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Al Bayt Stadium, Qatar; Welcome to the opening ceremony of FIFA World Cup Qatar 2022

Prevalence of Diabetes Distress among People with Type 2 Diabetes at Primary Health Care in Qatar: A cross-sectional Study

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Editorial

In this issue we have papers from Germany, UK, Qatar, Yemen, Saudi Arabia, Turkey, Lebanon, Australia, Jordan, and Pakistan. We also feature a new section on the Covid 19 pandemic.

The world has been plagued by way of the pandemic of COVID-19. It has spread rapidly in a speedy time affecting around 210 countries and causing much death that is increasing daily or through the hour. Thus, it needed an efficient health system that acts swiftly to limits it spread and complication. The region is not far away from the problem. Over the past six months there were growing interest in the issue of Corona Virus epidemic that is affecting the whole area. We are starting in in this issue a special section on COVID-19 for opinion and papers from the Region. In the past issues a paper from Pakistan looked at the grim looking trajectory for the COVID 19 in Pakistan. A second paper attempted to quantitatively analyze the impact of type of contact and duration of contact with infectivity of novel corona virus. A Sociological Appraisal of the corona virus came from Iran as well.

In this issue we have four papers on Corona epidemic. Aseel, M et al., looked at Family Medicine Residents Mentoring During Covid-19 Pandemic and Beyond. With the Covid-19 pandemic, it was expected that residents will be working under pressures that may lead to mental health and other challenges as we are dealing with a virus that we still know less about it. The authors stressed that a structured mentoring program did help supporting residents accommodate faster during the difficult time of Covid-19 especially during the early time. More frequent meetings between mentors and mentees are to continue for the first few months after the pandemic to ensure that the residents are ready to continue learning and for better achievements. Moussa R et al; looked at the implications of COVID -19 pandemic on Family medicine Residency training program & and ACGME requirements at Qatar. The authors stressed that Disasters like Covid -19 pandemic can turn in to opportunities for sustainable development. They stressed the following elements that family medicine residents can learn during the epidemic including leadership role and responsibility during the crisis, Covid -19 implications on ACGME-I Requirements and Residents Rotations and safety. The authors concluded that Crisis could be an opportunity for continuous development in the presence of adequate mentoring and leadership.

Sumathipala, S discussed the Trust and psychological safety in a virtual healthcare team. The author stressed that as the face of healthcare delivery has changed with the COVID 19 pandemic, virtual interactions between clinicians and their patients have increased. He indicated that Trust in virtual teams is positively associated with job satisfaction and improved working relationships. He concluded that with developments in technology and the impact of disease, working patterns in healthcare continue to change. Interacting remotely, not just with a patient but also with colleagues, is becoming more common, such that clinicians are now likely to be part of virtual teams. Alnaser F.A., looked at the Role of Family Doctors and Primary Health Care in COVID-19 Pandemic. He stressed that The Primary Health Care (PHC) is the first level of contact between the patients and the health system. Family doctors (FDs) are considered the gatekeepers in the fight against any outbreaks or illnesses. They, by the nature of their work, are very close to the patients and their families. Therefore, they have a greater chance for knowing about their patients' ailments and any new changes in their health conditions.

Abdalla H et al., did a cross-sectional study with a sample size of 350 on type 2 diabetes people aged 30 - 65 years at West Bay Health Centre in Qatar. The authors were looking at the Prevalence of Diabetes Distress among People with Type 2 Diabetes at Primary Health Care in Qatar. Overall prevalence of diabetes distress was 40.3% and expected to range between 35.2% and 45.5% with 95% confidence. Participants with high distress constituted 15.1%. The authors concluded that their study is the first of its kind in Qatar. The significant high prevalence highlights the importance of regular screening of diabetes distress, especially for those at high risk. Alfaqeeh A.S et al., looked at Risk factors and complications of cataract disease in type two diabetic patients in Taif city. They did a retrospective study was done where medical records of 110 diabetic patients were reviewed. About half of the participants (49.1%) were exposed to the sun, and 65.5% reported exposure to radiations. About 45% of the participants (45.5%) reported that they had a family history of cataract, of them 77,6% reported that those having cataract were of the 1st degree relatives. The authors concluded that long duration of DM, no commitment to medication, radiation exposure and aging were risk factors of cataract in diabetic patients. Diabetic patients should be continuously evaluated by an ophthalmologist.

Mathkhor A.J et al., investigated the prevalence of fibromyalgia and allied symptoms in patients with psoriasis. Seventy patients with psoriasis (40male and 30 female) and 70 age and sex matched controls were enrolled in the study.
A total of 37 (52.9%) patients with psoriasis were found to have widespread pain. A total of 21 patients met the criteria of FMS. The authors concluded that
FMS and allied symptoms are more prevalent in patients with psoriasis than in the general population. Women with psoriasis are more frequently affected by FMS than are men. Awareness of this comorbidity is an essential part in the treatment of psoriasis. Because of the strong association between disease severity and FMS, proper treatment that reduces skin involvement and disease severity may be associated with the alleviation of FMS and its allied symptoms.

Raza & Ahmed, reviewed irritable bowel syndrome. The authors stressed that Irritable Bowel Syndrome (IBS) is a highly prevalent gastrointestinal disorder affecting over 10% of the global population. It is a condition managed mostly in primary care but can often result in referral to secondary care. There is no test for diagnosing IBS and it is largely a diagnosis of exclusion. The pathogenesis of IBS is understood to be multifactorial therefore the treatments options are diverse, seeking to address the IBS patient using a holistic approach. In this review, they put a spotlight on IBS and in particular focus on the pathophysiology of IBS and how this understanding shapes how we manage IBS based on the current medical guidelines.

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Prevalence of Diabetes Distress among People with Type 2 Diabetes at Primary Health Care in Qatar: A cross-sectional Study

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Abstract

Background: Overwhelming demands of living with diabetes may lead to diabetes distress. It is linked to poor glycemic control which may result in high morbidity, mortality and increased health care costs. Our aim is to determine the prevalence of diabetes distress among people with type 2 diabetes and the associated factors.

Subjects and methods: A cross-sectional study with a sample size of 350 was conducted on type 2 diabetes people aged 30 - 65 years at West Bay Health Centre in Qatar. We used non-probability convenience sampling technique and written consent was secured from participants who met inclusion and exclusion criteria. Interviews were performed to fill out the diabetes distress scale DDS-17 which involves 4 subscales; emotional burden, physician distress, regimen distress and interpersonal distress. Mean item score of 2.0 - 2.9 was considered as moderate distress and ≥ 3.0 was considered as high distress. Approval notice was obtained from Research Committee. We used SPSS version 23 for data analysis.

Results: Overall prevalence of diabetes distress was 40.3% and expected to range between 35.2% and 45.5% with 95% confidence. Participants with high distress constituted 15.1%. For subscales; regimen distress had the highest prevalence (46.3%), followed by emotional burden (43.4%), interpersonal distress (38.6%), and physician distress (35.1%). A multivariate discriminant model to predict study participants with diabetes distress showed association in the following order of importance; Qataris/Arabs nationality, female gender, poor control of diabetes, receiving injections with treatment, obesity grade 2 and 3, age group ≥45 years, intensive diabetes control and being diagnosed with retinopathy. The discriminant model was statistically significant and able to classify individuals into distressed and non-distressed groups with 62% overall accuracy.

Conclusions: This study is the first of its kind in Qatar. The significant high prevalence highlights the importance of regular screening of diabetes distress, especially for those at high risk.

Key words: Diabetes distress, prevalence, Qatar

Introduction

Diabetes mellitus is a common metabolic disorder, characterized by high levels of blood glucose. Among the different types of the disease, type 2 diabetes mellitus is the most common, representing about 91% of total cases [1]. Diabetes mellitus has profound negative impacts on emotional and psychological well-being.

Diabetes distress overlaps with several conditions such as depression, anxiety, and stress but is distinct from clinical depression. Unlike depression, there is a significant relationship between diabetes distress and high levels of HbA1c [2]. It refers to worries, frustrations, concerns and emotional burdens that diabetics experience when managing a demanding chronic disease like diabetes [3]. Concerns related to diabetes distress include; general emotional distress, disordered eating, fear of hypoglycemia, and fear of short and long-term complications of diabetes [4]. A longitudinal study done by Fisher and his colleagues [5] concluded; the prevalence of affective and anxiety disorders was higher among people with diabetes compared to the general population. The persistence of diabetes distress over time was significantly greater than the persistence of affective and anxiety disorders, which tended to be episodic. This persistence strengthens the importance of diabetes distress screening at each patient visit, not just at specific intervals especially for high risk categories like females, younger adults, and those with comorbidities and/or complications.

In Qatar, the prevalence of diabetes mellitus was 16.7% [6], almost double that of the global estimate of 9.3% prevalence rate [7]. According to the results of a standardized online literature search using PubMed, Microsoft Academic and Google Scholar search engines targeting the term diabetes distress, no study has been done before in Qatar about diabetes distress and its prevalence. Determining the magnitude of the problem and the associated factors among people with type 2 diabetes will help to raise the awareness of the physicians to this important problem and motivate them to screen and address it on regular basis. This strategy may prove helpful to prevent further psychological deterioration and associated medical complications among diabetics. We believe that this study will have a positive impact on diabetes standards of care, diabetes control and better cost-effectiveness in health care.

Materials and Methods

1. Study Design
A cross-sectional study.

2. Setting
The study was executed at family medicine clinics at West Bay Health Center during the one-year study period extending from February 2019 - February 2020. This is one of 27 primary health care centers currently operated by the Primary Health Care Corporation (PHCC) in Qatar. Diabetes distress scale for type 2 diabetes DDS17 [8] was used. This valid and reliable tool involves 4 subscales; emotional burden, physician distress, regimen distress and interpersonal distress. Mean item score of 2.0 - 2.9 is considered as moderate distress, and ≥ 3.0 considered as high distress. A moderate or high distress are considered worthy of clinical attention.

The study protocol was approved for ethics and science by the Research Committee of PHCC. Informed written consent was secured from all study participants. A personal (face to face) interview was used to complete the questionnaire forms (English and Arabic translated version). Diabetes control was assessed according to American Diabetes Association, Standards of Medical Care in Diabetics - 2018 [9]. Active medications, recent ophthalmologist notes and HbA1c levels were extracted from the electronic medical recording system maintained by PHCC (Cerner Millennium).

3. Participants
Only people with type 2 diabetes were enrolled in the study. The reason for this selection is that the prevalence of diabetes distress is different for type 1 and type 2 diabetes, and the scales used for each type are also different. Adults aged 30 - 65 years were targeted in this study, since type 2 diabetes is more common among this age group. In addition, elderly people more than 65 years old may have multiple comorbidities, which might confound any observed association for diabetes distress.

Some factors may be considered as confounders and were therefore excluded from sampling. They included: end stage renal failure, Kidney/pancreas transplant, any condition that changes red blood cell turnover as it affects HbA1c, pregnant women, alcoholics, any patient diagnosed with cancer or any terminal illness, patients with learning difficulties, patients younger than 30 and older than 65 years and patients with language barrier and no staff available for translation.

4. Sampling Technique
Non-probability convenience sampling technique.

5. Study Size

The calculation of sample size was based on formula for estimating a single proportion, which is suitable for a cross-sectional study [10]. The formula used was:

$$x = Z(^{c}/_{100})^{2} r(100-r)$$

$$n = {}^{N\,x}/_{((N-1)\,E^{2} + x)}$$

$$E = \text{Sqrt}\,[{}^{(N-n)\,x}/_{n(N-1)}]$$

N is the population size, r is the fraction of responses that we are interested in (estimated proportion), and Z(c/100) is the critical value for the confidence level c. The population size (N) is 3,831. This is the number of type 2 diabetes patients who attended West Bay Health Centre in 2018. This information was obtained from Business and Intelligence Department at PHCC.

The estimated proportion of type 2 diabetics with distress (fraction of responses that we are interested in) was set at 50%. This would result in the largest possible sample size, since no previous studies in Qatar were available to give an estimate for this figure. The calculated sample size was 350 for estimating the proportion of diabetics with distress with a 5% margin of error (95% confidence level). By the end of data collection, 350 fully-answered questionnaires were included in analysis.

6. Statistical Analysis

Data were translated into a computerized database structure. The database was examined for errors using range and logical data cleaning methods, and inconsistencies were remedied. Expert statistical advice was sought. Statistical analyses were done using IBM SPSS version 23 computer software (IBM Statistical Package for Social Sciences) in association with Microsoft Excel.

The statistical significance of differences between averages for parameters of normal distribution was assessed using the Student's t-test, and for parameters deviating from normal distribution the nonparametric Mann-Whitney test and the median test were used. In the second stage, we used the Pearson's chi-squared test or Fisher's exact test to assess frequency differences of specified levels of qualitative variables, presented in nominal scales. The results of these variables were presented as proportions. We assumed the level of statistical significance at $p < 0.05$. All analyzed tests were bilateral.

Frequency distributions for selected variables were done first. To measure the strength of association between 2 categorical variables, the odds ratio (OR) was used.

Discriminant analysis is a multivariate model used to rank a set of explanatory variables according to their ability to predict diabetes distress. The model can provide a formula that helps in classifying diabetics into those with distress and those without distress.

Results

The analysis was based on a sample size of 350 type 2 diabetes patients. A half of study participants (50.6%) were between 30 and 54 years old [Table 1 - next page]. Two thirds (68%) of the sample were males. Asians constituted more than half (52.6%) of the sample, followed by Qataris (38.3%) and 9.1% for other Arabs. Most of the sampled individuals were overweight or obese (84%). About a quarter of the sample (27.1%) reported receiving injections with treatment. The HbA1c results were classified into four categories; about a quarter (24%) of subjects classified as intensive control (HbA1c <6.5%), 15.4% classified as recommended control (HbA1c 6.5-6.9%), 22.3% classified as less stringent control (HbA1c 7-7.9%) and 38.3% had poor diabetes control (HbA1c ≥8%). Only 13.7% of the study participants were diagnosed with retinopathy.

The overall prevalence of diabetes distress was 40.3% in the current sample, and expected to range between 35.2% and 45.5% in the reference population with 95% confidence [Table 2]. The prevalence rate for subscales of diabetes distress ranged between as low as 35.1% for physician distress to as high as 46.3% for regimen distress.

The high diabetes distress category (mean score of 3 and higher) was 15.1%, and moderate diabetes distress (mean score 2-2.9) was 25.1% [Table 3].

Risk of having moderate to high diabetes distress (mean score ≥3) increased in older age group (45-65 years) by 36% compared to younger age (30-44 years) [Table 4]. This observed age association was however not statistically significant. Female gender was associated with a statistically significant increase in risk of having the outcome by 62% compared to males. Only the extremely obese group (grade 2 and 3) was associated with a noticeable, but not statistically significant increase in the risk of having the outcome by 48% compared to subjects with BMI<25 Kg/m2. Compared to other Asian nationalities which had the lowest prevalence of diabetes distress (32.1%), Qatari nationality was associated with a statistically significant 2.1 times increase in risk of having distress. In addition, the other Arabic nationalities group was associated with 87% increase in risk of having distress compared to other Asians group, but the association failed to reach the level of statistical significance. Receiving injections with the therapeutic regimen for diabetes increased the risk of having distress by 41% compared to those on oral hypoglycemics, however this association was not statistically significant. Compared to the recommended diabetes control category, only the uncontrolled group was associated with a noticeable, though not statistically significant increase in the risk of having distress by 59%. The categories including duration of diabetes and being diagnosed with retinopathy had no obvious or statistically significant association with diabetes distress.

The logistic regression model for the association of gender with moderate to severe distress was not statistically significant after adjusting for the obesity [Table 5]. The accuracy of a positive prediction for distress cases was only 13.5%. Female gender was associated with 50% increase (partial OR=1.5) in risk of having moderate to severe distress compared to males after adjusting for obesity.

Eight explanatory variables were selected for inclusion in a multivariate discriminant model to predict study participants with moderate diabetes distress or higher, discriminating them from those with no distress [Table 6]. The single most important explanatory variable in predicting distressed diabetics was a Qatari/Arab nationality as opposed to that of other Asians nationalities which favored a non-distressed status. Unlike males, female gender predicted a distressed status and ranked second in its explanatory power. In the third rank was the poor control of diabetes (HbA1c ≥8%) which positively predicted a distressed individual when compared to those with HbA1c 6.5-7.9%. Receiving injections with treatment ranked fourth in the list. The fifth and sixth ranks were occupied by obesity grade 2 and 3, and older age (45-65 years). The explanatory variables with the weakest prediction were intensive diabetes control (HbA1c <6.5%) and those diagnosed with retinopathy. The discriminant model was statistically significant and able to classify individuals into distressed and non-distressed with 62% overall accuracy. The model provided a formula for calculating the discriminant score (D). If the calculated D exceeds 0.048, then we are more than 50% confident about predicting diabetes distress. The higher the D score beyond the 0.048 cut-off value, the higher probability of having diabetes distress. The formula shows that Qatari/Arab nationality or having poor control of diabetes reflected by having HbA1c ≥8% when combined with another predictor may be enough for having diabetes distress.

Table 1: Frequency distribution of the study (sample size 350) by sociodemographic and selected characteristics

Variables and values	Frequency	%
Age group (years)		
30-44	64	18.3
45-54	113	32.3
55-65	173	49.4
Gender		
Female	112	32.0
Male	238	68.0
Nationality		
Qatari	134	38.3
Other Arabs	32	9.1
Other Asian	184	52.6
BMI categories (Kg/m2)		
Acceptable (<25)	56	16.0
Overweight (25-29.9)	151	43.1
Obese Grade-1 (30-34.9)	77	22.0
Obese Grade-2 and 3 (≥35)	66	18.9
Duration of diabetes (years)-quartiles		
First, lowest quartile (≤2)	99	30.2
Average, interquartile range (2.1-10)	148	45.1
Fourth, highest quartile (>10)	81	24.7
Receiving injections		
Negative	255	72.9
Positive	95	27.1
Diabetes control (HbA1c %)		
Intensive control (<6.5%)	84	24.0
Recommended control (6.5-6.9%)	54	15.4
Less stringent control (7-7.9%)	78	22.3
Poor control (≥8%)	134	38.3
Diagnosed with retinopathy		
Negative	302	86.3
Positive	48	13.7

Table 2: Prevalence of diabetes distress and subscales

Mean score of diabetes distress and subscales	Frequency	%	95% CI
Moderate diabetes distress or higher (total DDS ≥2)	141	40.3	(35.2 to 45.5)
Moderate emotional burden or higher (mean item score ≥2)	152	43.4	(38.3 to 48.7)
Moderate physician distress or higher (mean item score ≥2)	123	35.1	(30.3 to 40.3)
Moderate regimen distress or higher (mean item score ≥2)	162	46.3	(41.1 to 51.5)
Moderate interpersonal distress or higher (mean item score ≥2)	135	38.6	(33.6 to 43.7)

Table 3: Frequency distribution of study sample by total diabetes distress mean score

Diabetes distress mean score	Frequency	%
No distress (<2)	209	59.7
Moderate distress (2-2.9)	88	25.1
High distress (≥3)	53	15.1
Total	350	100.0

Table 4: Relative frequency of having moderate diabetes distress or higher (Total DDS ≥2) by selected explanatory variables

Variables and values	Total Frequency	DDS ≥2 Frequency	%	OR	Inverse OR	95% CI OR	P
Age group (years)							
30-44	64	22	34.4				
45-54	113	47	41.6	1.36	**	(0.72 - 2.57)	0.345[NS]
55-65	173	72	41.6	1.36	**	(0.75 - 2.47)	0.312[NS]
Gender							
Male	238	87	36.6				
Female	112	54	48.2	1.62	**	(1.03 - 2.55)	0.039
Nationality							
Other Asian	184	59	32.1				
Qatar	134	67	50	2.12	**	(1.34 - 3.35)	0.001
Other Arabs	32	15	46.9	1.87	**	(0.87 - 4)	0.107[NS]
BMI (Kg/m2)							
Acceptable (<25)	56	21	37.5				
Overweight (25-29.9)	151	59	39.1	1.07	**	(0.57 - 2.01)	0.836[NS]
Obese Grade-1 (30-34.9)	77	30	39	1.06	**	(0.52 - 2.16)	0.864[NS]
Obese Grade-2 and 3 (≥35)	66	31	47	1.48	**	(0.71 - 3.05)	0.293[NS]
Duration of diabetes (years)							
First (lowest) quartile (≤2)	99	39	39.4				
Average (interquartile) (2.1−10	148	60	40.5	1.05	**	(0.62 - 1.76)	0.857[NS]
Fourth (Highest) quartile (>10)	81	33	40.7	1.06	**	(0.58 - 1.93)	0.854[NS]
Receiving injections							
Negative	255	97	38				
Positive	95	44	46.3	1.41	**	(0.87 - 2.26)	0.161[NS]
Diabetes control (HbA1c%)							
Recommended control (6.5-6.9)	54	19	35.2				
Less stringent control (7-7.9)	78	25	32.1	0.87	1.15	(0.42 - 1.81)	0.707[NS]
Intensive control (<6.5)	84	35	41.7	1.32	**	(0.65 - 2.67)	0.447[NS]
Poor control (≥8)	134	62	46.3	1.59	**	(0.83 - 3.05)	0.167[NS]
Diagnosed with retinopathy							
Negative	302	121	40.1				
Positive	48	20	41.7	1.07	**	(0.58 - 1.98)	0.834[NS]

Table 5: Multiple logistic regression model with the risk of having moderate to severe distress as the outcome

Variable	P	Adjusted OR
Female gender compared to male	0.07[NS]	1.5
Obese grade 2 and 3 compared to BMI <35 Kg/m2	0.48[NS]	1.2
Constant	≤0.001	0.562

P (Model) = 0.09[NS]
Overall classification accuracy = 59.7%
The accuracy of negative classification (mild or no distress) = 90.9%
The accuracy of positive classification (having moderate diabetes distress or higher) = 13.5%

Table 6: Discriminant model with selected explanatory variables to predict diabetics with moderate diabetes distress or higher discriminating them from those with no distress

Variable	Pooled within-groups correlations*
Qatari/Arab nationality compared to Asians	0.745
Female gender compared to male	0.463
Poor control (HbA1c ≥8%) compared to HbA1c control 6.5-7.9%	0.401
Receiving injections with treatment compared to oral medications	0.313
Obesity grade 2 and 3 compared to BMI <35 Kg/m2	0.273
Older age group (≥45 years) compared to those younger than 45 years	0.237
Intensive control (HbA1c <6.5%) compared to HbA1c control 6.5-7.9%	0.066
Being diagnosed with retinopathy	0.047

* Between discriminating variables and standardized canonical discriminant functions (variables ordered by absolute size of correlation within function)
Overall prediction accuracy = 62%
Wilks' Lambda = 0.945
P (Model) = 0.013
D = -1.699 + (0.103 x Older age group (≥45 years) compared to those younger than 45 years) + (0.808 x 1 if female gender compared to male) + (0.257 x 1 if obese grade 2 and 3 compared to BMI <35 Kg/m2) + (1.361 x 1 if Qatari/Arab nationality compared to Asians) + (0.101 x 1 if receiving injections with treatment compared to oral medications) + (0.627 x 1 if intensive control compared to HbA1c 6.5-7.9%) + (1.343 x 1 if poor control compared to HbA1c 6.5-7.9%) + (-0.213 x 1 if being diagnosed with retinopathy)
If D > 0.048, probability of having moderate diabetes distress or higher is more than being equivocal (50%)

Discussion

Our study calculated the overall prevalence rate of diabetes distress of 40.3%, a figure that requires attention and intervention. A systematic review and meta-analysis conducted on fifty-five international studies, the majority of them from United States, Canada, Australia and Europe concluded an overall prevalence of diabetes distress among people with type 2 diabetes was 36% [11].
For diabetes distress subscales, regimen distress had the highest prevalence of diabetes distress (46.3%) in the current study, followed by emotional burden (43.4%), interpersonal distress (38.6%), and physician distress had the lowest prevalence (35.1%). Family Medicine Model was introduced in PHCC two years ago. In this model of care, the patients assign themselves and their families to a specific doctor. They can also take appointments with their doctors by phone, which ensures continuity of care. This may explain why physician distress was the lowest among subscales.

Qataris had a significantly higher diabetes distress prevalence (50%), followed by other Arabs (46.9%), and Asians (32.1%), most of them were Indians. A cross sectional study performed in India showed a similar prevalence of diabetes distress of 27.9% [12]. Despite health care system differences between India and Qatar, there may be social and cultural factors explaining nationality and ethnic group differences. This ethnic group effect on diabetes distress was highlighted in two published studies, which showed that African Americans were at a higher risk for diabetes distress compared to White Americans [13], while diabetes distress scores were higher among Hispanics than African Americans [14].

It is known from previous studies that female gender is strongly associated with depression and anxiety [15]. In our study, a much lower proportion of males had diabetes distress (36.6%) compared to females (48.2%). Although females were at a higher risk, the association of gender with moderate to severe distress was not statistically significant after adjusting for the obesity. Women usually report higher levels of psychological distress than men, possibly because they are more expressive, face more stressors, and lack coping resources [16]. One published meta-analysis [11] showed a statistically significant increase in prevalence of diabetes distress among females.

Obesity grade 2 and 3 was associated with a prevalence rate of diabetes distress of 47%, compared to 39% in overweight and obesity grade 1, and 37.5% with BMI category <25 Kg/m2. Although this association was not statistically significant in the present study, a study from India reported a statistically significant positive association between diabetes distress and obesity [12]. Duration of diabetes showed no obvious or statistically significant association with diabetes distress. Despite this, diabetes distress level was shown to increase with a longer duration of diabetes as it is related to the threats of complications, functional impairment and the demanding regimens [17].
The present study showed that older age group (≥45 years) increased the risk of having distress by 36% compared to younger ages where the prevalence of distress was as low as 34.4%. This association couldn't be generalized to the population of type 2 diabetes because of failure to attain the level of statistical significance. In contrast to this study, younger ages were found to be at higher risk for diabetes distress [18]. Younger adults may show more reactions to stressors and may have less capacity to cope with stress than older adults [19].

Although not statistically significant in the present study, type 2 diabetics on only oral hypoglycemic medications had a lower prevalence of 38% for diabetes distress, compared to 46.3% for those on injections. Including injections in the management plan of type 2 diabetes was found significantly to affect diabetes distress in another recent study [12]. Fear of hypoglycemia, pain related to injections, stress associated with storing injections in a suitable place and social stigma may contribute to higher levels of distress. It was reported that in type 1 diabetes patients, the main concern linked to diabetes distress was fear of hypoglycemia, and that may explain why they have higher levels of distress compared to type 2 diabetics as management of type 1 diabetes is mainly insulin injections [20].

Although retinopathy failed to show any important association with having moderate or higher distress in the present study, other literature demonstrated that retinopathy affects vision level, family dynamics, relationships and may lead to social isolation [21]. Retinopathy may not be foreseen as a major health problem in the current study sample, probably because it is diagnosed at an early stage, since it is a routine health service for all diabetics.
Regarding association with diabetes control, the highest prevalence of diabetes distress (46.3%) was found in the poor control group, and the lowest prevalence (35.2%) among diabetics with recommended control. According to literature review there is a significant relationship between diabetes distress and poor control of HbA1c. Change in diabetes distress is associated with both short and long-term changes in glycemic control for patients with poorly controlled type 2 diabetes mellitus. Self-management education plays a major role to improve diabetes distress and leads to improvement in glycemic control [22]. A position statement of the American Diabetes Association advised for routine monitoring of diabetic people for diabetes distress, particularly at the onset of diabetes complications, or when treatment targets are not achieved (grade B) [23].

Interestingly, intensive diabetes control group had also a higher prevalence of diabetes distress (41.7%), compared to recommended control (35.2%). Diabetic patients with diabetes distress might have higher awareness of their glucose levels, and intensive control is associated with a higher probability of significant hypoglycemia. In the ACCORD study, intensive diabetes control was associated with a higher mortality rate compared to the standard treatment arm (1.41% vs. 1.14% per year), which led to termination of the study. There was no clear explanation of this result according to ACCORD data analysis [24]. American Diabetes Association recommends intensive diabetes control for only those who have short duration of diabetes and without significant hypoglycemia and/or cardiovascular disease (grade C) [9].

Study Limitations

This study was performed on type 2 diabetes patients who attended clinics at West Bay Health Center, Primary Health Care in Qatar, which is the educational center for Family Medicine Residency Program (ACGME-I accredited). Although this may affect generalizability of our study, we think this study is an important start in a field lacking such research. Multiple heath centers and secondary care would contribute to a better understanding of the size of the problem in the future.

Diabetes distress might not be properly assessable through interviews. In the future we may consider an online application to get the correlation between self-reported scores, home measurements of blood glucose levels and behavioral interventions for diabetes distress.

Conclusions

Prevalence of diabetes distress was 40.3%. Regimen distress had the highest prevalence among subscales, followed by emotional burden, interpersonal distress, and physician distress respectively. Associated factors in order of importance included; Qataris/Arabs nationality, female gender, poor control of diabetes, receiving injections with treatment, obesity grade 2 and 3, age group ≥45 years, intensive diabetes control, and being diagnosed with retinopathy.

This high prevalence of diabetes distress highlights the importance of regular screening of diabetes distress at each patient visit at primary health care, especially for those at high risk. Those who have diabetes distress need interventions and follow up. Self-management education, cognitive restructuring, goal setting and problem-solving play major roles to change the levels of diabetes distress.

Ethical Approval

We got an approval notice to conduct this study from the Independent Ethics Committee (IEC) and the Department of Clinical Research at Primary Health Care Corporation in Qatar.

Conflict of Interest

The authors declare that there is no conflict of interest regarding publication of this paper.

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References

(1) Xu G, Liu B, Sun Y, Du Y, Snetselaar LG, Hu FB, Bao W. (2018). Prevalence of diagnosed type 1 and type 2 diabetes among US adults in 2016 and 2017: population-based study. BMJ 2018;362: k1497. https://doi.org/10.1136/bmj.k1497

(2) Fisher L, Skaff MM, Mullan JT, et al. (2007). Clinical depression vs. distress among patients with type 2 diabetes: Not just a question of semantics. Diabetes Care, 30(3): 542-548. https://doi.org/10.2337/dc06-1614

(3) Fisher L, Hessler DM, Polonsky WH, Mullan JT. (2012). When is diabetes distress clinically meaningful? Diabetes Care, 35(2): 259-264. https://doi.org/10.2337/dc11-1572

(4) Polonsky WH, Anderson BJ, Lohrer PA, Welch BG, Jacobson AM, Aponte JE, Schwartz CE. (1995). Assessment of diabetes related distress. Diabetes Care 18(6): 754-760. https://doi.org/10.2337/diacare.18.6.754

(5) Fisher L, Skaff MM, Mullan JT, Arean P, Glasgow RE, Masharani U. (2008). A longitudinal study of affective and anxiety disorders, depressive affect and diabetes distress in adults with type 2 diabetes. Diabetic Medicine, 25(9): 1096-1101. https://doi.org/10.1111/j.1464-5491.2008.02533.x

(6) Al-Thani A., Bakri AH. Chronic disease risk factor surveillance. Qatar Stepwise Report 2012: 1-124. http://www.who.int/chp/steps/Qatar_2012_STEPwise_Report.pdf

|(7) Saeedi P et al. (2019). Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Research and Clinical Practice. https://doi.org/10.1016/j.diabres.2019.107843

(8) Polonsky WH, Fisher L, Earles J, et al. (2005). Assessing psychosocial stress in diabetes. Diabetes Care, 28(3): 626–631. https://doi.org/10.2337/diacare.28.3.626

(9) Glycemic targets: standards of medical care in diabetics-2018. Diabetes Care 2018 Jan; 41(Supplement 1): S55-S64. https://doi.org/10.2337/dc18-S006

(10) Raosoft sample size calculator. http://www.raosoft.com/samplesize.html

(11) Perrin NE, Davies MJ, Robertson N, Snoek FJ, Khunti K. (2017). The prevalence of diabetes-specific emotional distress in people with type 2 diabetes: a systematic review and meta-analysis. Diabetic Medicine 34(11): 1508-1520. https://doi.org/10.1111/dme.13448

(12) Sankar P et al. High prevalence of distress among patients with type 2 diabetes – a hospital based cross sectional study from south India. Diabetes 2018 Jul; 67(Supplement 1). https://doi.org/10.2337/db18-61-LB

(13) Hausmann LR, Ren D, Sevick MA. (2010). Racial differences in diabetes-related psychosocial factors and glycemic control in patients with type 2 diabetes. Patient Prefer Adherence, 7, 4: 291-299. https://doi.org/10.2147/ppa.s12353

(14) Spencer MS, Kieffer EC, Sinco BR, Palmisano G, Guzman JR, James SA, Graddy-Dansby G, Two Feathers J, Heisler M. (2006). Diabetes-specific emotional distress among African Americans and Hispanics with type 2 diabetes. J Health Care Poor Underserved, 17(2 Suppl): 88-105. https://doi.org/10.1353/hpu.2006.0095

(15) Altemus M, Sarvaiya N, Epperson CN. (2014). Sex differences in anxiety and depression clinical perspectives. Front Neuroendocrinol, 35(3): 320–330. https://doi.org/10.1016/j.yfrne.2014.05.004

(16) Thoits PA. Gender differences in coping with emotional distress. The social context of coping 107-138.

(17) Gonzalez JS, Fisher L, Polonsky WH. (2011). Depression in diabetes: have we been missing something important? Diabetes Care 2011; 34:236–239. https://doi.org/10.2337/dc10-1970

(18) Stoop CH et al. Diabetes-specific emotional distress in people with type 2 diabetes: a comparison between primary and secondary care. Diabetic Medicine 31(10): 1252-1259. https://doi.org/10.1111/dme.12472

(19) Schieman S, Van Gundy K, Taylor J. (2002). The relationship between age and depressive symptoms: a test of competing explanator suppression influences. J Aging and Health, 2002;14:260–285. https://doi.org/10.1177/089826430201400205

(20) Hagger V, Hendrieckx C, Sturt J, Skinner T, Speight J. Diabetes distress among adolescents with type 1 diabetes: a systematic review. Current Diabetes Reports 16, 9 (2016). https://doi.org/10.1007/s11892-015-0694-2

(21) Fenwick et al. (2011). Social and emotional impact of diabetic retinopathy: a review. Clinical & Experimental Ophthalmology, 40(1): 27-38. https://doi.org/10.1111/j.1442-9071.2011.02599.x

(22) Zagarins SE, Allen NA, Garb JL, Welch G. (2011). Improvement in glycemic control following a diabetes education intervention is associated with change in diabetes distress but not change in depressive symptoms. Journal of Behavior Medicine, 35(3): 299-304. https://doi.org/10.1007/s10865-011-9359-z

(23) Hyman DY, Groot MD, Briggs FH, Gonzalez JS, Hood K, Peyrot M. (2016). Psychological care for people with diabetes, a position statement of the American Diabetes Association. Diabetes Care 39(12): 2126-2140. https://doi.org/10.2337/dc16-2053

(24) The action to control cardiovascular risk in diabetes study group ACCORD. (2008). Effects of intensive glucose lowering in type 2 diabetes. New England Journal of Medicine 358: 2545-2559. https://doi.org/10.1056/NEJMoa0802743

Risk factors and complications of cataract disease in type two diabetic patients in Taif city

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Abstract

Diabetic retinopathy has been regarded as the most common cause of visual loss, and diabetes mellitus is also known as an important risk factor for cataract. The present study aimed to detect the risk factors and complications of cataract in type two diabetic patients in Taif city. A retrospective study was done from April 2019 to April 2020 at the diabetic tertiary care hospital in Taif city. Medical records of 110 diabetic patients were reviewed. A predesigned checklist was prepared to collect demographic data, data about diabetes mellitus, and data about cataract and its risk factors and complications. Of the studied patients, 86.4% had DM type 2, 63.6% had a DM duration more than 10 years, 50% were using antihyperglycemic agents as DM medication, 87.3% reported that they were committed to the medication used, and 50.9% had HTN. About half of the participants (49.1%) were exposed to the sun, and 65.5% reported exposure to radiations.. About 45% of the participants (45.5%) reported that they had a family history of cataract, of whom 77.6% reported that those having cataract were 1st degree relatives.

Conclusion: Long duration of DM, no commitment to medication, radiation exposure and aging were risk factors for cataract in diabetic patients. Diabetic patients should be continuously evaluated by an ophthalmologist.

Key words: risk, complications, cataract, diabetes, Taif

Introduction

Cataract is the primary cause of blindness worldwide [1]. It is defined as a decrease in the transparency of the crystalline lens and can be further differentiated into nuclear, cortical, or posterior subcapsular cataract (PSC) [2]. Diabetes mellitus has been reported as the most critical factor causing visual loss. Among the various complications of diabetes mellitus in the eyes, diabetic retinopathy has been regarded as the most common cause of visual loss [3]. Diabetes mellitus is also known as an important risk factor for cataract [3].

In a study performed to quantitatively evaluate the prevalence and risk factors of cataracts in Korean patients with type 2 diabetes mellitus, the duration of diabetes was the most significant risk factor for cataracts in patients with diabetes [3]. This finding indicates that the accumulated effect of hyperglycemia is related to lens transparency in patients with diabetes [3].

Another study done in the UK on newly diagnosed diabetes patients (≥40 years) found that diabetes is associated with an approximately two-fold increased detection rate of cataract. The risk of cataract associated with diabetes is highest at younger ages [4]. Patients with diabetic macular edema are at an increased risk for cataract as well as patients with long-standing diabetes [4].

Another study done in 2004 in Iran showed that the age-adjusted incidence rate of cataract was 20% greater among insulin-treated than non-insulin-treated type 2 diabetes mellitus clinic attenders and it increased with age [5]. Another study done in 2010 in India found that mixed cataracts were more common than monotype ones [6]. The prevalence of cataract was higher in women [6]. The risk factors for any type of cataract were increasing age, macroalbuminuria and increasing glycosylated hemoglobin; higher hemoglobin was the protective factor [6]. The risk factors for nuclear cataract included increasing age and high serum triglyceride [6]. For cortical cataract, increasing age and poor glycemic control were the risk factors; increasing hemoglobin was the protective factor [6].

For posterior subcapsular cataract, the risk factors included increasing age, being of the female sex, employment and duration of diabetes [6]. Tobacco smoking is also associated with dysfunctional tear syndrome, cataracts, and likely contributes directly to the development of diabetes mellitus [7].

Previous studies have found that DM is associated with early and rapid development of cataracts and diabetic patients are more likely to have cortical and posterior subcapsular cataracts [8]. Other studies found that the presence of cataracts were significant factors contributing to visual impairment and blindness in diabetics [9,10].
A study done in southern Saudi Arabia showed that the prevalence of bilateral blindness <3/60 was 3.3% [11]. Cataract was the leading cause of blindness (58.6%); followed by posterior segment diseases (20%), which included DR (7; 3.3%) [11]. The prevalence of sight-threatening diabetic retinopathy was 5.7%. Unlike in non-diabetic eyes, choroidal thickness in diabetic patients decreased following cataract surgery [12].

Another study was done in KSA in 2011 to estimate the prevalence of visual impairment and identify its causes and associated factors among the adult population attending primary health care (PHC) centers in Aljouf province, in northern Saudi Arabia. This study found that the main cause among patients who had chronic disease was diabetic retinopathy (39.1%) followed by cataract (32.6%) [13].

A recent Saudi study was done to determine the prevalence, patterns and predictors of diabetes complications among patients with type 2 diabetes. In those patients diabetic retinopathy was found among 16.7% of them [14].
The aim of this study was to detect the risk factors and complications of cataract in type two diabetic patients in Taif city.

Subjects and methods

Study design: The present study was a retrospective study.

Study duration: 1 year, from April 2019 to April 2020.
Study settings: This study was done at the diabetic tertiary care hospital (King Abdelaziz Specialized Hospital (KASH) in Taif city, Saudi Arabia.

Sampling methodology: Medical records of all diabetic patients were reviewed. The inclusion criteria were both genders of all ages who attended the diabetic centre of KASH at the time of the study. The excluding criteria were being non-diabetic patients, type 1 diabetic patients and non-cataract patients of type 2 diabetic patients.

Tools of data collection: A predesigned checklist was prepared to collect 3 sets of data from the medical records:.1) demographic data age, gender, etc), 2) data about diabetes mellitus, 3) data about cataract and its risk factors and complications.

Statistical design: Data was collected and analysed using the SPSS statistical program version 20. Qualitative data was expressed as frequencies and percentages. Chi-squared test was used to assess the relationship between variables. A p-value of less than 0.05 was considered significant.

Results

In the present study, 87.3% of the participants were in the age group less than 20 years, 52.7% were females, and 96.4% were of Saudi nationality. Of the participants, 12.7% were smokers and 50% of the smokers smoked less than 10 cigarettes/day and 71.4% had a smoking duration of more than 5 years. About half of the participants (48.2%) had a smoker as a family member and 25.5% were passive smokers (Table 1).

Table 1: Distribution of the studied patients according to their demographic characteristics, and smoking status (No.110)

Variable	No. (%)
Age	
more than40	5 (4.5)
20-40	9 (8.2)
lessthan20	96 (87.3)
Gender	
male	52 (47.3)
female	58 (52.7)
Nationality	
Saudi	106 (96.4)
non-Saudi	4 (3.6)
Smoking	
No	96 (87.3))
Yes	14 (12.7)
No. of cigarette\day (No.:14)	
lessthan10 cigarettes	7 (50)
10-20 cigarettes	5 (35.7)
more than20 cigarettes	2 (14.7)
Smoking duration	
5 years or less	4 (28.6)
more than5 years	10 (71.4)
Smoker in family members	
no	57 (51.8)
yes	53 (48.2)
Passive smoking	
no	82 (74.5)
yes	28 (25.5)

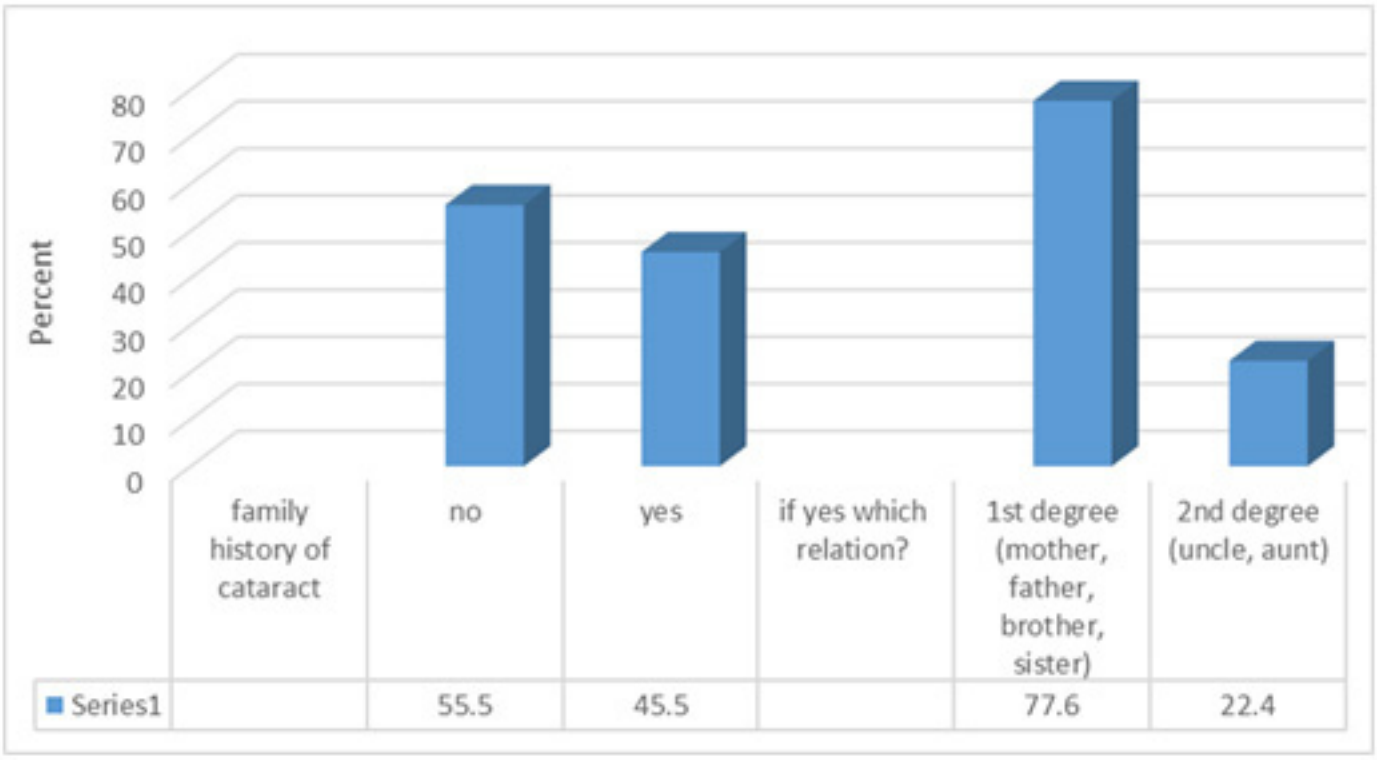
Of the studied diabetic patients, 86.4% had DM type 2, 63.6% had a DM duration more than 10 years, 50% were using antihyperglycemic agents such as DM medication, 87.3% reported that they were committed to the medication used, and 50.9% had HTN. About half of the participants (49.1%) were exposed to the sun, and 65.5% reported exposure to radiation (Table 2).

Table 2: Distribution of the studied patients according to DM type, duration, medication used, medication commitment, exposure to radiation and sun and presence of HTN (No.110)

Variable	No. (%)
DM type	
type (1)	15(13.6)
type (2)	95 (86.4)
Duration of DM	
lessthan5 years	19 (17.3)
5-10 years	21 (19.1)
more than10 years	70 (63.6)
DM medication used	
Antihyperglycemic agents	55 (50)
Insulin	52 (47.3)
Lifestyle change	3 (2.7)
medication commitment	
No	14 (12.7)
Yes	96 (87.3)
Exposure to radiation	
no	28 (34.5)
yes	72 (65.5)
Sun exposure	
no	56 (50.9)
yes	54(49.1)
if yes which time? (No.=54)	
from 7am to 10am	30 (55.6)
from 11am to 1pm	9 (16.7)
after1pm	9 (16.7)
from 5 pm until sunset	6 (11.1)
HTN	
no	54 (49.1)
yes	56 (50.9)

About 45% of the participants (45.5%) reported that they had a family history of cataract, of whom 77.6% reported that those having cataract were 1st degree relatives (Figure 1).

Figure 1: Distribution of the studied patients according to the presence of f amily history of cataract, and the type of family relation with those having cataract in the family (No. =110)



Of the participants, 66.4% had chronic headache, 30% had myopia, 25.5% had hyperopia, and 49.1% had previous correction surgery (Table 3).

Table 3: Distribution of the studied patients according to the presence of chronic headache, myopia, hyperopia and correction surgery (No. =110)

Variable	No. (%)
chronic headache	
no	73 (66.4)
yes	37(33.6)
myopia or hyperopia	
myopia	33 (30)
hyperopia	28(25.5)
non	49 (44.5)
correction surgery	
no	56 (50.9)
yes	54 (49.1)
If yes what were the outcomes (No.=54)	
progress	33 (61.1)
no difference	16 (29.6)
regress	5 (9.3)

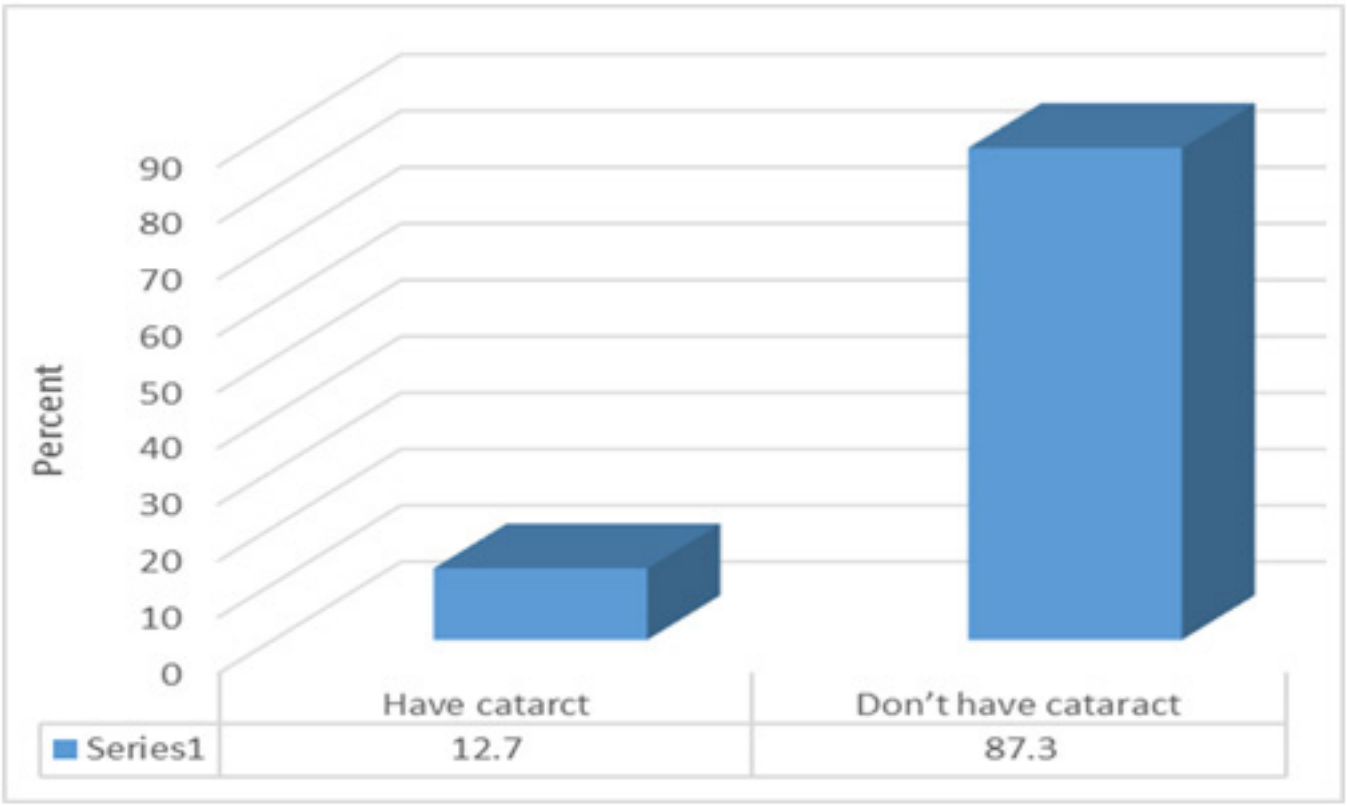
According to the presence of eye complications, 40.9% of patients had difficulty in reading, 27.3% had difficulty in night driving, and 34.5% had difficulty in seeing things correctly. Of them, 11.8% had poor vision, 6.4% had diplopia, 0.9% had difficulty coordinating clothes, 54.5% had blurred vision, and 3.6% had lack of vision in the extremities (Table 4).

Table 4: Distribution of the studied patients according to the presence of eye complications (No.=110)

Variable	No. (%)
Any difficulty in reading?	
no	65 (59.1)
yes	45 (40.9)
Any difficulty in night driving?	
no	80 (72.7)
yes	30 (27.3)
Any difficulty in seeing things correctly?	
no	72 (65.5)
yes	38 (34.5)
Any poor vision?	
no	97 (88.2)
yes	13 (11.8)
Any diplopia?	
no	103 (93.6)
yes	7 (6.4)
Any difficulty coordinating clothes?	
no	109 (99.1)
yes	1 (0.9)
Any blurred vision?	
no	50 (45.5)
yes	60 (54.5)
Any lack of vision in the extremities?	
no	106 (96.4)
yes	4 (3.6)

Figure 2 shows that of the studied diabetic patients, 14 (12.7%) were diagnosed with cataract.

Figure 2: Distribution of the studied patients according to the presence of cataract (No. =110)



Of the cataract patients, 8.9% had difficulty in reading, 16.7% had difficulty in night driving, 18.4 had difficulty in seeing things correctly, 23.1% had poor vision, 14.3% had diplopia, 18.3% had blurred vision, and 25% had lack of vision in the extremities. None of the participants suffered difficulty coordinating clothes. Only (64.3%) of patients who suffered from cataract had cataract surgery, of them 44.4% suffered eye erythema, 33.3% suffered eye itching and discharge, and 22.2% suffered haziness at the middle of their vision after surgery (Table 5).

Table 5: Distribution of the presence of eye complications among patients diagnosed with cataract (No. =14)

Variable	No. (%)
Any difficulty in reading?	
yes	4 (8.9)
Any difficulty in night driving?	
yes	5 (16.7)
Any difficulty in seeing things correctly?	
yes	7 (18.4)
Any poor vision?	
yes	3 (23.1)
Any diplopia?	
yes	1 (14.3)
Any difficulty coordinating clothes?	
yes	0 (0.0)
Any blurred vision?	
yes	11 (18.3)
Any lack of vision in the extremities?	
yes	1 (25)
Had cataract surgery	
No	5 (35.7)
Yes	9 (64.3)
If you had a cataract operation, did you complain of any one of these after the operation, choose all the right answers:	
- Eye erythema	4 (44.4)
- Eye itching	3 (33.3)
- Eye swelling	0 (0.0)
- Eye discharge	3 (33.3)
- Haziness at the middle of the vision	2 (22.2)
- Loss of vision completely	0 (0.0)

Table 6 shows that cataract prevalence was significantly higher among those with an age more than 40 years, those having DM duration more than 10 years, among those having lifestyle change as a DM therapy, and among those with no medication commitment (p=< 0.05). On the other hand, a non-significant difference was found between those having cataract and those who had not according to their gender and DM type (p=> 0.05).

Table 7 shows that cataract prevalence was significantly higher among those who had exposure to radiation (p=< 0.05). On the other hand, a non-significant difference was found between those having cataract and those have not according to smoking, exposure to sun, presence of HTN, and family history of cataract (p=> 0.05).

Table 6: Relationship between the presence of cataract and age, gender, DM type, duration, medication used, and medication commitment

Variable	cataract No. (%)	cataract No. (%)	χ2 test	p-value
Age				
more than40	2 (40)	3 (60)	11.76	0.003
20-40	7 (77.8)	2 (22.2)		
lessthan20	87 (90.6)	9 (9.4)		
Gender				0.82
male	45 (86.5)	7 (13.5)	0.04	
female	51 (87.9)	7 (12.1)		
DM type				0.08
type (1)	11 (73.3)	4 (26.7)	3.03	
type (2)	85 (89.5)	10 (10.5)		
Duration of DM				0.04
lessthan5 years	18 (94.7)	1 (5.3)	6.16	
5-10 years	21 (100)	0 (0.0)		
more than10 years	57 (81.4)	13 (18.6)		
DM medication used				0.014
antihyperglycemic agents	50 (90.9)	5 (9.1)	8.53	
insulin	45 (86.5)	7 (13.5)		
Lifestyle change	1 (33.3)	2 (66.7)		
Medication commitment				0.006
No	9 (64.3)	5 (35.7)	7.63	
Yes	87 (90.6)	9 (9.4)		

N.B.: χ2 =Chi-square test

Table 7: Relationship between the presence of cataract and smoking, exposure to radiation and sun, presence of HTN, and family history of cataract

Variable	Don't have cataract No. (%)	Have cataract No. (%)	χ2 test	p-value
Smoking				
No	86 (89.6)	10 (10.4)	3.62	0.05
Yes	10 (71.4)	4 (28.6)		
Exposure to radiation				
no	37 (97.4)	1 (2.6)	5.32	0.02
yes	59 (81.9)	13 (18.1)		
Sun exposure				
no	49 (87.5)	7 (12.5)	0.005	0.94
yes	47 (87)	7 (13)		
HTN				
no	49 (90.7)	5 (9.3)	1.14	0.28
yes	47 (83.9)	9 (16.1)		
Family history of cataract				
no	55 (90.2)	6 (9.8)	1.03	0.31
yes	41 (83.7)	8 (16.3)		

N.B.: χ2 =Chi-square test

Discussion

Cataract is the primary cause of blindness worldwide [1]. Diabetes mellitus is known as an important risk factor for cataract [3]. A previous study was done in Abha city in Saudi Arabia and demonstrated that retinopathy is a common complication of diabetes in diabetic patients at Abha and Aseer region and that the situation is no different from other regions of Saudi Arabia [15].

The present investigation aimed to examine the risk factors and complications of cataract on type 2 diabetic patients in Taif city, Saudi Arabia. Cataract prevalence was significantly higher among those with an age more than 40 year, those having a DM duration more than 10 years, among those having lifestyle change as a DM therapy, and among those with no medication commitment. The duration of DM was reported to be a risk factor of diabetic retinopathy in other studies [16]. Another study demonstrated that cataract risk increased with increasing diabetes duration for 10 years or more [17].

Other studies revealed that the longer duration of diabetes was associated with increased frequency of both cortical cataracts and cataract surgery [18].

In the present study, cataract prevalence was significantly higher among those with an age more than 40 years. This finding agrees with reports in an Indian study, where greater age at baseline was a risk factor for cumulative incidence and progression of most types of cataract [19]. The same was observed in other studies where risk factors of cataract among type 2 diabetic included age [20]. On the contrary, the risk of cataract associated with diabetes is higher at younger ages in another study [21].

In the present study, a non-significant relationship was found between the occurrence of cataract among the studied patients and the presence of HTN. In a study done in Sudan, the concurrent presence of chronic medical disorders such as hypertension, ischaemic heart disease, chronic kidney disease and dyslipidaemia amplifies the risk for the development of microvascular sequelae [22]. And previous studies have found that 24.9% of type 2 diabetic patients had a 10-year cumulative incidence of cataract surgery [23].

In a national study done in Jazan, Saudi Arabia, neuropathy was the most prevalent micro-vascular complication and hypertension and obesity were very significant predictors of diabetes complications [24].

Poor pupillary dilatation can be seen in diabetic patients as the result of damage to pupillary parasympathetic supply and elevated prostaglandin levels [25]. This means that pupil dilation is also a problem for these patients. The effects of DM on the ocular surface include neurogenic effects (subbasal nerve abnormalities) and impaired corneal stem cell and epithelial cell division, which can result in keratoepitheliopathy and leads to corneal epithelial defects/abrasions, which may heal slowly [26,27].

It has also been shown that corneal endothelial cell loss is higher in people with diabetes than in non-diabetics [23,28]; this means that routine evaluation of diabetic patients using specular microscopy is recommended. Moreover, surgeons should take greater care to reduce endothelial stress during surgery [29].

In the present study, cataract patients had complications such as difficulty reading (40.9%), difficulty night driving (27.3%), difficulty seeing correctly (34.5%), poor vision (11.8%), diplopia (6.4%), lack of peripheral vision (3.6%) and difficulty coordinating clothes (0.9%). Other complications were lack of extremities vision (25%), poor vision (23.1%), difficulty seeing correctly (18.4%), blurred vision (18.3%), difficulty night driving (16.7%), diplopia (14.3%) and difficulty reading (8.9%).

Progression of retinopathy after cataract surgery is another problem in diabetic patients [30]. The duration and complexity of cataract surgery are the main risk factors for progression of retinopathy [31]; it is therefore important to reduce the time and complexity of the surgery.

Among patients who did cataract surgery the most common complications were erythema (44.4%), eye itching (33.3%), discharge (33.3%) and haziness at the middle of the vision (22.2%).

A study done in Turkey reported that patients with diabetes have multiple issues to be evaluated preoperatively, perioperatively and in the postoperative period and these patients can, like other cataract patients without diabetes, recover excellent vision [32].

Limitations

Limitations of the present study were the small sample size and some difficulties related to the administrative aspects to collect data from medical records at the studied center.

Conclusion

Of the studied diabetic patients, 12.7% were diagnosed with cataract. Cataract prevalence was significantly higher among those with an age more than 40 years, those having a DM duration more than 10 years, among those having lifestyle change as a DM-therapy and among those with no medication commitment. Cataract prevalence was significantly higher among those who had exposure to radiation. Diabetic patients should be continuously evaluated by an ophthalmologist. The study calls for future longitudinal studies to identify modifiable risk factors that could prevent or delay cataract formation.

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References

1. Bourne RRA, Stevens GA, White RA, Smith JL, Flaxman SR, Price H, et al. Causes of Vision Loss Worldwide, 1990-2010: A Systematic Analysis. Lancet Glob Health. 2013;1(6): e339-49.
2. Asbell PA, Dualan I, Mindel J, Brocks D, Ahmad M, Epstein S. Age-related cataract. Lancet. 2005;12-18;365(9459):599-09
3. Seong Il Kim, MD and Sung Jin Kim, MD. Prevalence and Risk Factors for Cataracts in Persons with Type 2 Diabetes Mellitus. Korean J Ophthalmol. 2006; 20(4): 201–4.
4. Becker C, Schneider C, Aballéa S, Bailey C, Bourne R, Jick S, et al. Cataract in patients with diabetes mellitus—incidence rates in the UK and risk factors. Eye. 2018; 32:1028–35
5. Janghorbani M, Amini M. Cataract in type 2 diabetes mellitus in Isfahan, Iran: Incidence and risk factors. Ophthalmic Epidemiol. 2004;11(5):347-58
6. Raman R, Pal SS, Adams JSK, Rani PK;,Vaitheeswaran K, Sharma T. Prevalence and Risk Factors for Cataract in Diabetes: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study, Report No. 17.. Invest Ophthalmol Vis Sci.2010;51(12):6253-61
7. Stone DU. Tobacco smoking and blindness - The ignored epidemic. Saudi J Ophthalmol. 2016;30(3): 149.
8. Chiang PP, Lamoureux EL, Zheng Y, Tay WT, Mitchell P, Wang JJ, et al. Frequency and risk factors of non-retinopathy ocular conditions in people with diabetes: the Singapore Malay Eye Study. Diabet Med. 2013;30(2):e32–40.
9. Klein R, Lee KE, Gangnon RE, Klein BE. The 25-year incidence of visual impairment in type 1 diabetes mellitus the Wisconsin epidemiologic study of diabetic retinopathy. Ophthalmology. 2010;117(1):63–70.
10. Rani PK, Raman R, Gella L, Kulothungan V, Sharma T. Prevalence of visual impairment and associated risk factors in subjects with type II diabetes mellitus: Sankara Nethralaya diabetic retinopathy epidemiology and molecular genetics study (SN-DREAMS, report 16). Middle East Afr J Ophthalmol. 2012;19(1):129–34.
11. Hajar S, Al Hazmi A, Wasli M, Mousa A, Rabiu M. Prevalence and Causes of Blindness and Diabetic Retinopathy in Southern Saudi Arabia. Saudi Med J. 2015; 36(4):449-55.
12. Torabi H, Sadraei M, Jadidi K, Alishiri A. Choroidal Thickness Changes Following Cataract Surgery in Patients With Type 2 Diabetes Mellitus. J Curr Ophthalmol. 2018 ; 11;31(1):49-54.
13. Al-Shaaln FF, Bakrman MA, Ibrahim AM, Aljoudid AS. Prevalence and causes of visual impairment among Saudi adults attending primary health care centers in northern Saudi Arabia.Ann Saudi Med. 2011;31(5): 473–80.

14. Albasheer OB, Sani M, Abbas A, Alfaifi M, Najmi M, Hakami K, et al. Prevalence, patterns and predictors of diabetes complications among patients with type 2 diabetes at Jazan Diabetic Centre, Saudi Arabia. Medical science. 2020; 24(101):83-9.
15. Ahmed RA, Khalil SN, Al-Qahtani MA. Diabetic retinopathy and the associated risk factors in diabetes type 2 patients in Abha, Saudi Arabia. J Fam Community Med. 2016;23:18-24.
16. Lee R, Y. Wong T, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye and Vision. 2015;2:17-25.
17. Becker C, Schneide, C, Aballéa S, Bailey C, Bourne R, Jick S, et al. et al. Cataract in patients with diabetes mellitus-incidence rates in the UK and risk factors. Eye. 2018;32:1028–35
18. Klein BE, Klein R, Lee KE. Diabetes, cardiovascular disease, selected cardiovascular disease risk factors, and the 5-year incidence of age-related cataract and progression of lens opacities: the Beaver Dam Eye Study. Am J Ophthalmol. 1998; 126: 782-90
19. Srinivasan S, Raman R, Swaminathan G, Ganesan S, Kulothungan V, Sharma T. Incidence, progression, and risk factors for cataract in type 2 diabetes. Invest Ophthalmol Vis Sci. 2017;58:5921–29
20. Laitinen A, Laatikainen L, Harkanen T, Koskinen S, Reunanen A, Aromaa A. Prevalence of major eye diseases and causes of visual impairment in the adult Finnish population: a nationwide population-based survey. Acta Ophthalmol. 2010;88:463–71.
21. Harding JJ, Egerton M, van Heyningen R, Harding RS. Diabetes, glaucoma, sex, and cataract: analysis of combined data from two case control studies. Br J Ophthalmol. 1993;77:2–6.
22. Husseina M, Menasrib S. Prevalence of Microvascular Complications in Type 2 Diabetics Attending a Primary Healthcare Centre in Sudan. Int J Diabetes Metab. 2019;10:1159.
23. Shih KC, Lam KS, Tong L. A systematic review on the impact of diabetes mellitus on the ocular surface. Nutr Diabetes. 2017; 7: e251
24. Albasheer OB, Sani M, Abbas A, Alfaifi M, Najmi M, Hakami K, et al. Prevalence, patterns and predictors of diabetes complications among patients with type 2 diabetes at Jazan Diabetic Centre, Saudi Arabia. Medical Science. 2020; 24(101): 83-9
25. Ferrari GL, Marques JL, Gandhi RA, Heller SR, Schneider FK, Tesfaye S, et al. Using dynamic pupillometry as a simple screening tool to detect autonomic neuropathy in patients with diabetes: a pilot study. Biomed Eng Online. 2010; 9: 26
26. Yoon KC, Im SK, Seo MS. Changes of tear film and ocular surface in diabetes mellitus. Korean J Ophthalmol. 2004; 18: 168-74
27. Inoue K, Kato S, Ohara C, Numaga J, Amano S, Oshika T. Ocular and systemic factors relevant to diabetic keratoepitheliopathy. Cornea. 2001; 20: 798-801
28. Morikubo S, Takamura Y, Kubo E, Tsuzuki S, Akagi Y. Corneal changes after small-incision cataract surgery in patients with diabetes mellitus. Arch Ophthalmol. 2004; 122: 966-9
29. Yang R, Sha X, Zeng M, Tan Y, Zheng Y, Fan F. The influence of phacoemulsification on corneal endothelial cells at varying blood glucose levels. Eye Sci. 2011; 26: 91-5
30. Henricsson M, Heijl A, Janzon L. Diabetic retinopathy before and after cataract surgery. Br J Ophthalmol. 1996; 80: 789-93
31. Mittra RA, Borrillo JL, Dev S, Mieler WF, Koenig SB. Retinopathy progression and visual outcomes after phacoemulsification in patients with diabetes mellitus. Arch Ophthalmol. 2000; 118: 912-17
32. Kiziltoprak H, Tekin K, Inanc M, Goker YS. Cataract in diabetes mellitus. World J Diabetes. 2019; 10(3): 140-53

Self-Medication with Antibiotics among Medical Students in Karachi: A Cross-Sectional Institution Based Study

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Abstract

Objectives:
1) To identify the factors responsible for students self-medicating with antibiotics in medical students at Sindh Medical College, Jinnah Sindh Medical University, Karachi.
2) To determine the class of self-medicating antibiotics used by medical students at Sindh Medical College, Jinnah Sindh Medical University, Karachi.

Study Design:
A Cross-sectional study.

Study Place:
Sindh Medical College
Jinnah Sindh Medical University, Karachi

Study Duration:
March 01, 2018 To June 04, 2018

Sampling Technique:
Non-Probability Purposive Sampling

Method:
A cross sectional study was conducted on a sample size of 359 students. The sample was taken through non-probability convenient sampling from all 05 batches of Sindh Medical College, Jinnah Sindh Medical University, Karachi within the month of January 2018 and informed verbal consent was taken from the participants. A pilot study was conducted to assess the authenticity of the questionnaire. A structured questionnaire was then distributed, was filled out and the data was entered and analyzed using SPSS version 23.0 with 95 % confidence interval in margin of error 5 % and p value of less than 0.05 was considered as statistical significance.

Results:
The percentage of self-medication among students of Sindh Medical College, Jinnah Sindh Medical University, Karachi is 52.1%. Age groups were (16-18 = 14.5%, 19-21 = 58.2% and 22-24 = 27.3%). Participants from all years were (01st = 20.6%, 02nd = 19.5%, 03rd = 20.6%, 04th = 19.5% and 05th = 19.8%). The minimum days an antibiotic course should be continued from the collected data were (3-5 Days = 69.6%). The most hazardous outcome of using inappropriate antibiotics reported by the students was (Drug resistance = 40.4%). The most frequently used antibiotics were (Co-amoxiclav = 11.7%, Metronidazole = 5.8%). Students normally stop taking antibiotics (At the completion of course = 42.1%, After symptoms disappear = 31.5%, After consulting doctor = 10.6%).

Conclusion:
This study suggests that students of Sindh Medical College, Jinnah Sindh Medical University, were found to self-medicate themselves with antibiotics. However, knowledge about drug resistance is required at individual level in order to refrain from doing so. In consideration of these results, adequate measures should be taken to educate students regarding the hazardous side effects of antibiotics.

Key words:
Self-medication, Antibiotics, Karachi,
Medical students

Introduction

Self-medication is described as the use of medicines by a person on his own or on the proposition of a nonprofessional or a lay person instead of seeking guidance from a health care provider (1,2). In the field of medicine, a prescription is written by a medical practitioner that enables a person to be issued with medicine from the competent authorities. Over the counter medicines are also included in the term of self-medication. It is an emerging problem in the developing countries, due to lack of knowledge and convenience for people. Due to this practice and especially with antibiotics, the strains of multiple bacteria are becoming resistant, leading to more complications. Self-medication increases the likelihood of improper use of drug and drug dependency along with masking the signs and symptoms leading to a delayed diagnosis (3). “Most antibiotic resistance mechanisms are associated with a fitness cost that is typically observed as a reduced bacterial growth rate. The magnitude of this cost is the main biological parameter that influences the rate of development of resistance, the stability of the resistance and the rate at which the resistance might decrease if antibiotic use were reduced (4). According to a study conducted by Kumarasamy et al in India, the appearance of the super bacteria New Delhi metallo betalactamase1 (NDM1) positive Enterobacteriaceae in 2010, which were highly resistant to many antibiotic classes, has raised alarm about antibiotic resistance (5). As well as the people of a country, medical students are also using antibiotics without a doctor’s prescription. Several studies have been conducted for both general population and students involved in health care. According to Damian and Lupuşoru in 2014 in Romania self-medication with antibiotics has been recorded among university students internationally from which 44% was found in Romania (6) and according to Fadare and Tamuno in 2011, it was found to be 39%

in Nigeria (7). According to Kumarathunga in 2010 the practice of self-medication in South Asian countries, such as Sri Lanka was found to be 13% (8). According to a study conducted by Banerjee and Bhadury in India in 2012, self-medication was widely practiced among the students of medical colleges (9). In this situation, faculties should create awareness and educate their students regarding advantages and disadvantages of self-medication. According to a study conducted in Karachi, Pakistan in the year 2017; out of 320 participants prevalence of self-medication was 66%, out of which antibiotic self-medication prevalence was 39% from different universities (10).

Self-medication has been reported throughout the world. In developing countries people are not only using non-prescription drugs like painkillers; but prescription drugs such as antibiotics without supervision of a health care provider. The World Health Organization has emphasized on the fact that steps to be taken to teach and to control self-medication properly (11 12).

Two terms are often used; 'misuse' and 'abuse' of medicines. The terms are often used conversely, but hey have precise meanings in the dictionary. Misuse is used in the context of medicine as using an OTC (over the counter) drug for a justifiable medical reason, but in inappropriate doses or for a longer duration than recommended. Abuse of drug is the use without a medical purpose (13).

In the developing countries, antibiotics which are used to treat potentially life threatening bacterial infections and are also for prophylaxis are available as OTC (over the counter) drugs. They are easily available without prescriptions. Although these medicines are available from many pharmaceutical companies and are intended for self-medication, due to lack of knowledge in terms of efficacy and safety they are not properly understood. Antibiotics can cause resistance and their inappropriate use due to lack of knowledge of their side effects and interactions could bring serious complications, especially in groups like children and lactating mothers (14).

In a systematic review and meta-analysis of the burden, risk factors and outcomes of using antibiotics in developing countries, Moses Ocan et al, in 2015 included a total of 34 studies involving 31,340 participants. The overall prevalence of antimicrobial self-medication was (38.8%) at (95%) confidence interval. Most studies evaluated non-prescription use of (50%) antibacterial agents. The common complaints treated were respiratory (50%), fever (47%) and gastrointestinal (45 %). Side effects of antibiotic self-medication reported were, allergies (5.9%), lack of cure (11.8%) and causing death (5.9%). The commonly reported positive consequence was recovery from illness (11.8 %) (15).

Our study aimed to find out the frequency of self-medication with antibiotics among medical students of both preclinical and clinical setups at Sindh Medical College, Jinnah Sindh Medical University Karachi.

Methodology

A cross sectional study was conducted on a sample size of 359 students. The sample was taken through non-probability convenient sampling from all 05 batches of Sindh Medical College, Jinnah Sindh Medical University, Karachi. Within the month of January 2018 informed verbal consent was taken from the participants. A pilot study was conducted to assess the authenticity of the questionnaire; th structured questionnaire was then distributed, filled out and the data was entered and analyzed using SPSS version 23.0 with 95 % confidence interval in margin of error 5 % and p value of less than 0.05 was considered as statistical significance.

Results

The percentage of self-medication among students of Sindh Medical College, Jinnah Sindh Medical University, Karachi is 52.1%. The response rate was 98.8%. The percentage of male participants were 25.1% and female participants were 74.9%. Age groups were (16-18 = 14.5%, 19-21 = 58.2% and 22-24 = 27.3%). The cross tabs were done between age groups and following variables.

Participants from all years were (01st = 20.6%, 02nd = 19.5%, 03rd = 20.6%, 04th = 19.5% and 05th = 19.8%) (p value = 0.000).

The minimum days an antibiotic course should be continued from the collected data were: (3-5 Days = 69.6%), when infection ends = 10.9%, Don't know = 10.3%, 1-2 Days = 4.5%, No course = 1.4%, When packet finishes = 0.8%) (p value = 0.000).

The most hazardous outcome of using inappropriate antibiotics were: (Drug resistance = 40.4%, Don't know = 17.3%, Diarrhea = 10.6%, Decreased immunity = 10.0%, Nausea = 8.4 %, Vomiting = 6.7%, Rash and No effect = 2.8%) (p value = 0.000).

The most frequently used antibiotics were: (Co-amoxiclav = 11.7%, Metronidazole = 5.8%, Amoxicillin = 3.9%, Erythromycin = 3.1%, Ciprofloxacin = 2.8%, Cefixime = 2.2%, Azithromycin = 1.9%, Others = 1.9%, Levofloxacin = 1.7 %, Doxycycline = 0.3%). Antibiotics in combination used were (Co-amoxiclav and Metronidazole = 8.4% and Amoxicillin and Co-amoxiclav = 6.7%, Erythromycin and Metronidazole = 0.6%, Metronidazole and Levofloxacin = 0.3%) (p value = 0.004).

Students normally stop taking antibiotics: (At the completion of course = 42.1%, After symptoms disappear = 31.5%, After consulting doctor = 10.6%, After antibiotics finished = 4.7%, A few days after recovery = 3.6%, After asking family or relative = 0.8%, Others = 0.6%, After consulting a doctor and at completion of course = 1.9%, After consulting a doctor and after symptoms disappear = 1.4%, After antibiotics finished and a few days after recovery = 0.3%) (p value = 0.002). Cross tabs of age group with other variables is shown on opposite page.

Figure 1: The age group of participants in the study

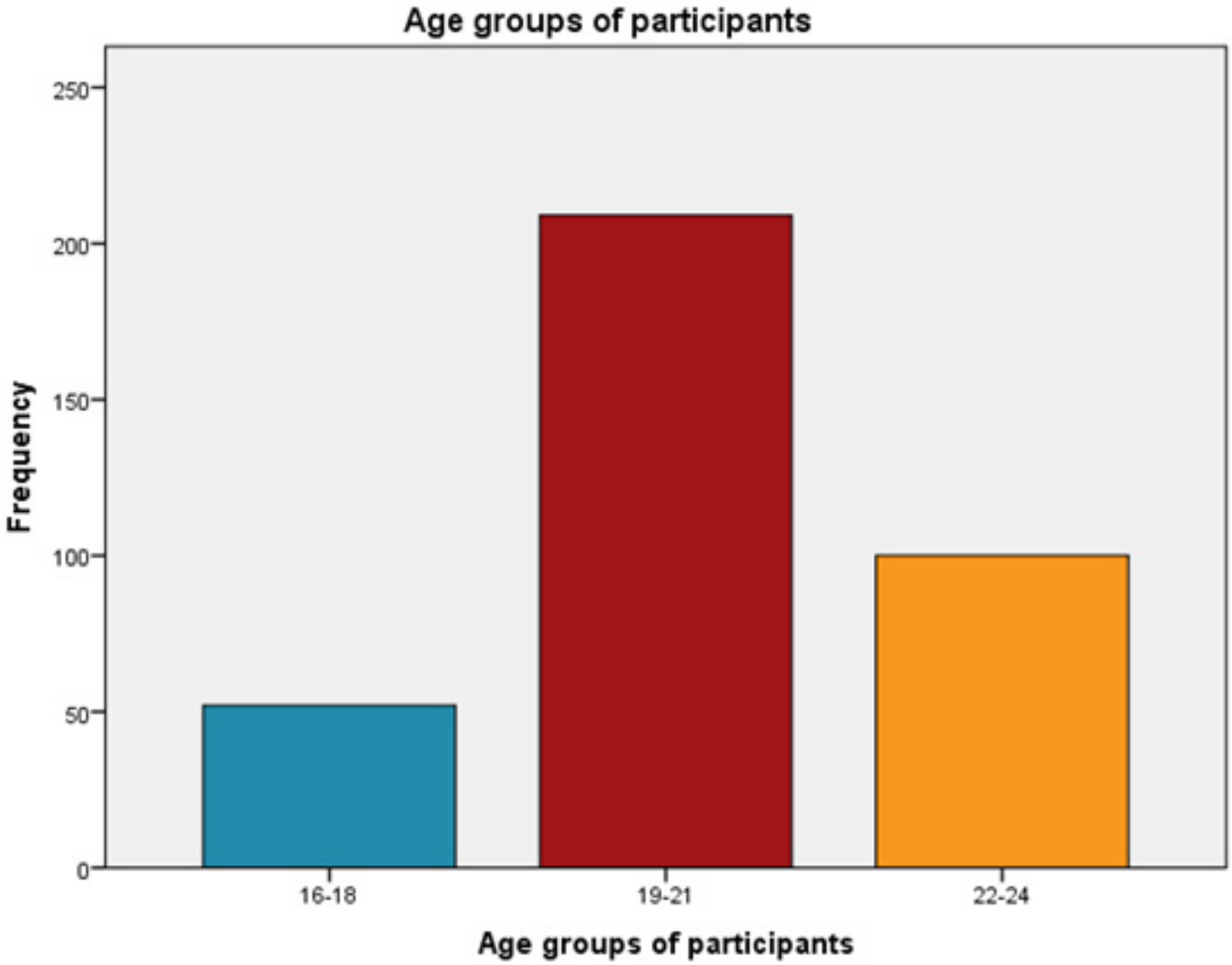


Figure 2 shows that Participants from all years were distributed as First Year 20.6%, Second Year 19.5%, Third Year 20.6%, Fourth Year 19.5% and Final Year were = 19.8% (p value = 0.000).

Figure 2: The year of study of participants in the study

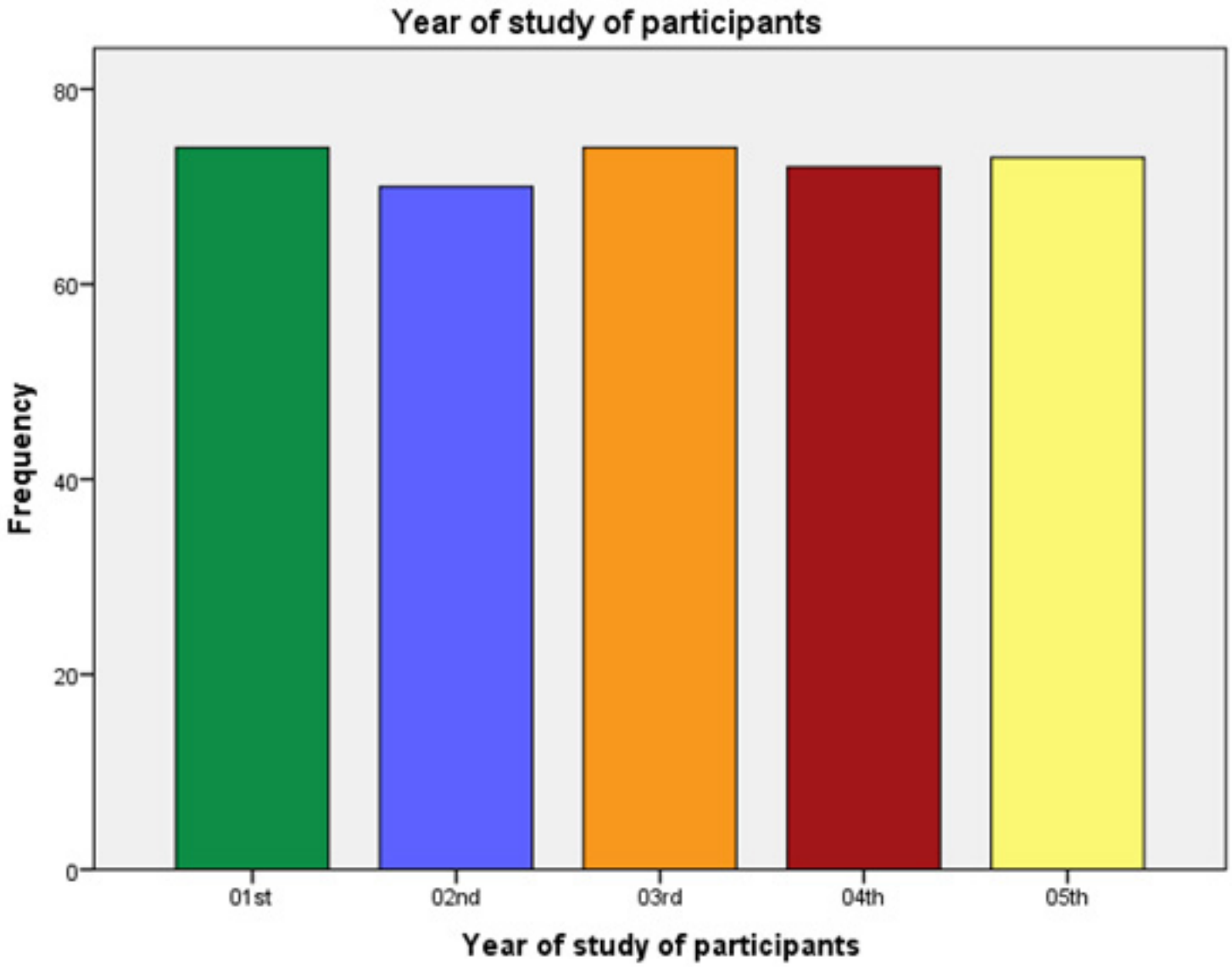


Figure 3 shows the responses of the participants when asked 'The minimum days an antibiotic course should be continued'. The responses showed that from 1-2 Days was stated by 4.5%, 3-5 Days was stated by 69.6%, When infection ends was stated by 10.9%; those who did not know were 10.3%, No course was stated by 1.4% and When packet finishes was quoted by 0.8% (p value = 0.000).

Figure 3: Frequency of course of antibiotics followed by medical students

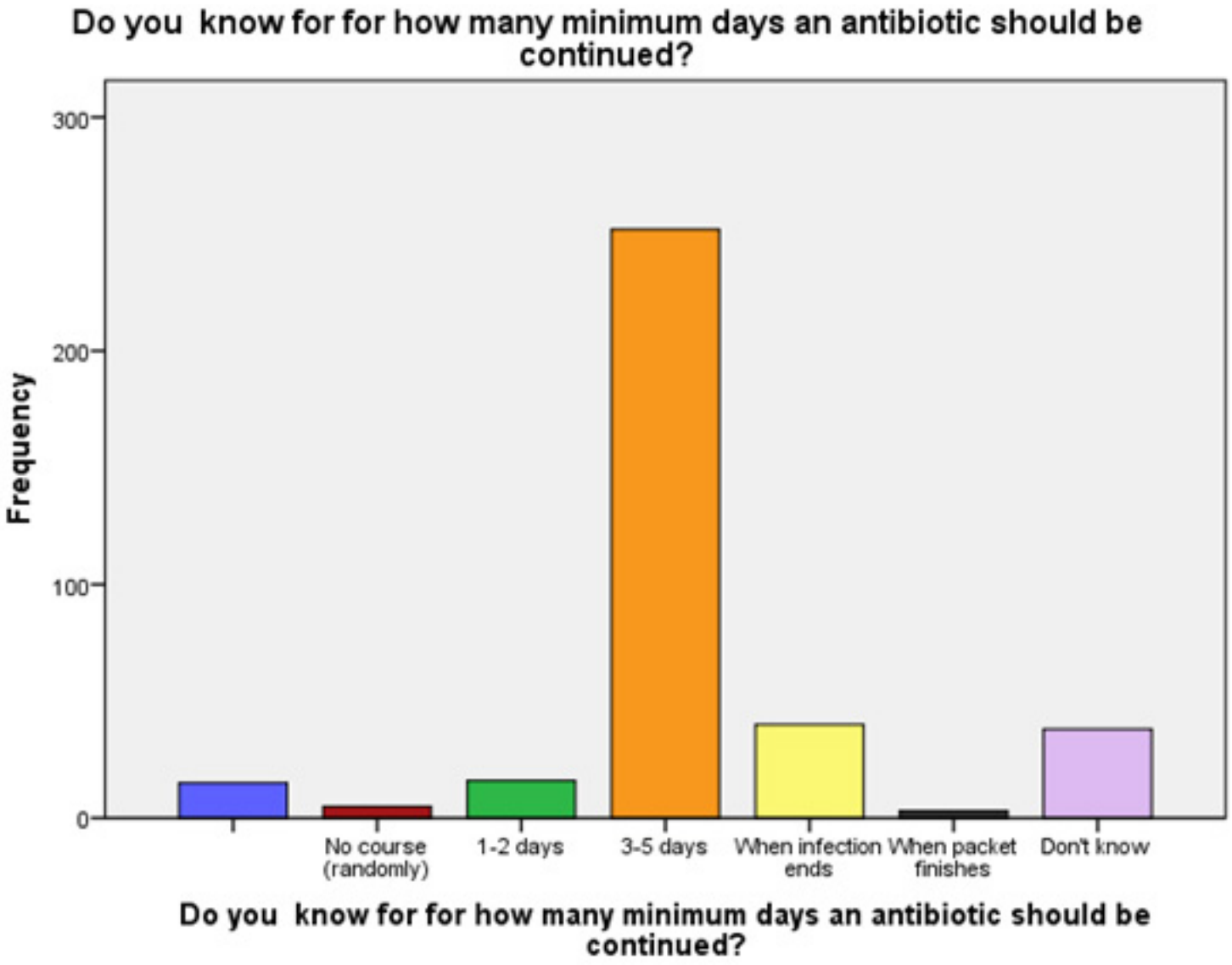


Figure 4 shows that when asked about the most hazardous outcome of using inappropriate antibiotics it was responded to as: drug resistance which was reported by 40.4%, those who did not know were 17.3%, diarrhea was stated by 10.6%, decreased immunity was mentioned by 10.0%, nausea was the response of 8.4 %, vomiting by 6.7%, rash and no effect was quoted by 2.8% (p value = 0.000).

Figure 4: Frequency of hazardous outcomes of antibiotics as reported by participants

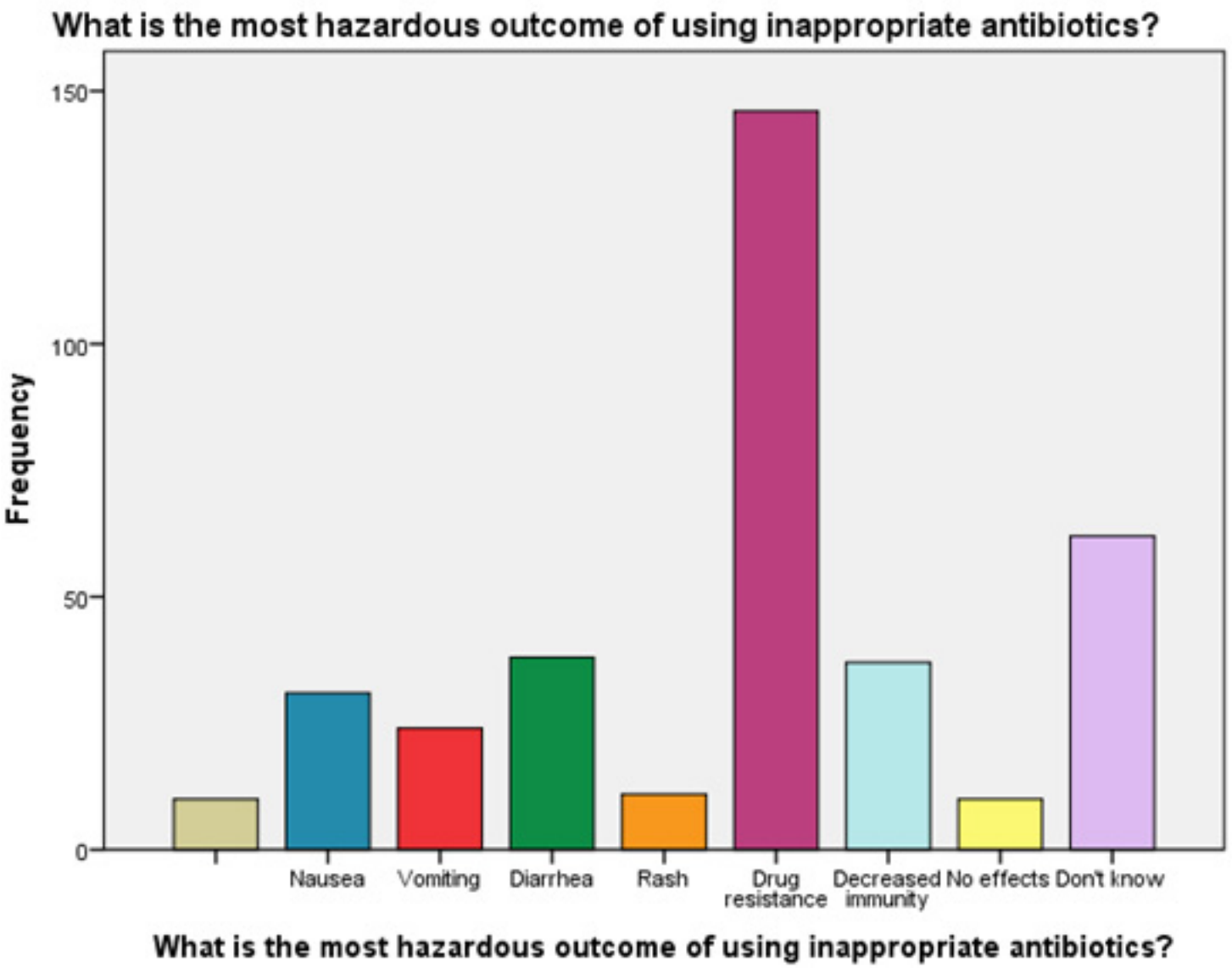
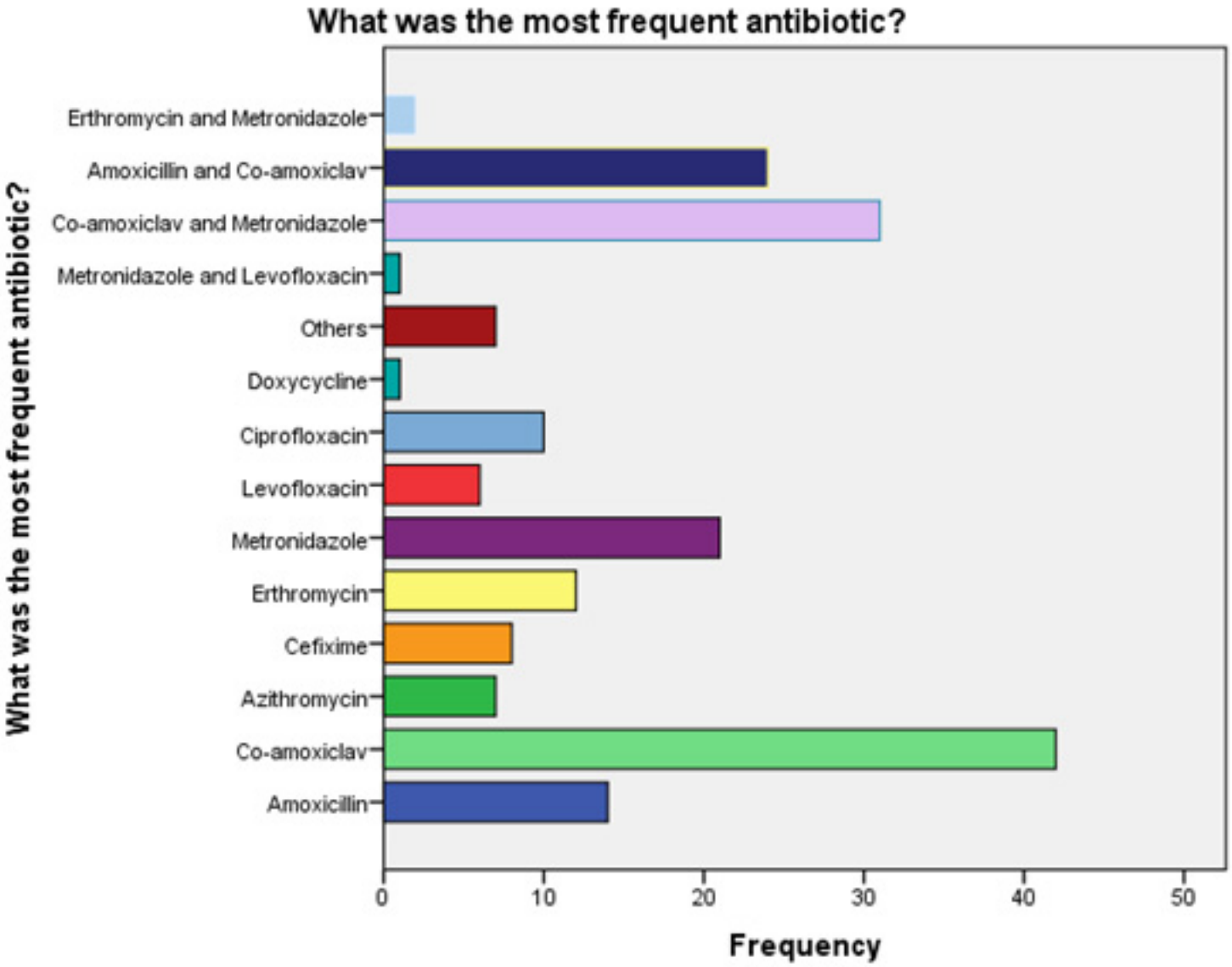


Figure 5 shows that the most frequently used antibiotics were Co-amoxiclav which was used by 11.7%, Metronidazole which was used by 5.8%, Amoxicillin which was used by 3.9%, Erythromycin which was used by 3.1%, Ciprofloxacin which was used by 2.8%, Cefixime which was used by 2.2%, Azithromycin which was used by 1.9%, Others which were used by 1.9%, Levofloxacin which was used by 1.7 %, and Doxycycline which was used by 0.3%). Antibiotics in combination used were Co-amoxiclav and Metronidazole which were used by 8.4% and Amoxicillin and Co-amoxiclav which were used by 6.7%, Erythromycin and Metronidazole which were used by 0.6% and Metronidazole and Levofloxacin which were used by 0.3% (p value = 0.004).

Figure 5



Discussion

The study was carried out to assess the level of self-medication with antibiotics among medical students of Sindh Medical College, Jinnah Sindh Medical University, Karachi.

A previous study was carried out on a sample of 400 students at 4 different universities of Sindh out of which (50%) were medical students. This study reported that (75%) males and (88%) medical students are analogously more aware about the uses of the medicines than females (67%). This study also revealed (39%) of males and (52%) of medical students are familiar with the complications that can arise after the use of medicines compared to the females (38%) (16). Our study showed the percentage of self-medication among students of Sindh Medical College is 52.1%. The percentage of male participants were 25.1% and female participants were 74.9%.

To determine the pattern of self-medication among undergraduate medical students, a study was conducted among 3rd year students at BUMDC (Bahria University Medical and Dental College) in 2013 in which Metronidazole (19%) and Amoxicillin Plus Clavulanic acid (17.3%) were the most commonly used antibiotics (17). According to our study, the most frequently used antibiotics for self-medication were (Co-amoxiclav - 11.7%, Metronidazole - 5.8%, Co-amoxiclav and Metronidazole - 8.4% and Amoxicillin and Co-amoxiclav - 6.7%).

Across-sectional study was conducted about pharmacology education and antibiotic self-medication among medical students at Faculty of Medicine and Allied Sciences in Rajarata University of Sri Lanka, Anuradhapura. The majority of the participants had taken the antibiotic for 1–3 days (68%) (18). According to our study, students used antibiotics for a minimum of; 3-5 days - 69.6%, when infection ends - 10.9%, don't know - 10.3%, 1-2 days - 4.5%, no course - 1.4%, when packet finishes - 0.8%.
A study by Kifayat Ullah on self-medication education with antibiotics among 1st professional medical students in Peshawar, Pakistan revealed that 72.2 % (n=144) of the participants self-medicated with antibiotics out of which 26.3% (n=38) self-medicated just once, while 29.1% (n=42) participants self-medicated with antibiotics more than five times in the last one year. Common causes for self-medication were; diseases not serious enough to consult a doctor (n=84, 58.3%) and past consumption of antibiotics (n=46, 31.9%) and common illnesses for which antibiotics were used; were sore throat (n=120, 83.3%), cough (n=68, 47.2%), fever (n=68, 47.2%) and runny nose (n=58, 40.2%). The choice of antibiotics was determined by previous doctor's prescription (n=100, 69.4%), opinion of others (n=86, 59.7%), self-experience (n=28, 19.4 %) and advertisement (n=6, 4.1%) (19).

Regarding self-medication practice and perceptions among undergraduate medical students; a cross-sectional Study conducted by Shivaraj B Patil et al showed that only (37.1%) of students who took antibiotics completed the full course of antibiotic regimen. The students should be educated about completing the course of antibiotic (20). However, our study showed that students normally stopped taking antibiotics at the completion of duration of antibiotic course (42.1%) and only 1.9% participants actually stopped taking the antibiotics after they were advised by a doctor so as to not indulge in self medication. According to self-medication practices with antibiotics among Tertiary level students in Accra, Ghana, in a cross-sectional study by Eric S. Donkor et al, 51% (215) of the respondents were aware that self-medication could cause adverse health effects such as antibiotic resistance, 41% (173) of the respondents had little knowledge about this, while 8% (34) of them were not aware at all of any health risk associated with self-medication (20). According to our study 40.4% students reported drug resistance as the most hazardous outcome and 17.3% did not know about it.

According to a report of the National Institute of Islamabad, the first known epidemic of extensively drug-resistant typhoid has been spreading through Pakistan since 2016. This resistance is expected to promulgate globally. Researchers have considered antibiotic resistance an international issue for the modern era to combat epidemics. According to WHO in Karachi, the capital of Sindh province, antibiotic resistance is increasing by 30 percent each year. Eric Mintz, an epidemiologist from CDC says, "It's a global concern at this point" (21).

Conclusion

This study suggests that students of Sindh Medical College, Jinnah Sindh Medical University, were found to self-medicate with antibiotics. However, knowledge about drug resistance is required at individual level in-order to refrain from doing so. In consideration of these results, adequate measures should be taken to educate students regarding the hazardous side effects of antibiotics.

References

1)Guidelines for the Regulatory Assessment of Medicinal Products for Use in Self-Medication. WHO guidelines for the regulatory assessment of medicinal products for use in self-medication, 2000.
2) Montastruc JL, Bagheri H, Geraud T, Lapeyre-Mestre M. Pharmacovigilance of self-medication. Therapie 1997; 52: 105-10.
3) World Health Organization. WHO guidelines for the regular assessment of medical products for use in self medication. WHO/EDM/Qs/00.1.2000. Accessed on 5 July 2011, URL:htt p://apps. Who.int/medicinedocs/pdf/s2218e/ s2218e.pdf
4) Andersson DI, Hughes D,. Antibiotic resistance and its cost: is it possible to reverse resistance? Nature Reviews Microbiology. 2010; 8(1): 260–271
5) Kumarasamy KK, Toleman MA, Walsh TR et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. The Lancet Infectious Diseases. 2010; 10: 597–602.

6) Damian L, Lupuşoru CE, Ghiciuc CM. Self-medication with antimicrobial drugs among university students in a Northeast region of Romania. Rev Med Chir Soc Med Nat Iasi. 2014;118(1):160–164.
7) Fadare JO, Tamuno I. Antibiotic self-medication among university medical undergraduates in Northern Nigeria. J Public Health Epidemiol. 2011;3(5):217–220.
8) Kumarathunga RMST. Assessment of self-medication practices among health sciences related students in University of Peradeniya [dissertation]. Peradeniya: University of Peradeniya; 2010.
9) Banerjee I, Bhadury T, Self-medication practice among undergraduate medical students in a tertiary care medical college, West Bengal. JPGM . 2012; 58 (2) : 127-131
10) Limaye D, Saeed F, Ahmad M. Self-medication practices among university students from Karachi, Pakistan.IJCMPH.2017;4(9): 3076-3081
11) Bradley C, Blenkinsopp A. Over the counter drugs: the future for self-medication. BMJ 1996; 312:835-837.
12) World Health Organization: The role of the pharmacist in self-care and self-medication. Report of the 4th WHO consultative group on the role of the pharmacist. The Hague, 1998. Available from http://www.who.int/medicines/library/dap/who-dap-98- 13/who-dap-98-13.pdf. Accessed on 20-9-2011
13) Hughes GF, McElnay JC, Hughes CM, McKenna P. Abuse/misuse of non-prescription drugs. Pharm World Sci 1999; 21: 251–255.
14) Murray MD, Callahan CM. Improving medication use for older Adults: An integrated research agenda. Ann Intern Med 2003; 139:2425-9.
15) Ocan M, M,ObukuEA, Bwanga F. Household antimicrobial self-medication: a systematic review and meta-analysis of the burden, risk factors and outcomes in developing countries. BMC Public Health.2015; 15:742
16) Syed N, Naseer M, Memon MQ. Prevalence of Self-Medication and its Practice among the Medical and Non-Medical Students. Jlumhs. May-August 2014; 13(2):79-82
17) Assad T, Karim N, Younus I, Feroz Z. Self-medication Patterns among Undergraduate Medical Students: A Cross Sectional Institution Based Study. Pharmacology, Toxicology and Biomedical Reports [Internet]. 2017;3(2):43-46.
18) Rathish D, Wijerathne B, Bandara S. Pharmacology education and antibiotic self-medication among medical students: a cross-sectional study. BMC Res Notes. 2017; 10: 337.
19) Ullah K, Khan SA, Ullah H, Bangash SS. Self-medication with antibiotics among first professional medical students inpeshawar, Pakistan. NJMS. 2016; 1(3):129-33
20) Patil SB, Vardhamane SH, Patil BV. Self-Medication Practice and Perceptions Among Undergraduate Medical Students: A Cross-Sectional Study. J Clin Diagn Res. 2014 Dec; 8(12): 20–23
21) Levine MM, Simon R. The Gathering Storm: Is Untreatable Typhoid Fever on the Way? mBio. 2018 Mar-Apr; 9(2):105-108

Prevalence and risk factors of non-alcoholic fatty liver disease in primary health care centers among subjects examined by abdominal ultrasound in Qatar: A case-control study

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Abstract

Background and study aim: Non-alcoholic fatty liver disease (NAFLD) is a cause of chronic liver disease and an important public health problem. The prevalence of NAFLD in patients with components of metabolic syndrome is high. Ultrasound is a non-invasive, available screening method to detect and follow up NAFLD with treatment options. The aim of this study is to explore NAFLD and its association with metabolic syndrome and other risk factors. It also aimed to identify a cohort of patients with fatty liver to perform a follow-up study.

Patients and methods: This is a retrospective case-control study nested in a cross-sectional design for NAFLD patients, diagnosed by ultrasonography. After assessing the size of cases, we initiated a case control study.

Results: NAFLD is prevalent in the study population (58.5%). The prevalence and risks were high in males (69.7% and 1.35) and in the 50-59 years age group (74.2% and 2.08 respectively). The prevalence and risk increased with increase in weight with the highest values in Grade III obese measuring 85.9% and 3.39, respectively. The difference in prevalence or risk between Qatari and expatriates or smoker and non-smoker patients was non-significant. The prevalence of NAFLD in cases of Metabolic syndrome was 81.7% and the risk was 1.89 and the prevalence and risk increased with increased number of metabolic syndrome components (the prevalence increased from 31.3% in 1 component to 90.2% in 5 components, and the risk increased from 1.71 in 1 component to 4.95 in 5 components).

Conclusion: Ultrasonography is the reference test for the detection of fatty liver at the population level in primary health care centers. NAFLD is a prevalent health problem in Qatar and is associated with metabolic syndrome and its components. A multifactorial intervention approach on the risk factors can restrict the appearance of more severe hepatic complications.

Key words: NAFLD, ultrasound, prevalence, risk factors, Qatar.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is an important public health problem and a cause of chronic liver disease [1]. It is considered the liver disease component of metabolic syndrome (MetS) [2]. It has two clinical entities known as nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH) [3]. NAFL is a benign, non-progressive clinical entity, while NASH can progress to cirrhosis or even hepatocellular carcinoma [4]. Diagnosis of NAFLD prevalence is based on: (1) nonalcoholic subjects (alcoholic liver disease occurs when daily alcohol consumption exceeds 20 g in women or 30 g in men), with lower levels of these alcohol consumptions, (2) patients with hepatic steatosis diagnosed by histology or imaging modalities, and (3) appropriate exclusion of other liver diseases such as chronic viral hepatitis, steatogenic medications, autoimmune hepatitis, hemochromatosis and Wilson's disease [2,4]. The prevalence of NAFLD is high with components of MetS, type 2 diabetics, and obese patients [5,6]. Most patients with NAFLD are asymptomatic, and diagnosis is predicted by an increased level of transaminases during a health checkup. Sometimes, accidental discovery of hepatomegaly or suggestive changes of fatty liver by other imaging modalities indicates NAFLD. However, the final diagnosis should be confirmed by liver biopsy [7,8]. Obesity has reached epidemic levels and is considered one of the priorities for intervention. Overweight or obese NAFLD patients are more likely to develop steatohepatitis and severe forms of liver disease [7]. Early detection of NAFLD is helpful and important for early intervention, thereby, targeting the associated factors and preventing the evolution of the disease to more severe forms [4]. Qatar occupies a high rank in the prevalence of obesity [9]. The prevalence of NAFLD using ultrasound in Italy was around 25%, and most of these cases had an association with features of MetS [10]. Ultrasound is a widely available, non-invasive screening method to detect NAFLD and help clinicians to select outpatients at highest risk. Thereby, ultrasonography improves diagnostic assessments and follow-up with treatment options [11,12].

The aim of this study is to explore the prevalence rate of NAFLD and its association with MetS and other risk factors. The objectives included (1) Determining the prevalence rate of fatty liver disease among patients undergoing abdominal ultrasound in primary health care settings in Qatar, (2) Study the association of demographic variables (age, gender, and nationality) and MetS with NAFLD, (3) Identify a cohort of patients with NAFLD to perform a follow-up study.

Patients and Methods

This is an observational case-control study nested in a cross-sectional design for all subjects with a valid ultrasound of the liver to verify the presence of fatty liver. Nested in the first design is another case-control sub-study. For the comparative study, only subjects that satisfied the requirements of completeness for defining MetS were included. After assessing the size of case groups, we drew an age- and gender-matched control group.

The inclusion criteria for the cross-sectional part of the study were all adult patients aged between 18 and 70 years with an abdominal ultrasound examination performed for any reason in PHCC centers in Qatar. Valid ultrasound scan results available on the official electronic medical record system (RIS PACS system) during the study period from 1st January 2018 to 31st December 2018 were reviewed. The case-control study part included subjects with complete information for lipid profile, blood pressure (or history of hypertension) and BMI. Fasting blood sugar (or a documented diagnosis of diabetes) was needed but was replaced by HbA1c when not available.

The exclusion criteria included documented alcohol intake, presence of chronic liver disease as hepatitis B and C, secondary causes of fatty liver (medications, human immunodeficiency virus, gastrointestinal by-pass surgery) and history of liver surgery.

We analyzed the whole population of study (3,853 subjects after exclusion of 81 subjects from the total number of 3,934 subjects according to the inclusion and exclusion criteria). The criteria of American Gastroenterology Association for Diagnosis of NAFLD and its grade were used in the study. We classified the study population into cases and non-cases. The prevalence rate of NAFLD was calculated at this stage stratified by age, gender, and nationality. After examining the age and gender frequency distribution of cases, we selected the control group from the population with a negative ultrasound diagnosis of NAFLD using a group age and gender matching technique. Subjects were considered as cases if they had fatty liver according to the ultrasound standard criteria of the American Gastroenterology Association. We reviewed all ultrasound images and reports. Fatty liver was diagnosed in the presence of one of the following standards [13]:

NAFL Grade I- Minimal diffuse rise in the fine echoes of the liver that are bright compared to the cortex of the kidney and normal appearance of diaphragm and intra hepatic vessel borders (Image 1).

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; EMR, Electronic Medical Records; FLD, fatty liver disease; HDL, high-density lipoprotein; HS, hepatic steatosis; LDL, low-density lipoprotein; MetS, metabolic syndrome; NAFL, nonalcoholic fatty liver; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic fatty steatohepatitis; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; PHCC, Primary Health Care Corporation; SH, steatohepatitis; T2DM, type 2 diabetes mellitus.

NAFL Grade II- Moderate diffuse rise in the fine echoes with slight diminished visualization of the intrahepatic vessels and diaphragm (Images 2, a, b).
NAFL Grade III- Noticeable increase in fine echoes with poor or no visualization of intrahepatic vessels and diaphragm and poor penetration of posterior segment of the right lobe of the liver (Image 3).

We calculated the one-year prevalence rate of NAFLD by this formula:

Prevalence = Count of subjects with a positive diagnosis of NAFLD during the study period ÷ Count of subjects with a valid ultrasound scan during the study period×100.

We evaluated the following variables requested from HIM department in subjects fulfilling the inclusion criteria as follows:(1) The abdominal ultrasound scan, (2) Socio-demographic variables: Age, gender, and nationality, (3) Personal history of liver disease or liver surgery, (4) The BMI measurement, (5) Presence of Type II diabetes mellitus, dyslipidemia, or arterial hypertension, (6) A history of alcohol intake, (7) Smoking habit, (8) History of drug used during previous six months, (9) Arterial blood pressure measurement, (10) Blood tests included measurement of hemoglobin, urea, creatinine, glucose, HbA1c %, lipid panel (cholesterol, triglycerides, HDL, LDL), liver function tests (ALT, AST, Alkaline Phosphatase, Albumin, Total protein, Total Bilirubin, including hepatitis markers (hepatitis B surface antigen virus and hepatitis C virus antibodies), (11) Diagnosis of MetS: Adapted national cholesterol education program adult treatment panel III (NCEP ATP III) component definitions were used for the study [14]. MetS is present if three or more of the following five criteria are met (or medication was taken to control them). Insulin Resistance (Serum Fasting Glucose≥100 mg/dl or HbA1c≥5.56) or a diagnosis of T2DM); blood pressure >130/>85 mmHg or a diagnosis of hypertension; fasting triglyceride >150 mg/dL (>1.7mmol/L); low, high-density lipoprotein (HDL) cholesterol (<40 mg/dL (<1.04 mmol/L) for males, <50 mg/dL (<1.3 mmol/L) for females; and waist circumference over 102 cm (40 inches) in men and 94 centimeters (37 inches) in women or obesity (BMI >30 [kg/m2]) [15].

Statistical analysis was computed using IBM SPSS version 23 computer software. A descriptive frequency distribution was done first. Assessment of the association between NAFLD and each of age group, gender, and nationality was done. Similarly, we used the statistical method to explore the association between NAFLD and each component of MetS.

Results

The frequency distribution of study population by selected socio-demographic variables is mentioned in Table 1. The age groups of the study population were as follows: <30 years (15.2%); 30-39 years (31.8%); 40-49 years (25.3%); 50-59 years (18.8%) and 60-69 years (8.9%). About 62.6% of the study population denoted female and 37.4% were male. About 22.3% of the population were Qatari, and 77.7% were expatriates. Around 84.4% of the subjects were non-smoker, 10.8% were current smoker and 4.7% were ex-smoker. In addition, 20.1% of the study population had an acceptable BMI (<25 kg/m2), 34.7% were overweight (25-29.9 kg/m2) and 45.2% were obese (≥30 kg/m2).

The overall prevalence of NAFLD was 58.5% in the study population. The prevalence and risk (prevalence ratio) of NAFLD by socio-demographic variables is as follows (Table 4): The prevalence in males and females was 69.7% and 51.8%, respectively. The risk in males was 1.35 compared to females. The prevalence and risk increased within the age groups of >30 years compared to the age groups of <30 years. Also, the highest prevalence and risk was observed in the 50-59 years age group, measuring 74.2% and 2.08, respectively. The prevalence and risk increased with increase in weight with the highest values in Grade III obese measuring 85.9% and 3.39, respectively.

The difference in prevalence or risk between Qatari and expatriates or smoker and non-smoker patients was non-significant.

The percentage of cases of positive MetS in our study was 56.4%. The prevalence of NAFLD in cases of MetS was 81.7% and the risk was 1.89. The prevalence and risk of NAFLD increased with the number of components defining MetS (Table 2). The prevalence increased from 31.3% in 1 component to 90.2% in 5 components, and the risk increased from 1.71 in 1 component to 4.95 in 5 components. The prevalence and risk of NAFLD by variables defining MetS were as follows (Table 2): (1) Obesity (BMI≥30 kg/m2 or central obesity (waist circumference over 102 cm (40 inches) in men and 94 cm (37 inches) in women)): The prevalence was 78.3%, and the risk was 1.53. (2) Insulin Resistance (Serum Fasting Glucose≥100 mg/dl or HbA1c≥5.56) or T2DM: The prevalence was 76.8%, and the risk was 1.78. (3) High blood pressure (over 130/85 mmHg) or a diagnosis of hypertension: The prevalence was 72.9%, and the risk was 1.6. (4) Low serum HDL (Fasting high-density lipoprotein (HDL) cholesterol level <1.04 mmol/L (<40 mg/dl) in men or <1.3 mmol/L (<50 mg/dl) in women: The prevalence was 72.7%, and the risk was 1.27. (5) High serum triglycerides (Fasting triglyceride level over 1.7 mmol/L (150 mg/dl): The prevalence was 81.9%, and the risk was 1.42. Table 3 shows that the prevalence of moderate (grade II) and severe (grade III) degrees of NAFLD increased with the increase in the number of components defining MetS. Table 5 shows that the three grades of NAFLD were more prevalent in males compared to females and the prevalence of grade III NAFLD was highest in obese Grade III, measuring 4.0%.

Image 1: Grade I NAFLD

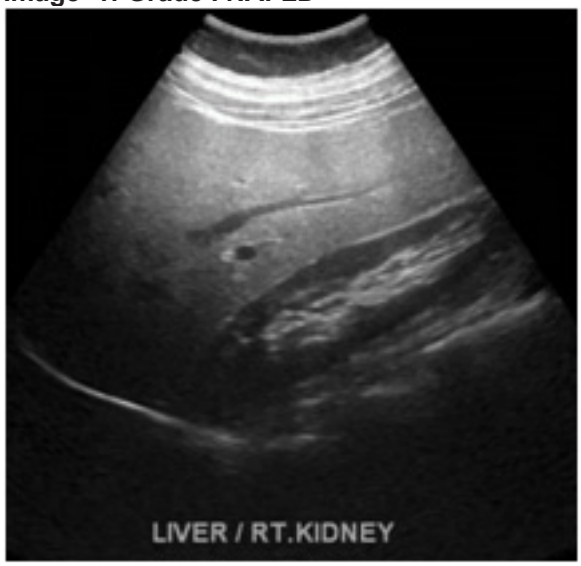

Image 2 (a and b): Grade II NAFLD.

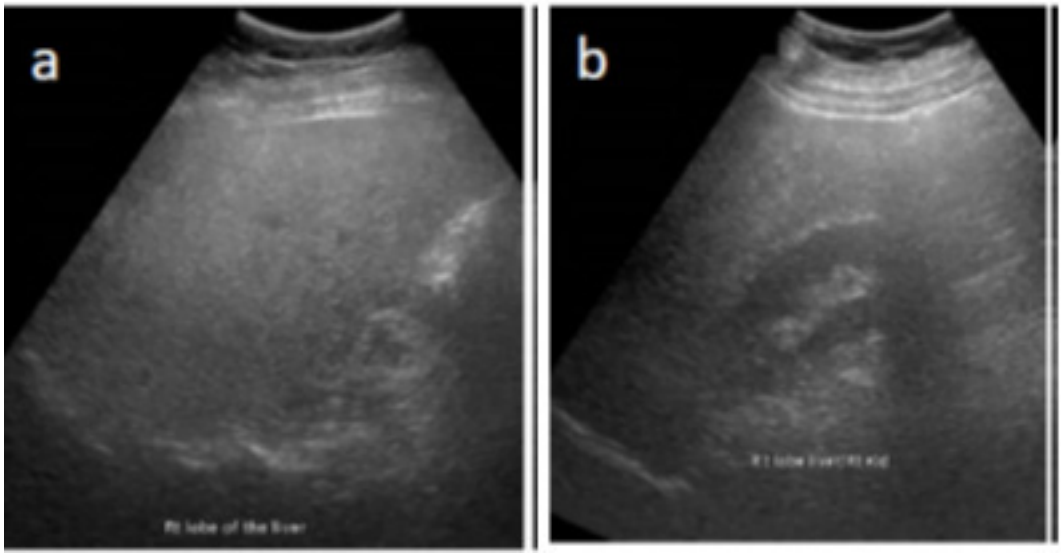

Image 3: Grade III NAFLD

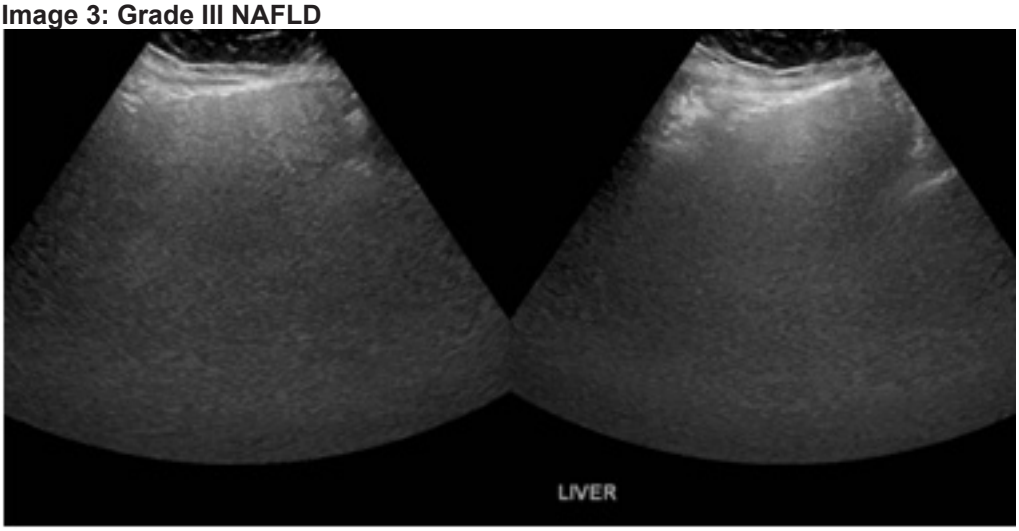

Table 1: Frequency distribution of study sample by selected socio-demographic variables

	N	%
Age group (years)		
<30	586	15.2
30-39	1225	31.8
40-49	975	25.3
50-59	724	18.8
60-69	343	8.9
Total	3853	100.0
Gender		
Female	2412	62.6
Male	1441	37.4
Total	3853	100.0
Nationality		
Ex-patriates	2995	77.7
Qatari	858	22.3
Total	3853	100.0
Smoking habit		
Non-smoker	2621	84.4
Current smoker	336	10.8
Ex-smoker	147	4.7
Total	3104	100.0
BMI categories (Kg/m2)		
Acceptable (<25)	776	20.1
Overweight (25-29.9)	1338	34.7
Obese Grade-I (30-34.9)	1017	26.4
Obese Grade-II (35-39.9)	473	12.3
Obese Grade-III (40+)	249	6.5
Total	3853	100.0

Table 2: The risk (prevalence ratio) of NAFLD by variables defining metabolic syndrome.

	Non-Alcoholic fatty liver disease								
	Negative		Positive		Total		Prevalence Ratio		
	N	%	N	%	N	%	estimate	95% CI	P
Count of positive criteria for Metabolic Syndrome									
0	157	81.8	35	18.2	192	100.0	Ref		
1	297	68.8	135	31.3	432	100.0	1.71	(1.23 - 2.38)	0.01
2	269	41.5	379	58.5	648	100.0	3.21	(2.36 - 4.36)	<0.001
3	196	24.0	621	76.0	817	100.0	4.17	(3.08 - 5.64)	<0.001
4	81	13.9	500	86.1	581	100.0	4.72	(3.49 - 6.38)	<0.001
5	24	9.8	221	90.2	245	100.0	4.95	(3.66 - 6.7)	<0.001
Metabolic Syndrome									
Negative	723	56.8	549	43.2	1272	100.0	Ref		
Positive	301	18.3	1342	81.7	1643	100.0	1.89	(1.77 - 2.02)	<0.001
Obesity (BMI>=30 kg/m2 or central obesity)									
Negative	705	48.9	738	51.1	1443	100.0	Ref		
Positive	319	21.7	1153	78.3	1472	100.0	1.53	(1.45 - 1.62)	<0.001
Insulin Resistance (Serum Fasting Glucose>=100 mg/dl or HbA1c>=5.56) or DM									
Negative	589	56.8	448	43.2	1037	100.0	Ref		
Positive	435	23.2	1443	76.8	1878	100.0	1.78	(1.65 - 1.92)	<0.001
High Blood Pressure (Systolic or Diastolic) or hypertensive									
Negative	465	54.5	388	45.5	853	100.0	Ref		
Positive	559	27.1	1503	72.9	2062	100.0	1.6	(1.48 - 1.73)	<0.001
Low serum HDL (<1.04 mmol/L in male and <1.3 mmol/L in female)									
Negative	625	43.0	830	57.0	1455	100.0	Ref		
Positive	399	27.3	1061	72.7	1460	100.0	1.27	(1.2 - 1.34)	<0.001
High serum Triglycerides (>=1.7 mmol/L)									
Negative	869	42.2	1190	57.8	2059	100.0	Ref		
Positive	155	18.1	701	81.9	856	100.0	1.42	(1.35 - 1.49)	<0.001

Table 3: The grade of NAFLD by variables defining metabolic syndrome

	Non-Alcoholic fatty liver disease grading system (American Gastroenterology Association)											
	No evidence		Grade-I		Grade-II		Grade-III		Total			
	N	%	N	%	N	%	N	%	N	%	Mean rank	P
Count of positive criteria for MS												<0.001
0	157	81.8	34	17.7	0	0.0	1	0.5	192	100.0	743	
1	297	68.8	124	28.7	11	2.5	0	0.0	432	100.0	920	
2	269	41.5	333	51.4	43	6.6	3	0.5	648	100.0	1298	
3	196	24.0	463	56.7	151	18.5	7	0.9	817	100.0	1628	
4	81	13.9	354	60.9	130	22.4	16	2.8	581	100.0	1810	
5	24	9.8	126	51.4	88	35.9	7	2.9	245	100.0	1988	
Metabolic Syndrome												<0.001
Negative	723	56.8	491	38.6	54	4.2	4	0.3	1272	100.0	1086	
Positive	301	18.3	943	57.4	369	22.5	30	1.8	1643	100.0	1746	
Obesity (BMI>=30 kg/m2 or central obesity)												<0.001
Negative	705	48.9	633	43.9	100	6.9	5	0.3	1443	100.0	1209	
Positive	319	21.7	801	54.4	323	21.9	29	2.0	1472	100.0	1702	
Insulin Resistance (Serum Fasting Glucose>=100 mg/dl or HbA1c>=5.56) or DM												<0.001
Negative	589	56.8	389	37.5	54	5.2	5	0.5	1037	100.0	1097	
Positive	435	23.2	1045	55.6	369	19.6	29	1.5	1878	100.0	1657	
High Blood Pressure (Systolic or Diastolic) or hypertensive												<0.001
Negative	465	54.5	323	37.9	62	7.3	3	0.4	853	100.0	1143	
Positive	559	27.1	1111	53.9	361	17.5	31	1.5	2062	100.0	1588	
Low serum HDL (<1.04 mmol/L in male and <1.3 mmol/L in female)												<0.001
Negative	625	43.0	649	44.6	168	11.5	13	0.9	1455	100.0	1331	
Positive	399	27.3	785	53.8	255	17.5	21	1.4	1460	100.0	1584	
High serum Triglycerides (>=1.7 mmol/L)												<0.001
Negative	869	42.2	951	46.2	221	10.7	18	0.9	2059	100.0	1333	
Positive	155	18.1	483	56.4	202	23.6	16	1.9	856	100.0	1760	

Table 4: The risk of NAFLD by sociodemographic variables

	Non-Alcoholic fatty liver disease									
	Negative		Positive			Total		Prevalence Ratio		
	N	%	N	%	95% CI	N	%	estimate	95% CI	P
Age group (years)										
<30	377	64.3	209	35.7	(31.9 to 39.6)	586	100.0	Ref		
30-39	591	48.2	634	51.8	(49 to 54.5)	1225	100.0	1.45	(1.28 - 1.64)	<0.001
40-49	349	35.8	626	64.2	(61.2 to 67.2)	975	100.0	1.8	(1.6 - 2.03)	<0.001
50-59	187	25.8	537	74.2	(70.9 to 77.3)	724	100.0	2.08	(1.85 - 2.34)	<0.001
60-69	94	27.4	249	72.6	(67.7 to 77.1)	343	100.0	2.04	(1.8 - 2.32)	<0.001
Total	1598	41.5	2255	58.5	(57 to 60.1)	3853	100.0			
Gender										
Female	1162	48.2	1250	51.8	(49.8 to 53.8)	2412	100.0	Ref		
Male	436	30.3	1005	69.7	(67.3 to 72.1)	1441	100.0	1.35	(1.28 - 1.42)	<0.001
Nationality										
Ex-patriates	1270	42.4	1725	57.6	(55.8 to 59.4)	2995	100.0	Ref		
Qatari	328	38.2	530	61.8	(58.5 to 65)	858	100.0	1.07	(1.01 - 1.14)	0.19[NS]
Smoking habit										
Non-smoker	1097	41.9	1524	58.1	(56.2 to 60)	2621	100.0	Ref		
Current smoker	120	35.7	216	64.3	(59.1 to 69.3)	336	100.0	1.11	(1.02 - 1.21)	0.2[NS]
Ex-smoker	39	26.5	108	73.5	(65.9 to 80.1)	147	100.0			
BMI categories (Kg/m2)										
Acceptable (<25)	579	74.6	197	25.4	(22.4 to 28.5)	776	100.0	Ref		
Overweight (25-29.9)	607	45.4	731	54.6	(52 to 57.3)	1338	100.0	2.15	(1.89 - 2.45)	<0.001
Obese Grade-I (30-34.9)	296	29.1	721	70.9	(68 to 73.6)	1017	100.0	2.79	(2.46 - 3.17)	<0.001
Obese Grade-II (35-39.9)	81	17.1	392	82.9	(79.3 to 86.1)	473	100.0	3.26	(2.87 - 3.7)	<0.001
Obese Grade-III (40+)	35	14.1	214	85.9	(81.2 to 89.8)	249	100.0	3.39	(2.97 - 3.86)	<0.001

Table 5: The grade of NAFLD by socio-demographic variables

	Non-Alcoholic fatty liver disease grading system (American Gastroenterology Association)											
	No evidence		Grade-I		Grade-II		Grade-III		Total			
	N	%	N	%	N	%	N	%	N	%	Mean rank	P
Age group (years)												<0.001
<30	377	64.3	173	29.5	32	5.5	4	0.7	586	100.0	1467	
30-39	591	48.2	517	42.2	114	9.3	3	0.2	1225	100.0	1773	
40-49	349	35.8	491	50.4	125	12.8	10	1.0	975	100.0	2031	
50-59	187	25.8	384	53.0	140	19.3	13	1.8	724	100.0	2281	
60-69	94	27.4	188	54.8	55	16.0	6	1.7	343	100.0	2218	
Total	1598	41.5	1753	45.5	466	12.1	36	0.9	3853	100.0		
Gender												<0.001
Female	1162	48.2	1000	41.5	236	9.8	14	0.6	2412	100.0	1784	
Male	436	30.3	753	52.3	230	16.0	22	1.5	1441	100.0	2166	
Nationality												0.006
Ex-patriates	1270	42.4	1358	45.3	337	11.3	30	1.0	2995	100.0	1903	
Qatari	328	38.2	395	46.0	129	15.0	6	0.7	858	100.0	2011	
Smoking habit												<0.001
Non-smoker	1097	41.9	1183	45.1	320	12.2	21	0.8	2621	100.0	1528	
Current smoker	120	35.7	162	48.2	47	14.0	7	2.1	336	100.0	1640	
Ex-smoker	39	26.5	79	53.7	26	17.7	3	2.0	147	100.0	1797	
BMI categories (Kg/m2)												<0.001
Acceptable (<25)	579	74.6	181	23.3	15	1.9	1	0.1	776	100.0	1248	
Overweight (25-29.9)	607	45.4	623	46.6	104	7.8	4	0.3	1338	100.0	1805	
Obese Grade-I (30-34.9)	296	29.1	555	54.6	158	15.5	8	0.8	1017	100.0	2170	
Obese Grade-II (35-39.9)	81	17.1	268	56.7	111	23.5	13	2.7	473	100.0	2486	
Obese Grade-III (40+)	35	14.1	126	50.6	78	31.3	10	4.0	249	100.0	2642	

Discussion

Our study showed that NAFLD is a prevalent disease in the Qatar population. It is associated with MetS and its components. The study provided appropriate data of the study population to create awareness among healthcare professionals about the disease and its risk factors. Guidance on lifestyle modification, diet and drugs from our primary care centers can avoid the progression of NAFLD to chronicity or complications. The second phase of the study will generate a cohort of patients, providing insights regarding the natural history of NAFLD (persistence, reversal, or progression of liver involvement). Ultrasonography is the preferred first-line detection procedure and is widely available for diagnosing steatosis [4]. The overall sensitivity and specificity of ultrasound in detection of moderate to severe fatty liver have been shown to be accurate and comparable to those of histology (gold standard). However, biopsy cannot be performed in the general population [16,17].

A previous meta-analysis of a very large population by Younossi et al. showed that the overall global prevalence of NAFLD diagnosed by imaging is around 25.24%. It showed that the highest prevalence of NAFLD is from the Middle East (31.79%) and South America and Asia (30.45%), whereas the lowest prevalence rate is reported from Africa (13.48%). The higher prevalence of NAFLD in these geographic areas can be explained by a higher prevalence of obesity in addition to genetic factors [18,19].

Our study showed that the prevalence of NAFLD by ultrasonography was around 58.5%. This high prevalence in Qatar can be due to the high number of overweight (34.7%) and obese (45.2%) patients apart from increased positive cases of MetS (56.4%).

Features of MetS are not only highly prevalent in patients with NAFLD, but its components also increase the risk of developing NAFLD. This bidirectional association between NAFLD and components of MetS has been strongly established [19].

Our study showed that the prevalence of NAFLD in positive cases of MetS was around 81.7% with the risk of 1.89. Also, our study showed that the prevalence and risk of NAFLD increased with the number of components defining MetS. The prevalence increased from 31.3% in 1 component to 90.2% in 5 components, and the risk increased from 1.71 in 1 component to 4.95 in 5 components.

Previous studies showed that obesity (excessive BMI and visceral obesity) is the most common and well documented risk factor for NAFLD. The entire spectrum of obesity, ranging from overweight to obese and severely obese, is associated with NAFLD. The majority (>95%) of patients with severe obesity undergoing bariatric surgery will have NAFLD [20].

Our study showed that the prevalence of NAFLD in cases of obesity (BMI≥30 kg/m2 or central obesity (waist circumference over 102 cm (40 inches) in men and 94 cm (37 inches) in women) was 78.3%, and the risk was 1.53.

Previous studies showed that there is a high prevalence of NAFLD in individuals with type 2 diabetes mellitus (T2DM). Some studies suggested that around one-third to two-thirds of diabetic patients have NAFLD [21]. It is also prudent to remember the importance of bidirectional association between NAFLD and T2DM. T2DM and NAFLD can develop almost simultaneously in patients, which confound the prevalence of NAFLD in patients with T2DM or the prevalence of T2DM in patients with NAFLD [19].

Our study agrees with previous studies and showed that the prevalence of NAFLD in cases of insulin resistance (Serum Fasting Glucose≥100 mg/dl or HbA1c≥5.56) or T2DM was 76.8%, and the risk was 1.78.

Previous studies showed that cases of dyslipidemia (high serum triglyceride (TG) levels and low serum high-density lipoprotein (HDL) levels) are also common in patients with NAFLD. The prevalence of NAFLD in individuals with dyslipidemia attending lipid clinics has been estimated to be 50%. In a cross-sectional study conducted among Taiwanese patients, attending a single clinic showed that the overall prevalence rate of NAFLD was 53.76% [19].

Our study showed that the prevalence of NAFLD in cases of high serum triglycerides (Fasting triglyceride level over 1.7 mmol/L (150 mg/dl)) was 81.9%, and the risk was 1.42. Also, our study showed that the prevalence of NAFLD in cases of low serum HDL (Fasting high-density lipoprotein (HDL) cholesterol level <1.04 mmol/L (<40 mg/dl) in men or <1.3 mmol/L (<50 mg/dl) in women) was 72.7%, and the risk was 1.27. It also showed that the prevalence of NAFLD in cases of patients with high blood pressure (over 130/85 mmHg) was 72.9%, and the risk was 1.6.

Previous studies showed that the prevalence of NAFLD may vary according to age, sex, and ethnicity [19,22]. Studies showed that both the prevalence of NAFLD and stage of liver disease increase with age, but this finding is controversial. Males are considerably a risk factor for NAFLD as the prevalence rate is 2 times higher than that in females [19,22].

Our study showed that the prevalence of NAFLD and grade of NAFLD increase with age. The highest is observed in the 50-59 years age group, followed by 60-69 years age group, measuring 74.2% and 2.08, and 72.6% and 2.04, respectively. It also showed that the prevalence in male and female population was 69.7% and 51.8% and the risk in the male population was 1.35 times higher.

The limitations of our case control study are related to the representativeness of the selected cases with respect to the whole population. Cases which are not suspected, not diagnosed or who do not consult in the primary care may be under-represented, but this possible selection bias will not be systematically introduced. Another limitation of the study is the use of hepatic ultrasonography for the diagnosis of fatty liver. Liver biopsy is the gold standard for diagnosis of NAFLD. However, studies comparing the diagnostic utility of ultrasonography with liver biopsy have shown a sensitivity of greater than 90% and a specificity of greater than 80% for ultrasonography in detecting the presence of NAFLD. The main limitation of ultrasonography is the difficulty in detecting fatty liver when the infiltration is less than 30% of the hepatic content [23]. Another limitation of ultrasonography is the lack of information regarding the histologic changes associated with disease progression, but ultrasonography is currently the test of reference for the detection of fatty liver at the population level [13].

Conclusion

Ultrasonography of the liver is the test of reference for the detection of fatty liver at population level. NAFLD is a prevalent health problem in our primary health care centers in Qatar and has a strong association with MetS and its components. Although the presence of this disease was approached as a minor problem, it must be considered that it may be potentially serious because of its possible evolution to chronicity and hepatic cirrhosis. On the other hand, its detection today in primary health care centers is relatively easy and accessible by ultrasonography. Also, a multifactorial intervention approach on the risk factors leading to its remission can restrict the appearance of more severe hepatic complications.

Competing interests: No conflict of interest

Ethical Considerations: The study was approved by the Primary Health Care Corporation (PHCC) Research Committee and the Research Section in the Department of Clinical Affairs.

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References

[1] Almobarak AO, Barakat S, Khalifa MH, et al. Non-alcoholic fatty liver disease (NAFLD) in a Sudanese population: What is the prevalence and risk factors? Arab Journal of Gastroenterology 2014; 15: 12–15

[2] Chalasani N, Younossi Z, Lavine J, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology 2012; 55: 2005- 23.

[3] Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and Management of Nonalcoholic Fatty Liver Disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology 2017; 67:328.

[4] Hashimoto E, Iwai M, and Suriawinata AA. Alcoholic Liver Disease and Nonalcoholic Fatty Liver Disease/ Nonalcoholic Steatohepatitis. In Hashimoto E, et al (Eds). Diagnosis of Liver Disease. 2nd Edition. Springer Nature Singapore Pte Ltd: 2019; p.79-84

[5] Chan WK, Tan AT, Vethakkan SR, et al. Non-alcoholic fatty liver disease in diabetics—prevalence and predictive factors in a multiracial hospital clinic population in Malaysia. J Gastroenterol Hepatol 2013; 28: 1375- 83.

[6] Yamazaki H, Tsuboya T, Tsuji K, Dohke M, Maguchi H. Independent association between improvement of nonalcoholic fatty liver disease and reduced incidence of type 2 diabetes mellitus. Diabetes Care 2015; 38: 1673-79.

[7] Caballería Ll, Auladell AM, Torán P, et al. Risk factors associated with non-alcoholic fatty liver disease in subjects from primary care units. A case-control study. BMC Gastroenterol 2008; 8: 44.

[8] Pagano C, Pacini G, Musso G, et al. Non-alcoholic steatohepatitis, insulin resistance and metabolic syndrome. Further evidence for an etiologic association. Hepatology 2002, 35:367-72.

[9] Al-Thani M, et al. The prevalence and characteristics of overweight and obesity among students in Qatar. Public Health 2018; 3:1-7.

[10] Bellentani S, Saccoccio G, Masutti F, et al. Prevalence of and risk factors for hepatic steatosis in Northern Italy. Ann Intern Med. 2000; 132:112–7.

[11] Wajeeha Imran Andrabi, Mubashir Dilawar, Nida Rauf, et al. Identifying Non-Alcoholic Fatty Liver Disease on Ultrasound and its Correlation with Obesity. P J M H S. 2017 Jul-Sep; 11(3):858-60.

[12] Mottin CC, Moretto M, Padoin AV, et al. The role of ultrasound in the diagnosis of hepatic steatosis in morbidly obese patients. Obes Surg. 2004; 14: 635–7.

[13] Sanyal AJ: AGA technical review on nonalcoholic fatty liver disease. Gastroenterology 2002, 123:1705-25.

[14] Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation 2005; 112:2735-52.

[15] Syed, M.A., Al Nuaimi, A.S., Latif Zainel, A.J.A. et al. Prevalence of metabolic syndrome in primary health settings in Qatar: a cross sectional study. BMC Public Health 2020; 20 (1):611.

[16] Hernaez R, Lazo M, Bonekamp S, et al. Diagnostic accuracy, and reliability of ultrasonography for the detection of fatty liver: a meta-analysis. Hepatology 2011; 54:1082–90.

[17] Mahale AR, Prabhu SD, Nachiappan M, et al. Clinical relevance of reporting fatty liver on ultrasound in asymptomatic patients during routine health checkups. The Journal of international medical research 2018, 46(11):4447–54.

[18] Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016; 64:73–84.

[19] Chalasani N, Younossi Z, Lavine JE, et al. PRACTICE GUIDANCE. The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance from the American Association for the Study of Liver Diseases. Hepatology 2018; 67(1): 328-57.

[20] Subichin M, Clanton J, Makuszewski M, et al. A. Liver disease in the morbidly obese: a review of 1000 consecutive patients undergoing weight loss surgery. Surg Obes Relat Dis 2015; 11:137-41.

[21] Leite NC, Salles GF, Araujo AL, et al. Prevalence and associated factors of non-alcoholic fatty liver disease in patients with type-2 diabetes mellitus. Liver Int 2009; 29:113-19.

[22] Fattahi MR, Niknam R, Safarpour A, et al. The prevalence of metabolic syndrome in non-alcoholic fatty liver disease; a population-based study. Middle East J Dig Dis 2016; 8:131-7.

[23] Caballería Ll, Auladell AM, Torán P, et al. Prevalence and factors associated with the
presence of non-alcoholic fatty liver disease in an apparently healthy adult population in primary care units. BMC Gastroenterology 2007; 7:41

Fibromyalgia in patients with psoriasis

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Abstract

Background: Fibromyalgia syndrome (FMS) and widespread pain are observed in many patients with autoimmune and inflammatory disorders. FMS may be underestimated in psoriasis, but not psoriatic arthritis.

The aim of this study was to investigate the prevalence of fibromyalgia and allied symptoms in patients with psoriasis.

Patients and methods: Seventy patients with psoriasis (40 male and 30 female) and 70 age and sex matched controls were enrolled in the study. Psoriatic area and severity index (PASI) was calculated for patients. A two stage classification process was applied to determine the presence of FMS in patients with psoriasis and controls. Stage 1: was answering the diffuse widespread pain questionnaire. In Stage 2, all patients with widespread pain were examined for 18 tender points.

Results: A total of 37 (52.9%) patients with psoriasis were found to have widespread pain. A total of 21 patients met the criteria of FMS with a prevalence rate of 30.0%; of them, 18 (85.7%) were women.

Conclusions: FMS and allied symptoms are more prevalent in patients with psoriasis than in the general population. Women with psoriasis are more frequently affected by FMS than are men. Awareness of this comorbidity is an essential part in the treatment of psoriasis. Because of the strong association between disease severity and FMS, proper treatment that reduces skin involvement and disease severity may be associated with the alleviation of FMS and its allied symptoms.

Key words: fibromyalgia, widespread pain, psoriasis, fibromyalgia allied symptoms, Psoriasis Area and Severity Index

Introduction

Psoriasis is defined as a chronic inflammatory disease of the skin; it usually presents as a red scaly rash over the extensor surfaces, the scalp, flexural areas of the body, palms and soles. It commonly affects the fingers and toenails [1]. The worldwide prevalence is approximately 2%, but it varies according to the geographic regions [1]. The prevalence rate is lower in Asian and some African populations, and is highly prevalent in Caucasians and Scandinavians [2–5]. Psoriasis Area and Severity Index (PASI) is used for the evaluation and measurement of psoriatic skin lesions [6], and its reduction is the standard tool of treatment response [7]. Psoriasis is known to be associated with a genetic predisposition and autoimmune pathogenesis [8]. Although the exact pathogenesis of psoriasis is still not well understood, it is demonstrated that; neurogenic inflammation has been involved in the induction and maintenance of psoriatic lesions [9–11]. A significant alteration of the expression and/or distribution of different neuropeptides and their receptors has been demonstrated in lesions of psoriasis. These neuropeptides are implicated in the pathogenesis of psoriasis and pruritus [12–14]. The exact cause of pruritus in psoriasis remains unknown; pruritic skin lesion was found to have abundant epidermal and papillary dermal innervation and an increase in substance P (SP)-containing nerve fibres, and many degranulating mast cells [15]. Studies suggest that stress may result in alterations in the psoriatic skin lesions by increasing this neuropeptide content [16]. Fibromyalgia syndrome (FMS) is chronic diffuse widespread pain disorder usually associated with other non-musculoskeletal symptoms like morning stiffness, anxiety, fatigue, sleep disturbance, and cognitive problems [17–19]. FMS prevalence rate is 1%-2% in the general population [20]. FMS often presents in association with other rheumatologic and inflammatory conditions such as axial spondyloarthritis, psoriatic arthritis, systemic lupus erythematosus, primary Sjogren's syndrome, rheumatoid arthritis, and scleroderma; the presence of FMS with such conditions is usually associated with greater severity of symptoms, impaired function, and greater disability [21–26]. The etiopathogenesis and development of FMS is correlated to stress; adverse life events, negative childhood experiences and post-traumatic stress [27]. Several neurotransmitters like glutamate, serotonin, and substance P demonstrated to be altered in patients with fibromyalgia, and could explain the increased pain sensitivity in these patients. SP has an important role in the neurotransmission of pain from the peripheral parts of the body to the central nervous system, and the physiological functions of SP are affected by the level of serotonin and coexist with glutamate [28]. Vaeroy et al. reported elevated levels of SP in cerebrospinal fluids obtained from FMS patients [29]. Therefore, stress and substance P, both have an important role in the pathogenesis and the development of both psoriasis and FMS. While the association between FMS and psoriasis may be underestimated, the association between psoriatic arthritis and FMS has been addressed in the literature [22,30,31]. However, to our knowledge, there is only one study evaluating the frequency of FMS in patients with psoriasis [32]. We therefore conducted this study to determine the prevalence of fibromyalgia and allied symptoms in patients with psoriasis.

Patients and Methods

This was a cross-sectional study carried out in the outpatient departments of Dermatology and Rheumatology in Basra Teaching Hospital from October 2018 to January 2020. A sample of 70 (40 male and 30 female) patients with psoriasis, diagnosed by dermatologist in the dermatology outpatient department, and 70 age and sex matched controls recruited from the general population were enrolled for this study. The exclusion criteria were psoriatic arthritis, other rheumatic diseases, any chronic diseases such as uncontrolled diabetes mellitus and heart or renal failure, thyroid disorders, psychiatric disorders, and history of cancer. The age, sex, disease duration, history of widespread pain, and medication history were determined for all patients. They were also assessed by the dermatologist, using the PASI. The PASI is a measure of the average redness, thickness, and scaliness of the lesions (each graded on a 0–4 scale), weighted according to the area of involvement [6]. A diagnosis of FMS was confirmed according to the two-stage classification process that was proposed by the 1990 ACR classification criteria for FMS [17]. Stage 1 was composed of the patients and controls answering the diffuse widespread pain questionnaire. Stage 2 comprised evaluation of all patients and controls complaining of diffuse pain; this evaluation included the assessment of 18 tender points and 4 control non-tender points through digital palpation with an approximate force of 4 kg (the amount of pressure required to blanch a nail). The four control non-tender points are: the middle of the forehead, the volar aspect of the mid forearm, the thumb nail, and the muscles of the anterior thigh. To meet the diagnostic criteria, musculoskeletal pain had to have been present for at least 3 months, and pain must have been present in 11 or more out of 18 specific tender points on digital palpation. All participants were also asked about the following FMS allied symptoms: morning stiffness, sleep disturbance, fatigue, headache, anxiety, and irritable bowel.

Ethical considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki, and verbal consent was obtained from all participants prior to their involvement.

Statistical analysis

SPSS Software version 25.0 was used for data analysis. Percentages and mean was used to present the data in tables. Comparison of study groups was carried out using chi-square and Fisher's exact test for categorical data, and Student's t-test for continuous data. P-value of < 0.05 was considered statistically significant.

Results

Table 1 shows the demographic distributions of both patients and control groups. From the total 70 patients with psoriasis; there were 40 (57.1%) males and 30 (52.9%) females. There were 37 (52.9%) patients with widespread pain compared with 5 (7.1%) individuals with widespread pain in the control group which is a statistically significant difference (P<0.05) as shown in Table 2. There were 21 (30.0%) (18 females and 3 males) patients who fulfilled the 1990 ACR criteria for classification of FMS in the patients group, compared to 1 (1.4%) in the control group which is also a statistically significant difference (P<0.05). Women were more obviously having FMS compared to men in a proportion of 6:1 as shown in Table 2. Table 3 shows high PASI in psoriasis patients with FMS compared to psoriasis patients without FMS; 57.9±4.6 and 15.5±3.4 respectively, (P<0.05) which is a statistically significant difference. The mean age and disease duration were 50.7±7.3 and 10.03± 2.5 respectively as shown in Table 1. FMS allied symptoms were more prevalent in patients with psoriasis than in the control group; the difference is statistically significant (all P<0.05) as shown in Table 4.

Table 1: The demographic distributions of both patients with psoriasis and controls

Characteristics	Psoriasis	Controls	P value
Total No.(%)	70(100%)	70(100%)	
Men	40(57.1%)	38(54.3%)	>0.05
Women	30(52.9%)	32(55.7%)	
Age	50.7±7.3	50.4±7.2	>0.05
Disease duration	10.03± 2.5		
Treatment	methotrexate, Topical		

Table 2: FMS in both men and women is more frequent in patients with psoriasis than in the controls

	Psoriasis	Controls	P value
Total No	70	70	
Widespread pain	37(52.9%)	5(7.1%)	<0.05
FMS:	**21(30%)**	**1(1.4%)**	<0.05
Men	3(14.3%)	0(0%)	
Women	18(85.7%)	1(100%)	

Table 3: Psoriasis patients with FMS have higher psoriatic area and severity index than psoriasis patients without FMS

Patient group	PASI
Psoriasis with FMS	57.9±4.6
Psoriasis without FMS	15.5±3.4
P value	<0.05

Table 4: FMS allied symptoms are more frequent in patients with psoriasis than in the controls

	Psoriasis	Controls	P value
TOTAL (%)	70(100%)	70(100%)	
Morning Stiffness	20(28.5%)	2(2.9%)	<0.05
Sleep Disturbance	20(28.5%)	2(2.9%)	<0.05
Anxiety	21(30%)	1(1.4%)	<0.05
Fatigue	20(28.5%)	1(1.4%)	<0.05
Headache	19(27%)	2(2.9%)	<0.05
Irritable Bowel	19(27%)	1(1.4%)	<0.05

Discussion

In this study, widespread pain was found to be more prevalent in the patients with psoriasis than in the control group in a percentage of 52.9% and 7.1% respectively, whereas the percentage of FMS among patients with psoriasis was found to be 30.0% which is higher when compared to a study done by Thune [32], who found FMS affected 13.0% of his study group. However, the prevalence rate of FMS in patients with psoriasis in our study was comparable to the prevalence rates of 25% in patients with RA (33), 30% in patients with SLE [23], and it seems to be low when compared to the prevalence rate of 37.5% and 50% in patients with psoriatic arthritis and Sjogren syndrome respectively [22,25]. The prevalence of FMS in our study population is considered high when compared to the prevalence rate in the general population [20]. This result may be explained by the psychological burden of this disfiguring disorder that contributes to stress. Stress is usually associated with exacerbation of psoriasis [16]; in addition stress plays an important role in the pathogenesis of FMS [27]. Another explanation for the increased prevalence rate of FMS in patients with psoriasis may be attributed to the common underlying pathway in the pathogenesis of both FMS and psoriasis, which is associated with the dysfunctional neurotransmitter systems, in particular the increased level of substance P in both disorders [15,28]. Women showed a 6-fold higher occurrence of FMS than men, whereas the ratio was 3:1 in the general population [20]. Therefore, FMS is more prevalent in women with psoriasis than women in the general population. This result is comparable with findings of other studies that found a female predominance of FMS in different inflammatory and rheumatic disorders [23,34,35]. In this study we found that psoriasis patients with higher PASI developed FMS more than those with lower PASI. This relationship is not addressed in the literature. This result, also may be explained by the psychological burden of this disfiguring disorder, or may be correlated to the increased level of substance P, that leads to the exacerbation of both psoriasis and FMS. Further studies, with larger patient sample are needed for the confirmation of this result. Morning stiffness, sleep disturbance, fatigue, irritable bowel, headache and anxiety were the most common non-musculoskeletal manifestations recorded in patients with psoriasis in this study. These FMS allied symptoms were more prevalent in psoriatic patients compared to the controls. The increased frequency of these symptoms also may be attributed to the common etiopathogenesis of both FMS and psoriasis. However, these symptoms were not addressed in previous studies; therefore, further studies are needed to estimate the prevalence of these FMS allied symptoms in patients with psoriasis. Prevalence of FMS allied symptoms in this study were found to be comparable with the findings of other studies conducted on acne vulgaris, another skin disorder associated with FMS [36,37].

Conclusion

FMS and allied symptoms are more prevalent in patients with psoriasis than in the general population. Women with psoriasis are more frequently affected by FMS than are men. Awareness of this comorbidity is an essential part in the treatment of psoriasis. Because of the strong association between disease severity and FMS, proper treatment that reduces skin involvement and disease severity may be associated with the alleviation of FMS and its allied symptoms.

Conflict of interest:
There is no any conflict of interest associated with this manuscript to be declared.

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All authors approve that the manuscript has been read and approved. All authors participated equally in the preparation of this manuscript by completing the questionnaires of the patients, preparing and writing the final manuscript preparing it for publishing.

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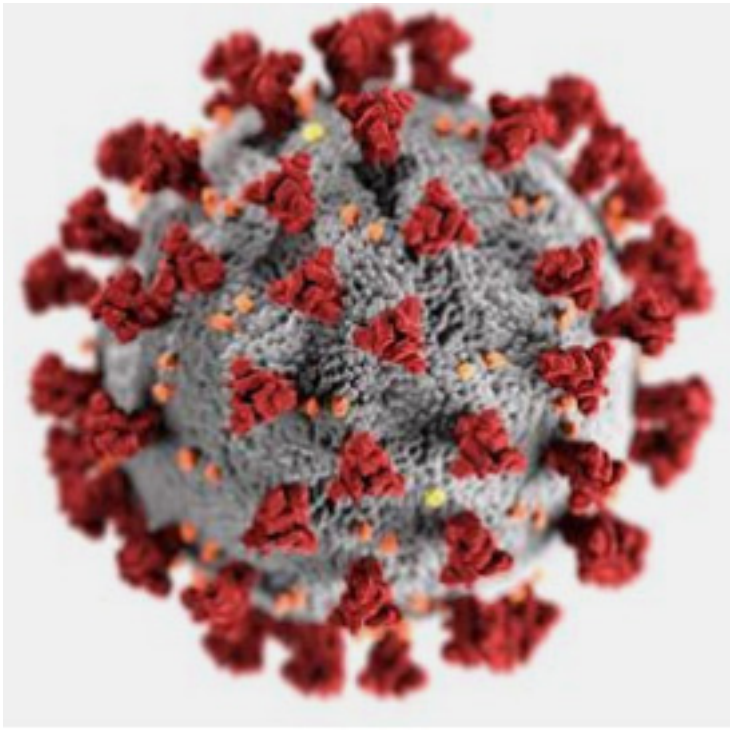
References

1. Langley RGB, Krueger GG, Griffiths CEM. Psoriasis: Epidemiology, clinical features, and quality of life. In: Annals of the Rheumatic Diseases. BMJ Publishing Group; 2005. p. ii18.
2. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. J Am Acad Dermatol. 2014 Mar;70(3):512–6.
3. Danielsen K, Olsen AO, Wilsgaard T, Furberg AS. Is the prevalence of psoriasis increasing? A 30-year follow-up of a population-based cohort. Br J Dermatol. 2013 Jun;168(6):1303–10.
4. Gibbs S. Skin disease and socioeconomic conditions in rural Africa: Tanzania. Int J Dermatol. 1996;35(9):633–9.
5. Parisi R, Symmons DPM, Griffiths CEM, Ashcroft DM. Global epidemiology of psoriasis: A systematic review of incidence and prevalence. J Invest Dermatol. 2013;133(2):377–85.
6. Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. Ann Rheum Dis. 2005;64(SUPPL. 2):65–8.
7. Torres T, Puig L. Treatment goals for psoriasis: Should PASI 90 become the standard of care? Actas Dermosifiliogr. 2015;106(3):155–7.
8. Trembath RC, Clough RL, Rosbotham JL, Jones AB, Camp RDR, Frodsham A, et al. Identification of a major susceptibility locus on chromosome 6p and evidence for further disease loci revealed by a two stage genome-wide search in psoriasis. Hum Mol Genet. 1997;6(5):813–20.
9. Saraceno R, Kleyn CE, Terenghi G, Griffiths CEM. The role of neuropeptides in psoriasis. Br J Dermatol. 2006;155(5):876–82.

10. Raychaudhuri SP, Farber EM. Neuroimmunologic aspects of psoriasis. Cutis. 2000;66(5):357–62.
11. Al'Abadie MSK, Senior HJ, Bleehen SS, Gawkrodger DJ. Neuropeptides and general neuronal marker in psoriasis - An immunohistochemical study. Clin Exp Dermatol. 1995;20(5):384–9.
12. Chan J, Smoller BR, Raychauduri SP, Jiang WY, Farber EM. Intraepidermal nerve fiber expression of calcitonin gene-related peptide, vasoactive intestinal peptide and substance P in psoriasis. Arch Dermatol Res. 1997;289(11):611–6.
13. Reich A, Orda A, Wiśnicka B, Szepietowski JC. Plasma concentration of selected neuropeptides in patients suffering from psoriasis. Exp Dermatol. 2007;16(5):421–8.
14. Eedy DJ, Johnston CF, Shaw C, Buchanan KD. Neuropeptides in psoriasis: An immunocytochemical and radioimmunoassay study. J Invest Dermatol. 1991;96(4):434–8.
15. Nakamura M, Toyoda M, Morohashi M. Pruritogenic mediators in psoriasis vulgaris: Comparative evaluation of itch-associated cutaneous factors. Br J Dermatol. 2003;149(4):718–30.
16. Harvima IT, Viinamaki H, Naukkarinen A, Paukkonen K, Neittaanmdki H, Harvima RJ, et al. Association of cutaneous mast cells and sensory nerves with psychic stress in psoriasis. Psychother Psychosom. 1993;60(3–4):168–76.
17. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The american college of rheumatology 1990 criteria for the classification of fibromyalgia. Arthritis Rheum. 1990;33(2):160–72.
18. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res. 2010 May;62(5):600–10.
19. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016 Dec;46(3):319–29.
20. Wolfe F, Ross K, Anderson J, Russell IJON, Hebert L. THE PREVALENCE AND CHARACTERISTICS OF FIBROMYALGIA IN THE GENERAL POPULATION. 1995;38(1):19–28.
21. Salaffi F, De Angelis R, Carotti M, Gutierrez M, Sarzi-Puttini P, Atzeni F. Fibromyalgia in patients with axial spondyloarthritis: Epidemiological profile and effect on measures of disease activity. Rheumatol Int. 2014;34(8):1103–10.
22. Magrey MN, Antonelli M, James N, Khan MA. High Frequency of Fibromyalgia in Patients with Psoriatic Arthritis: A Pilot Study. 2013;2013.
23. Middleton GD, Mcfarlin JE, Lipsky PE. The prevalence and clinical impact of fibromyalgia in systemic lupus erythematosus. Arthritis Rheum. 1994;37(8):1181–8.
24. Perrot S, Peixoto M, Dieudé P, Hachulla E, Avouac J, Ottaviani S, et al. Patient phenotypes in fibromyalgia comorbid with systemic sclerosis or rheumatoid arthritis: Influence of diagnostic and screening tests. Screening with the FiRST questionnaire, diagnosis with the ACR 1990 and revised ACR 2010 criteria. Clin Exp Rheumatol. 2017;35:35–42.
25. Torrente-Segarra V, Corominas H, Sánchez-Piedra C, Fernández-Castro M, Andreu JL, Martínez-Taboada V, et al. Fibromyalgia prevalence and associated factors in primary Sjögren's syndrome patients in a large cohort from the Spanish Society of Rheumatology registry (SJOGRENSER). Clin Exp Rheumatol. 2017;35:28–34.
26. Haliloglu S, Carlioglu A, Akdeniz D, Karaaslan Y, Kosar A. Fibromyalgia in patients with other rheumatic diseases: Prevalence and relationship with disease activity. Rheumatol Int. 2014;34(9):1275–80.
27. Van Houdenhove B, Egle U, Luyten P. The role of life stress in fibromyalgia. Curr Rheumatol Rep. 2005;7(5):365–70.
28. Russell IJ, Orr MD, Littman B, Vipraio GA, Alboukrek D, Michalek JE, et al. Elevated cerebrospinal fluid levels of substance p in patients with the fibromyalgia syndrome. Arthritis Rheum. 1994;37(11):1593–601.
29. Vaeroy H, Helle R, Forre 0, Kass E, Terenius L: Elevated CSF levels of substance P and high incidence of Raynaud's phenomenon in patients with fibromyalgia: new features for diagnosis.
Pain 32:21-26, 1988
30. Brikman S, Furer V, Wollman J, Borok S, Matz H, Polachek A, et al. The effect of the presence of fibromyalgia on common clinical disease activity indices in patients with psoriatic arthritis: A cross-sectional study. J Rheumatol. 2016;43(9):1749–54.
31. Ulus Y, Akyol Y, Bilgici A. The impact of the presence of fibromyalgia on fatigue in patients with psoriatic arthritis: comparison with controls. 2020;1–7.
32. Thune PO. The prevalence of fibromyalgia among patients with psoriasis. Acta Derm Venereol. 2005;85(1):33–7.
33. Wolfe F, Cathey MA, Kleinheksel SM. Fibrositis (Fibromyalgia) in rheumatoid arthritis. J Rheumatol. 1984;11(6):814–8.
34. Amiri AH, Sedighi O. Prevalence of fibromyalgia in patients with ankylosing spondylitis. 2014;7(3):338–41.
35. Jobanputra C, Richey RH, Nair J, Moots RJ, Goebel A. Fibromyalgia in Behçet's disease: a narrative review. Br J Pain. 2017;11(2):97–101.
36. Grahame V, Dick DC, Morton CM, Watkins O, Power KG. The psychological correlates of treatment efficacy in acne. Dermatology Psychosom. 2002;3(3):119–25.
37. Golchai J, Khani SH, Heidarzadeh A, Eshkevari SS, Alizade N, Eftekhari H. Comparison of anxiety and depression in patients with acne vulgaris and healthy individuals. Indian J Dermatol. 2010;55(4):352–4.



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Family Medicine Residents Mentoring During Covid-19 Pandemic and Beyond

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Family medicine residency training program in Qatar is a 4 year program established in 1995 where residents graduate after completing the Arab Board of Medical Specialization requirements for Family Medicine. The program gained the ACGME-I initial accreditation in 2013 and currently has advanced accreditation.

Mentoring was already there in the Family Medicine Residency Program since it started but it was not in an official manner and there was no structured curriculum. With the continuous change and development in residency training in response to the country's needs, and to match with the accreditation standards, the program developed a structured mentorship curriculum that was officially implemented in 2018, being the first residency training program in Qatar to officially implement a structured mentorship program.

Covid-19 pandemic was announced by WHO on March 11th 2020 (1) and in Qatar the MoPH applied precautions in response to that and this included holding all face-to-face group activities and in collaboration with HMC and PHCC, a number of facilities dedicated to caring for Covid-19 patients opened and our family medicine residents worked as part of the front line team in these facilities.

With the Covid-19 pandemic, it was expected that residents will be working under pressure that may lead to mental health and other challenges as we are dealing with a virus that we still know little about. And every day we know new information about how it spreads, its severity, immunity, etc especially, that there is no effective vaccine or treatment approved for it et. With that, residents were expected to work under pressure being worried about their family's health as well as their own health. Adding to that, initially there was no clear vision on how the educational activities will continue and the residents were worried about having their previously scheduled clinical rotations delayed which made them anxious about the future.

Providing mentorship and support for mentees during the pandemic represented a challenge to many when considering the difficulty of face-to-face meetings, and the rising needs. Our mentorship curriculum included other alternatives to face-to-face meetings between minors and mentees including virtual methods and other ways of communication. We decided that the mentors need to communicate with their mentees more frequently and that this communication is to be more unofficial communication. Most of the communication was through phone calls, emails and messaging. The program agreed that the initial communication was to mainly discuss the new situation, responsibilities and expectations and to agree on the best way of communication during the Covid-19 pandemic. The mentors were to ensure that residents are working in teams with support and supervision immediately available where residents are to be aware about where, when, and how to ask for help and support at any of the Covid-19 and other related sites. The Program Director maintained continuous communication with mentors to ensure that all the residents did have a chance of communicating with their mentors while maintaining the confidentiality of information being discussed between residents and their mentors from the faculty members. Additional support is being provided by the program through maintaining communication with residents through emails, being available to respond to phone calls, and face-to-face meetings when needed. The program continued receiving feedback about all the residents working in Covid-19 sites. An important aspect that mentors considered whenever they communicate with mentees was the mental and physical wellness of the residents.

With this support being provided through the mentoring program, it was observed that the residents were able to adapt to the new situation faster and that was reflected on the degree of satisfaction whenever they communicate with their mentors. Adding to that, the program did continue receiving positive feedback about our Family Medicine Residents with no single complaint raised against our residents. The program did observe that the residents positively benefited from the new experience and that was reflected in many aspects including improved communication skills and being involved in more research and other scholarly activities with teams from other hospital departments.

In conclusion, a structured mentoring program did help supporting residents accommodate faster during the difficult time of Covid-19 especially during the early period. More frequent meetings between mentors and mentees are to continue for the first few months after the pandemic to ensure that the residents are ready to continue learning and for better achievements. There are still other ways to support residents and learners during such situations and sharing experience can help programs improve and better prepare for similar situations if that happens in the future.

Reference

1. WHO. WHO Director-Generals opening remarks at media briefing on Covid-19 11 March 2020. https://www.who.int/dg/speeches/detail/who- director-general-s-opening-remarks-at-the- media- briefing-on-covid-19 - 11-march-2020 (2020).

Trust and psychological safety in a virtual healthcare team

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Abstract

Virtual teams are a common feature in many organizations. Given the need to improve the management of disease, and harness advances in technology, virtual teams are increasingly seen in healthcare. Two ingredients considered necessary for an effective team are trust and psychological safety. There are differences between co-located and virtual teams, including face to face interaction and social interaction. Understanding how to develop and maintain trust and psychological safety is crucial to ensure that a virtual team works effectively.

Key words: Virtual team; Healthcare; Trust; Psychological Safety.

Introduction

As the face of healthcare delivery has changed with the COVID 19 pandemic, virtual interactions between clinicians and their patients have increased (1). Clinicians have worked in virtual settings before, for instance in certain types of multidisciplinary meetings (2). The pandemic is likely to see clinicians increasingly likely to work as part of virtual teams.

A virtual team is considered to possess certain characteristics: (3)

- That it is a functioning team
- The members of the team are geographically dispersed
- There is a reliance on technology mediated communication to accomplish a task

Virtual teams have several advantages, such as not requiring the individual to leave to travel to undertake a face to face interaction, thereby saving time travel and cost. There is the opportunity to include individuals from a wider pool who might otherwise not be able to join a physically co-located team (4).

Virtual teams are particularly vulnerable to breakdown of communications, conflicts, power struggles and mistrust (5) 70 to 80% of medical errors were related to interactions within the health care team (6). Two conditions considered important for a team to accomplish a task effectively are trust and psychological safety. Trust is likened to the “glue of the workplace” (7). Psychological safety allows team members to think freely and take risks with confidence (8).

Trust

Trust in virtual teams is positively associated with job satisfaction (9) and improved working relationships (10). Trust has been defined in terms of vulnerability and control (11). One individual (trustor) is willing to be vulnerable to the other individual (trustee) when the trustee cannot be monitored or controlled by the trustor. There are also three antecedent characteristics of trust:

- Ability refers to the skills that allow a trustee to be perceived as being able to be competent within a certain context.
- Integrity is the perception that the trustee is reliable through demonstrating a set of principles, such as work habit.
- Benevolence is the perception that the trustor will act in a good way, demonstrating "interpersonal care and concern…beyond an egocentric profit motive" (12).

The triad of antecedent characteristics is thought to arise at different stages in the formation of trust. Early on, trust is considered to develop from perceptions from the trustor about the ability and integrity of the trustee (12). Judgements based on benevolence would be made later in the relationship between trustor and trustee (13).

Trust can develop even when there is limited time to form interpersonal relationships. This is termed swift trust (14) and can develop in co-located as well as virtual teams (12). Swift trust is considered to arise from the trustor's own inclination to trust and an initial assumption of trustworthiness, based upon factors such as the trustee's reputation. However, the trustor's swiftly formed opinion about the trustee is confirmed or refuted with the passage of time. As such, swift trust is considered fragile (15).

Trust has been described as the glue of the global workspace, but technology does not do much to create relationships (16). Technology can enable communication in a virtual team, but non-verbal cues will be less apparent. Trust is influenced by the ability to directly see what colleagues are doing (17). In the virtual setting, it is important for team members to communicate what they are doing. This will avoid resentment of other members socially loafing (18), thereby undermining the perception of integrity. Task deadlines also need to be met so as not to undermine the belief in ability.

Technologically enabled communication should include a focus on developing social bonds. For instance, starting an email with a salutation such as "Hi" enhances trust in the setting of a distributed team (19). Other methods include allowing colleagues to discuss hobbies and interests. These social bonds will help to introduce benevolence and affective trust which will help to maintain trust.

Hunsaker and Hunsaker (20) suggested five things a leader should do to boost trust in virtual teams:

1. Create face time. For instance, this helps individuals to get to know each other, appreciate non-verbal cues and develop team cohesion.
2. Set goals and expectations. This will make clear the team agenda and what deadlines need to be met.
3. Provide ongoing feedback. Well delivered feedback yields increased job satisfaction, less depression and increased mental and physical longevity (21).
4. Show-case team members' competence. It is especially important that early interaction between colleagues includes sufficient information such as previous work or accomplishments.
5. Foster cultural understandings, such as particular ways of greeting one another or asking for advice may be different according to cultural practices, and these differences need to be recognized (22).

Psychological safety

If trust is considered to focus on the benefit of doubt that is given to others, psychological safety is concerned with the benefit of doubt given to the individual by others (23). It is a group phenomenon, allowing team members to think freely and take risks which are key aspects of learning, with confidence that there is mutual respect and trust within the team (8).

Furthermore, with respect to trust, the long-term consequences of trusting another person are considered, whereas the calculus inherent in psychological safety considers the very short-term interpersonal consequences expected from engaging in a specific action (24).

Researchers originally suggested that psychological safety was a response to organizational change and postulated that, during the change process, it would enable the individual to have a pro-active approach to team goals rather than a focus on self-protection (25).

When three factors (co-worker relations, co-worker norms and supervisor relations) were assessed, supervisor relations had the strongest relationship with psychological safety (26). If the supervisor or leader is authoritarian and not welcoming the opinions of others, the team has low psychological safety, potentially leading to disastrous consequences (27).

In health care, learning and improvement can be made harder if communication must cross traditional hierarchical lines of status (23). Status differences which challenge good communication have been identified as contributory to many medical errors (28). A hostile team diminished the members' willingness to take part in problem solving activities (29).

It has been suggested that health care providers should be high reliability organizations preoccupied with the possibility of failure (30). Research has found that high-performing medical teams reported more mistakes than their low-performing teams. Those high performing teams possessed greater levels of psychological safety in comparison to low performing teams (8).

When Google's People Analytics Unit assessed the characteristics of high performing teams, psychological safety was found to be the most important characteristic (31). The ability of team members to have their opinions heard was one of the keys to success. Previous research has also found "groups where a few people dominated the conversation were less collectively intelligent than those with a more equal distribution of conversation turn- taking" (32, at page 688).

Team members are more inclined to speak up in the team if a leader is democratic and supportive, welcoming questions and challenges (29). Psychological safety facilitated learning, experimenting and new practice production in intensive care units within 23 hospitals (33). Units with greater learning behaviors had lower risk adjusted mortality rates after 2-3 years of observation (34).

With respect to the virtual team setting, leaders need to consider certain factors:
1. The way the team is configured to avoid ingroup and outgroup if there is one large and one smaller subgroup (35).
2. Team members require familiarity with the technology that is being used to communicate. If there is a reporting system that is in place, then this should be designed to be easy to use and not disruptive to the normal ebb and flow of patient care (36).
3. In the virtual meetings, expectation is established that everyone gets an equal chance to speak and active listening is encouraged from co participants (32).
4. The leadership approach needs to be one which facilitates a sense of safety from team members to express themselves authentically.
5. Most of the research on psychological safety has been undertaken in Western countries, so its interpretation might require adaptation if the virtual team spans other countries (37).

Communication within a virtual team

There are barriers to successful communication in virtual teams including communication that is lacking contextual information, providing inaccurate information, interpretation of silence and technical problems (38).

The lack of convenient nonverbal cues in digital communication can make virtual team working challenging, for instance, it is less conducive for the establishment of mutual knowledge (39).

Communication media can be considered to exist on a continuous scale based on the ability to communicate a complex message efficiently. Videoconferencing, for instance, is richer than using emails. The richer the media, the more efficiently it can clarify ambiguous issues (40). Use of richer media in virtual teams helps to increase an individual contribution being noticed and valued and reduces perceived social loafing (41).

Although it might be assumed that individuals would choose to communicate messages using richer media, when sending more equivocal messages, rather than voice mail, the less rich medium of email was used (42). The ideal communication system for a virtual team would feature a variety of types of media, with a range of media richness, in which team members are able to choose the media that is best suited for them and the task (43).

Summary

With developments in technology and the impact of disease, working patterns in healthcare continue to change. Interacting remotely, not just with a patient but also with colleagues, is becoming more common, such that clinicians are now likely to be part of virtual teams.

For these virtual teams to be effective, trust and psychological safety need to be developed and maintained. Though they are not identical, one commonality is the need for bonds to develop between colleagues based upon confidence that a task can be completed, and any questions can be raised.
For those bonds to develop, the communication systems that are used and the interface between team members and the team leader need to facilitate exchange of information, both formal and informal, easily, and ideally, as close to face to face exchanges as possible.

Key Learning points
Team members need to be confident in the ability and integrity of colleagues and go on to build emotional bonds with them. They need to feel able to express themselves, for instance in a team meeting, and not feel at risk of ridicule when doing so.

Team leaders need to understand how trust and psychological safety are fostered and maintained in their teams. They need to take care not to stifle the informal aspects of teamwork. They should ensure that team members feel able to approach them with suggestions or concerns.

The technology used to communicate in the virtual team needs to provide as many types of media possible to facilitate timely communication and foster bonds within the team to allow for work to be done effectively and with positive participation.

References

1. Webster P. Virtual health care in the era of COVID-19. The Lancet. 2020;395(10231):1180-1181.
2. Munro A, Swartzman S. What is a virtual multidisciplinary team (vMDT)? British Journal of Cancer. 2013;108(12):2433-2441.
3. Gibson C, Cohen S. Virtual teams that work. San Francisco, California: Jossey-Bass; 2013.

4. Bergiel BJ, Bergiel EB, Balsmeier PW. Nature of virtual teams: a summary of their advantages and disadvantages. Management Research News. 2008; 31(2): 99-110.
5. Malhotra A, Majchrzak A, Rosen B. Leading Virtual Teams. Academy of Management Perspectives. 2007;21(1):60-70.
6. Schaefer H, Helmreich R, Scheidegger D. Human factors and safety in emergency medicine. Resuscitation. 1994;28(3):221-225.
7. Kirkman B, Mathieu J. The Dimensions and Antecedents of Team Virtuality. Journal of Management. 2005;31(5):700-718.
8. Edmondson A. Psychological Safety and Learning Behavior in Work Teams. Administrative Science Quarterly. 1999;44(2):350.
9. Morris S, Marshall T, Rainer Jr. R. Impact of User Satisfaction and Trust on Virtual Team Members. Information Resources Management Journal. 2002;15(2):22-30.
10. Sharifi S, Pawar K. Virtually co-located product design teams. International Journal of Operations & Production Management. 2002;22(6):656-679.
11. Mayer R, Davis J, Schoorman F. An Integrative Model of Organizational Trust. The Academy of Management Review. 1995;20(3):709.
12. Jarvenpaa S, Knoll K, Leidner D. Is Anybody out There? Antecedents of Trust in Global Virtual Teams. Journal of Management Information Systems. 1998;14(4):29-64.
13. Schoorman F, Mayer R, Davis J. An Integrative Model of Organizational Trust: Past, Present, and Future. Academy of Management Review. 2007;32(2):344-354.
14. Kramer R, Tyler T, Meyerson D, Weick K. Trust in organizations. Thousand Oaks (Calif.): Sage publ.; 1996.
15. Crisp C, Jarvenpaa S. Swift Trust in Global Virtual Teams. Journal of Personnel Psychology. 2013;12(1):45-56.
16. O'Hara-Devereaux M, Johansen R. Globalwork. San Francisco, California: Jossey-Bass; 1996.
17. Aubert B, Kelsey B. Further Understanding of Trust and Performance in Virtual Teams. Small Group Research. 2003;34(5):575-618. Cited in Ford RC, Piccolo RF, Ford LR. Strategies for building effective virtual teams: Trust is key. Business Horizons. 2017; 60: 25-34.
18. Peñarroja V, Orengo V, Zornoza A. Reducing perceived social loafing in virtual teams: The effect of team feedback with guided reflexivity. Journal of Applied Social Psychology. 2017;47(8):424-435.
19. Walther J, Bunz U. The Rules of Virtual Groups: Trust, Liking, and Performance in Computer-Mediated Communication. Journal of Communication. 2005;55(4):828-846.
20. Hunsaker P, Hunsaker J. Virtual teams: a leader's guide. Team Performance Management: An International Journal. 2008;14(1/2):86-101. Cited in Gazor H. A Literature Review on Challenges of Virtual Team's Leadership. Journal of Sociological Research. 2012;3(2):134-145.
21. Nowack K. Taking the Sting Out of Feedback. Talent Development Magazine. 2014;(68):50-54.
22. Shachaf P. Cultural diversity and information and communication technology affects global virtual teams: An exploratory study. Information & Management. 2008; 42(2): 131-142.
23. Edmondson AC. Managing the Risk of Learning: Psychological Safety in Work Teams. In West M, Tjosvold D, Smith K. International handbook of organizational teamwork and cooperative working. New York: Wiley; 2008.
24. Edmondson AC. Psychological Safety, Trust and Learning: A Group-level Lens. In Trust and Distrust in Organizations: Dilemmas and Approaches, edited by Roderick Kramer and Karen Cook, 239–272. New York: Russell Sage Foundation; 2004.
25. Schein E, Bennis W. Personal and organizational change via group methods. New York: John Wiley; 1965.
26. May D, Gilson R, Harter L. The psychological conditions of meaningfulness, safety and availability and the engagement of the human spirit at work. Journal of Occupational and Organizational Psychology. 2004;77(1):11-37.
27. Bienefeld N, Grote G. Silence That May Kill. Aviation Psychology and Applied Human Factors. 2012;2(1):1-10. Cited in Marsden, E. Psychological safety. Risk Engineering. 2020. Available from: https://risk-engineering.org/concept/psychological-safety.
Accessed 24/7/2020
28. Institute of Medicine. Keeping Patients Safe: Transforming the Work Environment of Nurses. National Academics Press. 2003
29. Nembhard I, Edmondson AC. Making it safe: the effects of leader inclusiveness and professional status on psychological safety and improvement efforts in health care teams. Journal of Organizational Behavior. 2006;27(7):941-966.
30. Reason J. Human error: models and management. BMJ. 2000;320(7237):768-770.
31. Bergmann B, Schaeppi J. A Data-Driven Approach to Group Creativity [Internet]. Harvard Business Review. 2020. Available from: https://hbr.org/2016/07/a-data-driven-approach-to-group-creativity. Accessed 27/11/2020
32. Woolley AW, Chabris CF, Pentland A, Hashmi N, Malone TW. Evidence for a Collective Intelligence Factor in the Performance of Human Groups. Science. 2010; 330: 686-688.
33. Tucker AL. An empirical study of system improvement by frontline employees in hospital units. Manufacturing & Services Operations Management. 2007; 9(4):492–505. Cited in Edmondson AC, Lei Z. Psychological Safety: The History, Renaissance, and Future of an Interpersonal Construct. Annual Review Organizational Psychology and Organizational Behavior. 2014; 1:23–43.
34. Edmondson A, Lei Z. Psychological Safety: The History, Renaissance, and Future of an Interpersonal Construct. Annual Review of Organizational Psychology and Organizational Behavior. 2014;1(1):23-43.
35. O'Leary M, Mortensen M. Go (Con)figure: Subgroups, Imbalance, and Isolates in Geographically Dispersed Teams. Organization Science. 2010;21(1):115-131.
36. Hartnell N, MacKinnon N, Sketris I, Fleming M. Identifying, understanding and overcoming barriers to medication error reporting in hospitals: a focus group study. BMJ Quality & Safety. 2012;21(5):361-368.

37. Hofstede G. Culture's consequences: Comparing values, behaviors, institutions, and organizations across nations. 2nd ed. Sage. 2001. Cited in Marsden, E. Psychological safety. Risk Engineering. 2020. Available from: https://risk-engineering.org/concept/psychological-safety.
Accessed 24/7/2020
38. Cramton C. The Mutual Knowledge Problem and Its Consequences for Dispersed Collaboration. Organization Science. 2001;12(3):346-371.
39. Cramton CD. Finding Common Ground in Dispersed Collaboration. Organizational Dynamics 30.4 (2002): 356-67
40. Carlson JR, Zmud RW. Channel Expansion Theory and the Experiential Nature of Media Richness Perceptions. The Academy of Management Journal. 1999. 42 (2): 153–170.
41. Bryant S. The effects of reward structure, media richness and gender on virtual teams. International Journal of Accounting Information Systems. 2009.10 (4): 190
42. El-Shinnawy M, Markus M. The poverty of media richness theory: explaining people's choice of electronic mail vs. voice mail. International Journal of Human-Computer Studies. 1997;46(4):443-467.
43. Workman M, Kahnweiler W, Bommer, W. The effects of cognitive style and media richness on commitment to telework and virtual teams. Journal of Vocational Behavior. Special Issue on Technology and Careers. 2003. 63 (2): 199–219

Implications of COVID-19 pandemic on Family Medicine Residency training program and ACGME requirements in Qatar

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Introduction

Disasters like Covid-19 pandemic can turn into opportunities for sustainable development. From the family medicine training perspective while responding to the most urgent needs as a front-line staff facing the unpredictable pandemic, one must take advantage of all opportunities for change to achieve the desired goals and sustainable recovery. It is a continuous dynamic multi-dimensional process through the efficient use of the best available resources.

Qatar reported its first Qatari case of Covid-19 coming from Iran on February 29, 2020, and 2 weeks later the first cluster had emerged. The state of Qatar, through Hamad Medical Corporation, has developed the system wide incident command committee, SWICC, to manage the crisis in the country. Family medicine residents were allocated to provide direct patient care along with the other residents as front-line staff to manage the situation.

Leadership role and responsibility during the crisis

- Adequate resources, training and supervision and putting resident's safety as a priority were all requisites of the accredited ACGME-I, family medicine training program in Qatar. The concept of Flexibility was always adopted to accommodate residents' training needs. Family medicine training program director along with the faculty team takes the initiative of raising our residents to be flexible in order to adjust to the real situation on the ground during and after the event.

- The program director monitors the educational activities, webinars, collaborating with Microsoft teams, providing close supervision and guidance to highlight residents' points of strength and encourage them by providing a personalized comprehensive feedback system which encompasses their strengths and weaknesses and empowers them to be safe, highly qualified physicians.

- Promoting their mental well-being; family medicine residents are encouraged to report fatigue, stress and other problems at site. Local support from the program director, assigned consultants and their chosen mentors along with the Mental Health team has been provided as well as relieving them from responsibilities when needed.

- The program director considers the circumstances, assesses readiness of each resident for autonomous practice, provides a final evaluation for each graduating trainee and be able to attest for future hospital privileges, licensure, and other purposes. The decision to graduate a resident is made by the program director, with input from the Core Competency Committee, based on that individual's ability to perform the medical, diagnostic, and/or surgical procedures considered essential for the area of practice. The Extension of the educational program/training may be necessary if the program director determines that an individual is not fully ready for autonomous practice.

Covid-19 implications on ACGME-I Requirements

Family medicine residency program in Qatar has been an accredited ACGME-I program since 2013; During the COVID crisis, ACGME/ ACGME-I has granted significant flexibility to allow our residents to meet increased clinical demands created by the pandemic(3). This advice is adapted from their advice to USA programs and is consistent with ACGME's commitment to patient and trainee safety as following.

1. Work Hour Requirements
ACGME Common Program Work Hour Requirements are unchanged. Safety of patients and trainees is their highest priority. All residents have received adequate rest between clinical duties. Therefore most deployed trainees are working around a 40-hour week and certainly not exceeding 80. Only daytime shifts or nighttime cover.

2. Adequate Resources and Training
ACGME expects that trainees be aware of and able to appropriately respond to Covid-19. Therefore, the residents caring for patients are fully trained in treatment and infection control protocols and procedures (e.g. PPE). Clinical learning environments provide adequate resources, facilities, and training to recognize and care for these patients presenting with COVID-19 signs and symptoms. They are using Microsoft Teams groups to share all the latest national treatment protocols and other relevant resources that help our residents in management of patients with COVID-19.

3. Adequate Supervision
All the residents who provide care to patients are working closely with supervising consultants for support and guidance according to their level and expertise. PGY 1 Residents are left mainly in their base program, but a few are deployed in COVID facilities.

Residents Rotations and safety

Over several months of very heavy pressure on the health care systems with additional patients who must be cared for, requiring significant trainee redeployment, several measures have been introduced such as and not limited to:
Prior to starting the reassignment, residents must receive appropriate safety and clinical training for the new setting which encompasses training on infection prevention and control (IPAK) measures, and swabbing techniques. They must always have appropriate supervision and adhere to work hour requirements.

Optimizing the quality of transitions/hand-offs; - a good system was established by Chief Residents including I-PASS handoff notes. The I-PASS handoff tool in Cerner is utilized to maintain adequate and proper handoff between different shifts. This allows social distancing between physicians and limits the need for paper endorsements.
Residents with chronic conditions or fitting the criteria of Covid-19 high risk group such as pregnancy or immunocompromised are exempted from the direct contact with Covid patient cases.

- According to HMC/SWICC; many trainees are deployed > 4 weeks because that is felt to be much safer for patients and for them, so this will be an issue for programs to assess. It may be that the experience can count towards training but that depends on their r curriculum and their deployment. E.g. ICU could count as an elective for an IM trainee. HMC/ SWICC also acknowledged that residents experience at centers handling the pandemic crisis might count towards aspects of training e.g. (professionalism, systems-based learning). Residents are encouraged to log the procedures they did in COVID hospitals into Med hub and ADS.

- Residents' time away from required rotations, or the program, may possibly, but not necessarily, affect their graduation from the Program, their promotion to the next year or indeed, their Arab Board eligibility.

- The Program can make their judgment based on exactly what the trainee has missed. Trainees cannot participate in operations that do not take place. Cancellation of clinics may adversely affect required volumes of clinic visits. If they have missed a core rotation, they may need the time (and arrangements made) to complete that. They may need additional time to gain the essential competencies for that training year.

- Program has had the opportunity to describe how this crisis has affected enrolled trainees and the resident's point of view has been highlighted via an anonymous survey.

- Arab Board have not given any specific guidance regarding eligibility requirements or time away from required rotations/the program related to COVID. Their examinations are delayed anyway, so with attention to individual needs, trainees may well be ready when the exams are deliverable

Didactics e.g. educational sessions, rounds, journal clubs, etc.

The Program continues to provide education to trainees, when feasible, utilizing remote conferencing technology, web-based resources, and other innovative tools. Programs document and record the educational activities that they are able to provide during the crisis and easily record the session for trainees who cannot make that time.

Face to face socially distanced sessions (if unavoidable) are carefully conducted in order not to put trainees or faculty at any extra risk.

Recommendations

Safety of residents and staff is a priority.

Continue applying physical distance and IPAK measures. Preparedness and Planning for any upcoming waves.

Increase the Funding on virtual communications like new web cam, lap tops, mics. etc.

Collaboration with educational medical institution and stakeholders for online OSCE Exam preparation.

Continuous comprehensive Training to faculties on the official virtual methods of communication and online training.

Keep an eye on promoting the mental health well-being for all team members and address any concern as early as possible.

Post-crisis reforming and planning.

Analysis of Residents' Pandemic Reflection survey and empower all positive aspects.

Encourage all the scholarly activities for both residents and faculties.

Conclusion

Crisis could be an opportunity for continuous development in the presence of adequate mentoring and leadership. Efficient educational resources, supervision, promoting residents well-being are all requisites of the, accredited ACGME-I, family medicine training program in Qatar. The concept of Flexibility was always sadopted to accommodate residents' training needs.

Conflict of interest
Nothing to be declared

References

1. Espana-Schmidt C, Ong E, Frishman W, Bergasa N, Chaudhari S. Medical Residency Training and Hospital Care During and After a Natural Disaster: Hurricane Sandy and Its Effects. The American Journal of Medicine. 2013;126(11):944-945.
2. Gómez Rosado J, Valdés Hernández J, Oliva Mompeán F. Considerations regarding the residency of General and Digestive Surgery during the health crisis caused by COVID-19. Cirugía Andaluza. 2020;31(2):161-163.
3. Kharbach Y, Khallouk A. Will COVID-19 drive innovation within medical education and residency training? Integrative Journal of Medical Sciences. 2020;7.
4. ACGME International > Accreditation Process > Requirements [Internet]. Acgme-i.org. 2020 [cited 29 July 2020]. Available from: https://www.acgme-i.org/Accreditation-Process/Requirements
5. M. Nasrallah, H. Tawfik and M. Aseel, "Medicine Residency Training Program during COVID-19: Qatari Experience", Pan African Medical Journal, vol. 35, 2020. Available: 10.11604/pamj.supp.2020.35.2.25005 [Accessed 30 August 2020].

Role of Family Doctors and Primary Health Care in COVID-19 Pandemic

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Abstract

The world has currently been plagued by way of the pandemic of COVID-19. It has spread rapidly in a speedy time affecting around 210 countries and causing much death that is increasing daily or by the hour. Thus an efficient health system is needed that acts swiftly to limit it spread and complications. Primary Health Care (PHC) is the first level of contact between the patients and the health system. Its main objectives are; to promote the health of the individuals and the community, to prevent illness of individuals and family members, to provide medical care for common illnesses, acute & chronic illnesses and to manage ongoing psycho-social problems that are either related to the problem or those that have been created by the medical illnesses. Family doctors (FDs) are considered the gatekeepers in the fight against any outbreaks or illnesses. They, by the nature of their work, are very close to the patients and their families. Therefore, they have a greater chance of knowing about their patients' ailments and any new changes in their health conditions. Hence, they could be very helpful in combating any outbreaks and its consequences, in particular Covid-19.

It is well known that to build up a well-developed strong nation, governments must ensure the provision of three main services that must not be endorsed to any third party; health, education, and housing. Because PHC is the care based on disease prevention, early detection, and safeguarding the public, it ought to be the foundation of any health services provided for the nations. The recent crisis has shown how vital PHC & Community Medicine is in being a shield, and protecting the whole community by setting measures for the containment of the diseases. In this review, we will discuss the expected role of the FDs and PHC team in combating disasters or pandemics.

Key words: Covid-19, Corona, Family Doctor, Pandemic, Epidemic, Primary Health Care

Introduction

The world has recently been plagued by the pandemic of COVID-19, which has spread swiftly and in a very short period affecting around 210 countries around the world and causing much death, which has been increasing not only on a daily but even on an hourly basis.

It all took place when pneumonia of unknown cause was detected in Wuhan, China which was first reported to the Chinese WHO Country Office on 31st of December 2019 (1).

On the 9th of January 2020, WHO issued a statement warning of the risk of human-to-human transmission (2). Then the outbreak was declared as a Public Health Emergency of International Concern on 30th of January 2020. While, on March 11th, 2020, the WHO announced COVID-19 a name for the new coronavirus disease and declared pandemicity of the problem affecting many countries around the world, which later lead to more than one-third of the world population being locked down (3).

COVID-19 is from the family of coronaviruses (Coronaviridae). The virus is very small with a diameter of 75 to a hundred and sixty nanometers (just to compare, a human hair is 60000 to one hundred thousand nm). It is a single-strand enveloped RNA virus. The coronavirus name derived from the Latin corona which means crown, as, under electron microscopy, the viral envelope appears crown-like because of small bulbar projections formed through spike (S) peplomers. It is stated that COVID-19 (SARS-CoV-2) is inhibited in bats and likely be transmitted to the human through pangolins (4).

Most people usually get infected with one of these virus families during the stages of their lives that do not cause any major health problems, except for some epidemics which have happened previously such as SARS (severe acute respiratory syndrome) that occurred in 2003, where 8000 people were infected and 800 died., and MERS (that is related to the respiratory syndrome of the Middle East) in 2012, affecting 1329 people and killing 525 (5).

When infected with COVID-19 virus, many people, 81%, do not show any major health problems but have mild to moderate disease and most recover from it without needing hospital treatment. While 14% will get severe illness and 5% become critically ill with breathing difficulties (6). Everybody is prone to catch COVID-19 and become seriously ill however people who are at more risk of COVID-19 and developing serious illness are; elderly, patients with chronic illnesses like DM, and diseases such as heart, liver, renal or respiratory illnesses, patients with low immunity, pregnant women, and people with disabilities (7).

COVID-19 could be very contagious to the extent that even people with very mild symptoms can transmit the virus. Patients can be infectious for as long as the symptoms last and even on clinical recovery. Some people may additionally act as super-spreaders; a study reported that an English citizen after attending a conference in Singapore was able to infect eleven other people while staying in an Alps resort and after returning to the UK (8,9). To highlight its contagiosity it was found that the first 100,000 cases occurred during 66 days, the second 100,000 in 12 days, the third in 3 days, after which the infection was almost at the rate of >50,000 per day. The total number of cases of Covid-19 till the 1st of July 2020 has reached more than 10.5 million cases around the world, (10) while the daily number of cases shows an increasing number without any signs of decline.

The percentage of distribution of cases among countries was reported to be the highest in the USA (>25.8%) then Brazil 13.1% and Russia 6.2%. However, these figures have been changing between countries each day (10). Nevertheless, the good news turned into approximately the recovery rate reaching >50 in some. And as of the 6th of May, the total recovery rate worldwide was around 34% which improved to almost 49% on the seventh of June (10). Despite that, WHO revealed that the mortality rate as of March 3 was 3.4%, (11) which contrasted from country to the next and from one time to another (for example, it reached sometimes to more than 10% in Italy). The number of deaths has been expanding during an extremely shorter timeframe. Statistics have indicated that the first 100,000 deaths came on around the fourteenth of April (105 days since the start of the pandemic), the second 100,000 deaths occurred (1st of May) after fifteen days, the third 100,000 deaths happened (on 15th of May) and the fourth 100,000 deaths took 22 days (6th of June). By the first of July, the USA was on the top list of the ten countries with the highest death rate with a record of >130,000 deaths.

COVID-19 is widespread and has not only impacted the prosperity of individuals but moreover, it has influenced every division of life starting from the economy to the other sectors. Some examples of what it has brought about are the following (12):

- 30 trillion dollars loss in the global economy
- 71 to 100 million people are pushed into extreme poverty (13)
- The sharp drop in oil and gas prices had a negative economic impact on nations
- It is reported that around 1.6 billion children worldwide are absent from school
- The restaurant and cafe sector in the United States has lost $225 billion
- There is a loss of $314 billion in the aviation sector
- The various sports including football and various other championships lost about $600 Billion.
- 75% drop in retail sales
- The share value of the car manufacturing industries has lost 25% of its value
- Loss in Cinema & film production, Cargo, Cruises
- 1 in 3 Americans did not pay their rent last month (as reported by the CNN in April 2020)
- The Arab League estimated that 7 million jobs were lost in the Arab countries (14).

Signs and Symptoms

The most widely recognized manifestations of COVID-19 are fever, dry cough, and tiredness. A few patients may complain of aches and pains, nasal congestion, sore throat or diarrhea, conjunctivitis, headache, loss of taste or smell, skin rash, discoloration of fingers or toes. These symptoms are usually mild and begin gradually. But, some will develop serious conditions and will have difficulty in breathing or shortness of breath, chest pain, and loss of speech or movement. In any case, individuals of any age who experience fever, cough, and difficulty in breathing should seek medical attention.

Family doctors and primary health care

Before we elaborate on what is anticipated from the PHC at some point in the pandemic, we will highlight in brief the concept of PHC and the attributes of FDs making them at the frontline all through any epidemics or disasters.

Notably, PHC is the first level of contact between the patients and the health system with the main objectives; to promote the health of the individuals and the community, to prevent, to provide medical care for common, acute & chronic illnesses and to manage ongoing psycho-social problems that are either related to the problem or those that have created the medical illnesses. The main principle of PHC service that makes it superior to other disciplines is: the provision of personal care to individuals, taking into consideration the family and population health and the concept of offering continuity of care. Moreover, the given care is efficient, appropriate, sustainable, affordable, and cost-effective. Most importantly, the care is accessible to everybody, and across all the disciplines making it inter-sectoral and interdisciplinary. In supporting the importance of PHC, the American Academy of Family Physicians stated in a document entitled “Delivering on the promise of primary care” that “PHC should be predominant because it provides better healthcare as people with access to PHC can live longer and healthier. It provides better care and studies have shown that with more PHC in any country, the infant mortality rate is reduced with “more equitable distribution of health to the population”. Also, PHC costs lower than other health care services by 33% because of less hospitalization and less duplication of services (15). It is reported that the health of the nation is better in areas with more primary care physicians and people receiving care from the primary care physicians are healthier. What’s more, for every one extra FD per 10,000 people is found to be associated with a 5.3% decrease in mortality (16). Reports from the USA during the 1990s showed that those U.S. states with higher proportions of primary care physicians to population had better health outcomes, including lower rates of all causes of mortality (17).

Role of FDs and PHC in COVID-19:
With this background of information, the expected role of PHC in COVID-19 could be summarized in the following:

- Detection of cases
- Helping to manage mild cases in the home
- Tracing contacts
- Psychological support of the family members
- Mass health education and raising public awareness during and post the pandemic
- Risk management and protection of the health care workers
- Role in returning to normality
- Role in research
- Role in E-medicine and medical digitalization

FDs role in detecting of cases
The EMR region of the World Health Organization issued a document expressing the importance of PHC stating that “health systems oriented to primary health care can react persistently to the new challenges in all countries, whether developing or developed, rich or poor, and in conflict or peace” (18). A Canadian report considered PHC as the initial point of contact for most Canadians attending the health care system, and FDs have the first opportunity to identify and diagnose communicable diseases of concern for public health. Moreover, FDs can empower an ideal public health response for any acute reportable illnesses such as viral illnesses (19). For that, FDs are considered the gatekeepers in the fight against any outbreaks (20).

During epidemics, there will be perpetually a requirement for a responsive and capacious primary health care system. Because, the very survival of any hospital would rely upon pre-hospital screening and pre-hospital and post-hospital care that are provided by the PHC. It is a fact that neither hospital emergency rooms nor the hospitals beds can admit and care for all the sick. Therefore there should be an alternative facility that is able to reduce the burden on hospitals. It is the PHC that is closer to the patients’ homes and that conveys efficient care by a trusted and familiar family doctor (21). For that, FDs have a greater chance to know about their patients’ ailments and any changes in their health conditions and are acquainted with the vulnerable groups within those families. Therefore, with such privileges, they would be in a more superior position than other health care workers to early detect or suspect cases of COVID-19.

FDs’ abilities to help in managing mild cases of Covid-19 at home
Since family medicine is a community-based discipline, the patient-doctor relationship is fundamental to all that it does. With FDs having the opportunity to know more about their patients’ present and past medical history, they will be as well more aware of their psychosocial status. In the present time, there are numerous factors playing a role in making home care a necessity and not a luxury, such as aging population, change in family structure from extended to nuclear, change in the disease pattern (more of NCD), increased focus on person-centered care and

need to have efficient and continuous care that extends beyond the facility. In highlighting the importance of home care, Dr. Ian R. McWhinney stated "We define family medicine in terms of relationships, and continuity of the patient-doctor relationship is one of our core values. How can we justify breaking our long-term relationships with patients whenever, in sickness or old age, they become housebound" (22).

During the COVID-19 epidemic, the advantages of the provision of home care are many, and include; avoiding the stress of being isolated in the hospital which may lead to decreased immunity making the patient more susceptible to complications. Additionally, it could avoid the stigma of being a COVID-19 case especially in the culture prevailing in our part of the world. Nevertheless, the corona patients will have a feeling of security by being surrounded by their family members. Appropriate home care could help in reducing or preventing the dissemination of the illness.
COVID-19 patients who are discharged from hospital need regular follow up and continuity of care. Such could be offered by the FD through an efficient home care system. The home environment will be ideal to increase the health awareness of the family and the close contacts about COVID-19. Rawaf et al, in supporting home care stated that "Primary care should be structured to deliver more effective services to suspected cases and contacts, as well as continue to provide the vital health care services as the first point of contact within the health system while maintaining a high level of continuity of care. Patients discharged from intensive care require follow-up and primary care should be well-positioned to do so" (23).

FDs have the skills in tracing contacts

Contact tracing is more or less similar to detective work, and to perform that job properly there should be a good doctor/patient relationship and effective patients confidence. The contact tracers who are supposed to interview people with contagious disease (positive COVID-19 test) ought to be well prepared to figure out who they may have lately been in contact with and at what point and time they were mixing with those individuals. They should also have the skills of convincing the suspected to isolate themselves, avoiding the spread of the disease any further. Experience from global countries such as South Korea and New Zealand have proved to be successful due to the forceful utilization of contact tracing in an attempt to control the outbreak (24).

Patrick Howell stated that for efficient contact tracing in the PHC there is a requirement for four main fundamental elements. The first is; recruiting numerous manual tracers; then protection of people's privacy against any abuse in the utilization of information; ensuring that contact tracing should cover as many people as possible, and finally, it has to be known that technology alone cannot help in contact tracing and cannot replace manual tracers as not everybody possesses smartphones (25).

FDs' role in psychological support of the patients and their family members

The fourth very important role of FDs during the COVID-19 pandemic is to provide psychological support to the patient's family members. With some 2.6 billion individuals around the globe in some sort of lockdown condition, it is without a doubt that such a factor is considered a high risk for psychological problems. Moreover, it is well known that having a suspected or confirmed case of COVID-19 in the home or just being isolated in addition to the created social stigma could all form a very stressful situation to the individuals and their family members that may lead to; fear, worry, and stress among the concerned but more in certain groups, such as old people, people with underlying certain health conditions (like NCDs or heart problems) and the care providers. The induced anxiety no doubt has a psychopathological impact on the person and their relatives that may induce depression which in turn could precipitate self-harm or suicidal attempts. Even though the reported important psychological impact to date is elevated rates of stress or anxiety, as new measures and impacts are introduced – especially quarantine and its effects on many people's routine activities– the levels of loneliness, depression, drug use, and self-harm or suicidal behaviour are also expected to rise (26).

FDs are known to be the most appropriate health care provider to offer support and palliative care to the families during any stressful situation because of their broad knowledge and the long-standing relationship with patients and their families making them aware of the personal attributes of each patient. They are also more familiar with the family members' interactions during an illness and how that affects the patient's health. Such provided palliative care depends very much on the medical treatment, the physical, psychological, social and the spiritual care provided (27, 28).

Provision of mass health education and raising public awareness

The FDs and the PHC team are in a better position to provide mass health education to the public to increase their awareness during and post the pandemic since the advice-giving method is part of their role and their professional competencies (29). Subsequently, it is expected from them to do the same during any epidemic or pandemic. It is most important that health care professionals working in PHC institutions acquire the knowledge, experience, and skills to promote health and educate and counsel the families and public, about healthy lifestyle behaviours (30). In this line, many studies have found that there is a strong relationship between health promotion counselling done by the FDs and the indicators of quality of life as reported by AlSayah et al (31).

Risk management and protection of the health care workers

One of the important FD tasks during epidemics is assessing and managing the risk induced by the disease to the health care workers and the community. FDs have the skills, knowledge, and abilities to perform that task.

During COVID-19 many PHC centres in different parts of the world led by FDs made changes in their services and their places of work to respond to this task.

Role in managing aftermath and returning to normality

FDs are the ones expected to manage the aftermath of contingencies (20). They, along with the PHC team could play a critical role in easing the burden of global lockdown adoption. Due to their attributes and their close contacts with the community they have major responsibilities in leading the public to go back to normal life, while adhering to the precautionary measures against the spread or the contraction of the disease. Also, they could stipulate the appropriate measures against the occurrence of the second wave of Covid-19 epidemics. They will as well keep a vigilant eye on the people under their care to continue educating and protecting them against COVID-19 and secure them from getting psycho-emotional problems due to long home confinement.

FDs as a researcher

To know more about Covid-19, FDs and Public health doctors are expected more than other health disciplines to respond to many unknown questions about the coronavirus. They would be at the front line of performing research to overcome any problems that are related to the pandemic and or to protect against the second wave of the Covid-19 epidemic.

Their role in E-medicine and medical digitalization

The health delivery system after COVID-19 will be different from before the pandemic. It is expected that there will be rapid adoption of the digitalization of medicine with fewer patients' physical consultation and less visits to the primary health care centres, in contrast to more over-the-phone or video consultations, more home visits and more e-health or e-medicine. The COVID-19 pandemic, as stipulated by the NHS, UK , has speeded up the timeline long-term plan that was promised to every patient for the right to digital primary care services by the year 2024 (32).

WHO defines e-Health as "the cost-effective and secure use of Information and communications technologies in support of health and health-related fields, including healthcare services, health surveillance, health literature, and health education, knowledge and research" (31). Clinical applications of e-Health include Electronic Health Records, TeleConsultations, Clinical Decision Making Support Systems, Vital Signs Monitoring Services, TeleHomeCare, Ambulatory e-Health—smart clothing, e-Wear, e-Clothing, e-Prescribing, e-Nursing, e-dissemination of personalized healthcare and professional Continuing Education using e-Learning tools (32).

Since, PHC is the care that is based on disease prevention, early detection and safeguarding the public, the health system should be restructured in a way that a healthy nation is ensured. However and unfortunately, many countries before the COVID-19 Pandemic have been considering seriously the concept of privatization of health services which could have had a disastrous impact during this crisis if it was implemented.

Finally, PHC in addition to community medicine, which aims at studying the nature of the illness and the characteristics of its causative agent, are both vital for the protection of the health of the whole nation. The recent crisis has indicated how significant both are in being a safeguard for the entire community against the devastating effect of Covid-19. That was reflected by the swift execution of measures for the containment of the disease. Therefore, they both ought to be the foundation of any health system offered to the public. The late Barbara Starfield stated "Family Medicine should always shape the health services reform and Not Vice Versa. And Family physicians have to be at the forefront of any health care reform". Due to that, it is recommended that Fifty percent of any physicians' workforce in any country should be constituted of Family Doctors (35). Policy makers have to be convinced that any long term investment in PHC will pay off as there are many successful stories in this line, such as in Sri Lanka which built its health system on a strong base of PHC that has led to a rise in life expectancy and reduction in mother, infant, and child mortality rates (36).

Conclusion

FDs and PHC teams have an extraordinary role in any health disaster including the COVID-19 Pandemic. Because of their close relationships with family members, they are expected to be safe-guards helping the community and taking measures to decrease the spread of infection and its unfavourable consequences. It is notable that to develop a solid well-developed nation, governments must ensure the provision of three fundamental services that must not be endorsed to any third party; health, education, and housing. Since a healthy population is the aim of any governmental services, such service should take the priority and be built on a strong foundation of primary health care services.

References

1. World Health Organization. Pneumonia of unknown cause - China. Geneva: World Health Organization; 5 January 2020 (https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/, accessed 27 April 2020).
2. World Health Organization. WHO statement regarding cluster of pneumonia cases in Wuhan, China. Geneva: World Health Organization; 9 January 2020 Available at https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-of-pneumonia-cases-in-wuhan-china, accessed 19 April 2020).
3. Buchholz K. What share of the world population is already on COVID-19 Lockdown? Statista (https://www.statista.com/chart/21240/enforced-covid-19-lockdowns-by-people-affected-per-country/, accessed 23 April 2020).

4. Muhammad Adnan Shereen, Suliman Khan, Abeer Kazmi, Nadia Bashir. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research Volume 24, July 2020, Pages 91-98
5. COVID-19, MERS & SARS, National Institute of Allergy and Infectious Diseases https://www.niaid.nih.gov/diseases-conditions/covid-19, April 6, 2020
6. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020.
7. People Who Are at Higher Risk for Severe Illness. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases (CDC). https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html. 14 May 2020.
8. Tanu Singhal, A Review of Coronavirus Disease-2019 (COVID-19) Indian J Pediatr. 2020; 87(4): 281–286. doi: 10.1007/s12098-020-03263-6
9. World Health Organization. Situation reports. Available at:https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/. Accessed 22 Feb 2020.
10. https://www.worldometers.info/coronavirus/
11. Lipsitch M. Seasonality of SARS-CoV-2: Will COVID-19 go away on its own in warmer weather? Center for Communicable Disease Dynamics, Harvard University (https://ccdd.hsph.harvard.edu/will-covid-19-go-away-on-its-own-in-warmer-weather/, accessed 19 April 2020).
12. Socio-economic impact of COVID-19. UNDP. https://www.undp.org/content/undp/en/home/coronavirus/socio-economic-impact-of-covid-19.html
13. Updated estimates of the impact of COVID-19 on global poverty https://blogs.worldbank.org/opendata/updated-estimates-impact-covid-19-global-poverty
14. http://uac-org.org/en/News/details/2566/7- Union of Arab Chambers Commerce Industry Agriculture. 1st June 2020.
15. Delivering on the promise of primary care. AAFP. https://www.aafp.org/dam/AAFP/documents/about_us/initiatives/infographics/promise.pdf
16. AAFP, Overview of Preventive Health. Preventive Health. https://www.aafp.org/advocacy/informed/pubhealth/prevstrategy.html.
17. Starfield Barbara, Shi Leiyu, Macinko James. Contribution of Primary Care to Health Systems and Health. Milbank Q. 2005 Sep; 83(3): 457–502. doi: 10.1111/j.1468-0009.2005.00409.x
18. Regional Committee for the EM/RC55/INF. DOC.6(a). Eastern Mediterranean September 2008. https://applications.emro.who.int/docs/EM_RC55_inf_doc_6a_en.pdf
19. Alexander Summers. Important role of family physicians in reporting communicable diseases Outbreak of hepatitis A in a kindergarten class. Can Fam Physician. 2018 Oct; 64(10): 742–743
20. Donald Kwok Tung Li. Challenges and responsibilities of family doctors in the new global coronavirus outbreak. BMJ Journal. Volume 8, Issue 1, 2020. https://fmch.bmj.com/content/8/1/e000333
21. Mazowita G. Role for primary care in epidemic surge capacity. Can Fam Physician. 2006 Aug 10; 52(8): 951.
22. McWhinney IR. Fourth annual Nicholas J. Piscano Lecture. The doctor, the patient, and the home: returning to our roots. J Am Board Fam Pract. 1997;10(6):430–5.
23. Rawaf S, Harumi Quezada Yamamoto HQ, Rawaf D. Unlocking towns and cities: COVID-19 exit strategy. East Mediterranean Health J. 2020;xx(x):xxx–xxx. https://doi.org/10.26719/emhj.20.028 in-press
24. Alejandro De La Garza. What Is Contact Tracing? Here's How It Could Be Used to Help Fight Coronavirus. Times APRIL 22, 2020. https://time.com/5825140/what-is-contact-tracing-coronavirus/
25. Patrick Howell. Five things we need to do to make contact tracing really work. Tech policy/Tech and health. April 28, 2020
26. Mental health and COVID-19. http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/novel-coronavirus-2019-ncov-technical-guidance/coronavirus-disease-covid-19-outbreak-technical-guidance-europe/mental-health-and-covid-19
27. De Silva N. Lecture Notes in Family Medicine. Colombo: Vishwa Lekha; 2006.
28. Ramanayake R.P.J.C., Dilanka G.V.A., Premasiri L.W.S.S. Palliative care; role of family physicians. J Family Med Prim Care. 2016 Apr-Jun; 5(2): 234–237
29. Roger Ladouceur. Family physicians and health promotion. Can Fam Physician. 2014 Feb; 60(2): 106
30. Kabasakal Esma, Kublay Gülümser. Health Education and Health Promotion Skills of Health Care Professionals Working in Family Health Centres. International Journal of Medical Research & Health Sciences, 2017, 6(3): 22-28
31. Al Sayah F, Agborsangaya C, Lahtinen M, Cooke T, Johnson JA. Mental health and the relationship between health promotion counseling and health outcomes in chronic conditions. Cross-sectional population-based study. Can Fam Physician. 2014;60:e113–20.
32. A Baird Beccy. How has general practice responded to the Covid-19 (coronavirus) outbreak? The Kings Fund. https://www.kingsfund.org.uk/blog/2020/04/covid-19-general-practice
33. Resolution 58/28 of the World Health Assembly, Geneva, 2005. https://apps.who.int/iris/bitstream/handle/10665/20398/A58_2005_REC1-en.pdf
34. Ganapathy K, E-Medicine: transforming healthcare with information and communication technology, Med J Armed Forces India. 2011 Apr; 67(2): 106–107. doi: 10.1016/S0377-1237(11)60003-8
35. Starfield Barbara. Family Medicine Should Shape Reform, Not Vice Versa. Fam Pract Manag. Jul-Aug 2009;16(4):6-7
36. Ratnasingam Gobith. Long Term Investment in Primary Health Care Pays Off in Sri Lanka. Phcpi. June 19, 2020. https://improvingphc.org/blog/2020/06/19/long-term-investment-primary-health-care-pays-sri-lanka

Perceptions of millennials of twenty first century regarding position of women in Pakistani society

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Abstract

Introduction: Millennials is a term referring to the people born between 1981–2000. Members of this demographic cohort are known as millennials because they were born around the turn of the third millennium A.D. This generation is generally associated with heightened technical knowledge and most of their active hours are spent on social media. It is a generation which claims to break all stereotypes engrained into our minds by society in the name of "culture".

Seeing that the reason for women being discriminated within households revolves around the closed, backward concepts of dowry and patriarchy, we targeted an audience of extremely privileged, well educated, socially and culturally aware university students to determine their view point on the issue at hand.

Objective : To determine the perceptions of millennials of twenty first century regarding position of women in Pakistani society in Karachi.

Material and method: A Cross-sectional study was conducted on a sample of 330 participants from various universities of Karachi. The study was conducted for a period of ten months from February 2019 To November 2019 .The Data was collected from Aligarh Institute of Technology, Bahria University, DHA Suffa University and Institute of Business Administration Karachi. The sample was taken through Non-Probability Purposive Sampling. A Pilot study was conducted to assess the authenticity of the questionnaire. Data collected was entered and analyzed using SPSS version 20, with 95% confidence interval. All ethical considerations were observed.

Results: Regarding faculties of the participants, 48.2% were from Engineering, 17.6% from Commerce, 3.3% from Arts and 30% from other fields. 100% of them were single. 65.5% of our participants thought women in Pakistan are treated differently than men of the same society. 89.1% thought mothers of sons get more respect in family matters and decision making than mothers of daughters while 10.9% thought they didn't. 85.2% of the participants believe women in Pakistan get treated differently if they become pregnant with daughters as compared to sons. When asked to specify what they meant by being treated differently, 16.97% said that society makes daughter bearing women feel bad, 34.85% thought society made them feel like they are bringing a burden into this world, 22.42% felt that the same level of health care wasn't provided to such women whereas 25.76% felt that women carrying daughters were treated better than those carrying sons. Only 3.6% of participants said that they would have a softer spot for a woman if she were having a boy, 7.6% said they would have a softer spot if she were having a girl, 24.8% said it wouldn't matter,

61.5% would care for any expecting woman while 2.4% would not care for any. When asked which parent can naturally decide the gender of a child 58% had misconceptions. 83.33% said men should not remarry a second or third time if they were having only daughters from their first marriage, 4.24% said men should be allowed to do so without prejudice and 12.42% refrained from sharing their point of view. When asked about their ideal family, 5.5% said only 1 child (daughter), 2.1% said only 1 child (son), 87% said both sons and daughters, 2.1% said only sons and 3.3% said they would ideally want only daughters.

Conclusion: The youth of Pakistan are well aware of the social stigmas around them. Even our targeted audience that comprised people living in urban areas have grown up seeing women mistreated for bearing daughters, but our study shows that this generation has realized the fault of their ancestors and there is hope that these young adults would bring a positive change in the future.

Key words: Perceptions, millennial, women status, Pakistani society

Introduction

The Urban Dictionary defines “Mum” as, “The woman who loves you unconditionally from birth, the one who puts her kids before herself and the one who you can always count on above everyone else.”

But unfortunately according to a study conducted by Sunita Puri in The U.S (who studied immigrant Indians) in 2011, “40% of the women interviewed had terminated prior pregnancies with female fetuses and that 89% of women carrying female fetuses in their current pregnancy pursued an abortion” (1) .

Seeing this drastic difference between what the place of a mother is in a child’s life and what are the common practices against female fetuses, one is intrigued to look further into the matter.

The main question arises; why would a person, who is biologically programmed to love the child growing inside them, suddenly decide to take its life away, just because that child is another female like herself?

Or maybe that’s what scares her the most, bringing another life into this world that would be doomed to the same gender discrimination that she faced her entire life. According to a study published in 2016, “The immense value placed on male children around the world, especially among patriarchal cultures in developing countries like Nigeria, has resulted in unfavorable disposition towards the continuous birth and welfare of females” (2).

According to a study conducted by Farah Qadir et al in Pakistan in 2011, “In Pakistan, preference for boys over girls is deeply culturally embedded. From birth, many women experience gendered disadvantages; less access to scarce resources, poorer health care, higher child mortality, limited education, less employment outside of the home and circumscribed autonomy.” The same study further stated that “Boys carry the family name, can continue the family trade, and are expected to provide for their parents in old age. Married women typically live with their in-laws, and are expected to provide care and support to their husband’s parents in their old age. Married sons are therefore a virtual necessity in countries with no state pension or welfare support for frail older persons” (3) .

According to a study by Nithin Kumar et al published in 2014 in India. “Various factors that can be attributed to the decline in sex-ratio include increased sex selective female abortions, and female feticide.” The study also states that, “The main reason for female feticide is based on a common perception that the female child is an economic burden on the family due to dowry problems and vulnerability of them for sexual harassment, whereas males carry out family business and support parents at a later age” (4).

According to a study by R. Kansal et al in India in 2010, the birth of female child is perceived as a curse with economic and social liability. The proliferation and abuse of advanced technologies coupled with social factors such as dowry, concerns with family name and looking up to the son as a breadwinner (5).

According to a Study conducted by Srivastav Shalini et al in India in 2011, “desire for male child manifests so blatantly that parents have no qualms about repeated, closely spaced pregnancies, premature deaths and even terminating a child before it is born” (6). According to a study conducted in Pakistan in 2015 psychological antenatal depression was very common in that country because of the constant ongoing stress faced by women (7). According to another study in Pakistan the findings showed that gender discrimination was not uniform in intensity and nature across the educated Pakistani society and there was neither any evidence of socio economic status nor of religiosity of men who were discriminating against women (8). According to another study there was a marked difference in educating children on the basis of gender. It was observed that due to the higher cost of private schooling and less availability of government schools within the community, parents are more reluctant to enroll their daughters in private schools because parents were somewhat less willing to invest in girls’ schooling compared to boys due to cultural constraints (9).

According to a study in India the level of education of parents did make a difference in nutritional status of girls (10).

Considering how concepts like dowry and daughters being given off forever to her husband's family seem illiterate and old fashioned, it was important to find out how the educated people of Pakistan today perceive the status of women around them today. This study aims to provide an insight into the thoughts of Millennials regarding core issues like patriarchy and the status of women in Pakistani society.

Objective

To determine attitudes and practices of millennials of the twenty first century regarding position of women in Pakistani society in Karachi.

Material and method

A Cross-sectional study was conducted on a sample of 330 participants from various universities of Karachi. The study was conducted for a period of ten months from February 2019 To November 2019 .The data was collected from Aligarh Institute of Technology, Bahria University, DHA Suffa University and Institute of Business Administration Karachi. The sample was taken through non-probability purposive sampling. A Pilot study was conducted to assess the authenticity of the questionnaire. Data collected was entered and analyzed using SPSS version 20, with 95% confidence interval. All ethical considerations were observed.

Results

Regarding faculties of the participants, 48.2% were from Engineering, 17.6% from Commerce, 3.3% from Arts and 30% from other fields. 100% of them were single. 65.5% of our participants thought women in Pakistan are treated differently than men of the same society. 89.1% thought mothers of sons get more respect in family matters and decision making than mothers of daughters while 10.9% thought they didn't. 85.2% of the participants believe women in Pakistan get treated differently if they become pregnant with daughters as compared to sons. When asked to specify what they meant by being treated differently, 16.97% said that society makes daughter bearing women feel bad, 34.85% thought society made them feel like they are bringing a burden into this world, 22.42% felt that the same level of health care wasn't provided to such women whereas 25.76% felt that women carrying daughters were treated better than those carrying sons. Only 3.6% of participants said that they would have a softer spot for a woman if she were having a boy, 7.6% said they would have a softer spot if she were having a girl, 24.8% said it wouldn't matter, 61.5% would care for any expecting woman while 2.4% would not care for any. When asked which parent can naturally decide the gender of a child 58% had misconceptions. 83.33% said men should not remarry a second or third time if they were having only daughters from their first marriage, 4.24% said men should be allowed to do so without prejudice and 12.42% refrained from sharing their point of view. When asked about their ideal family, 5.5% said only 1 child (daughter), 2.1% said only 1 child (son), 87% said both sons and daughters, 2.1% said only sons and 3.3% said they would ideally want only daughters.

Figure 1 shows faculties of the participants as; 48.2% from Engineering, 17.6% from Commerce, 3.3% from Arts and 30% from other fields.

Figure 1

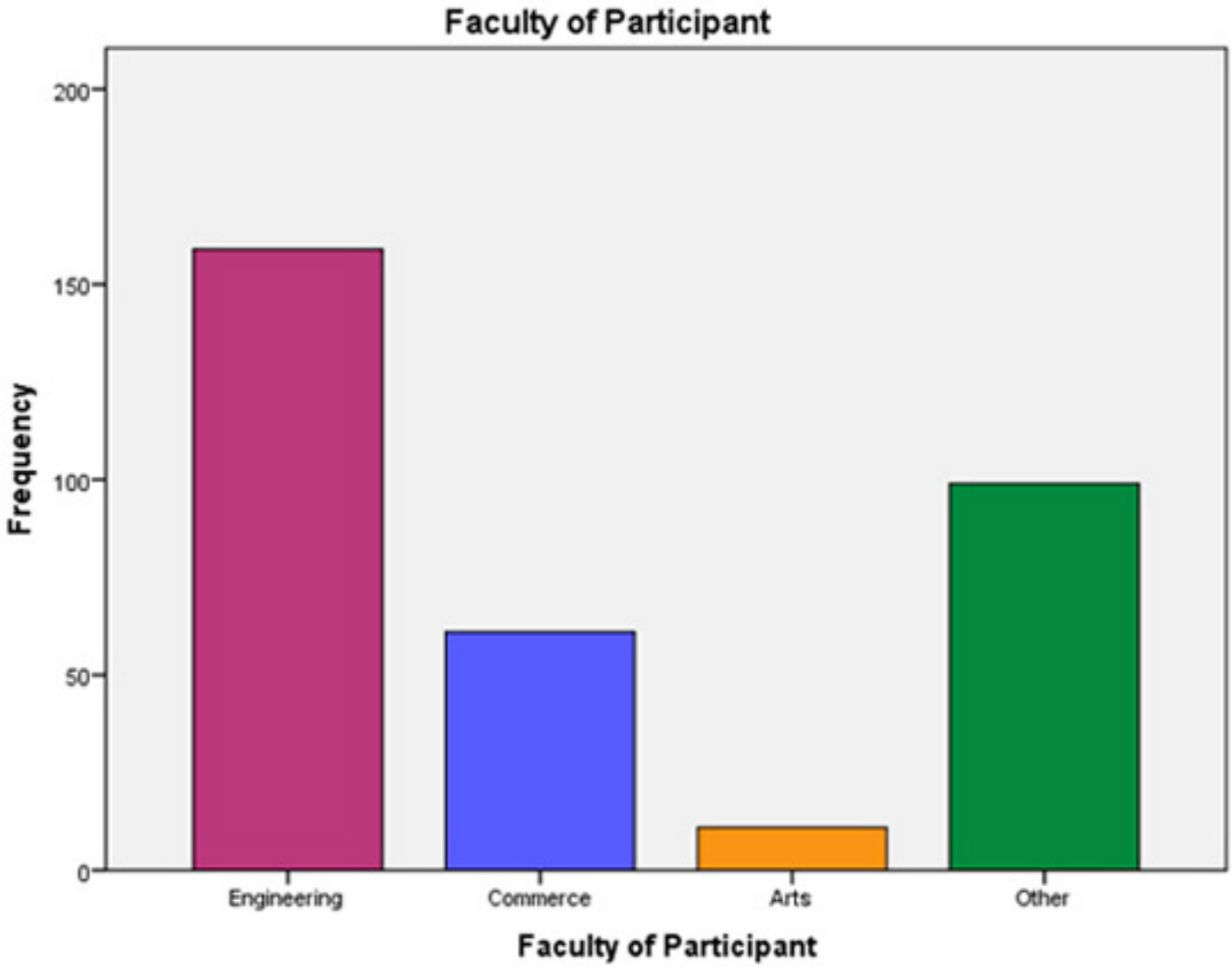


Figure 2 shows 65.5% of our participants think women in Pakistan are treated differently than men of the same society.

Figure 2

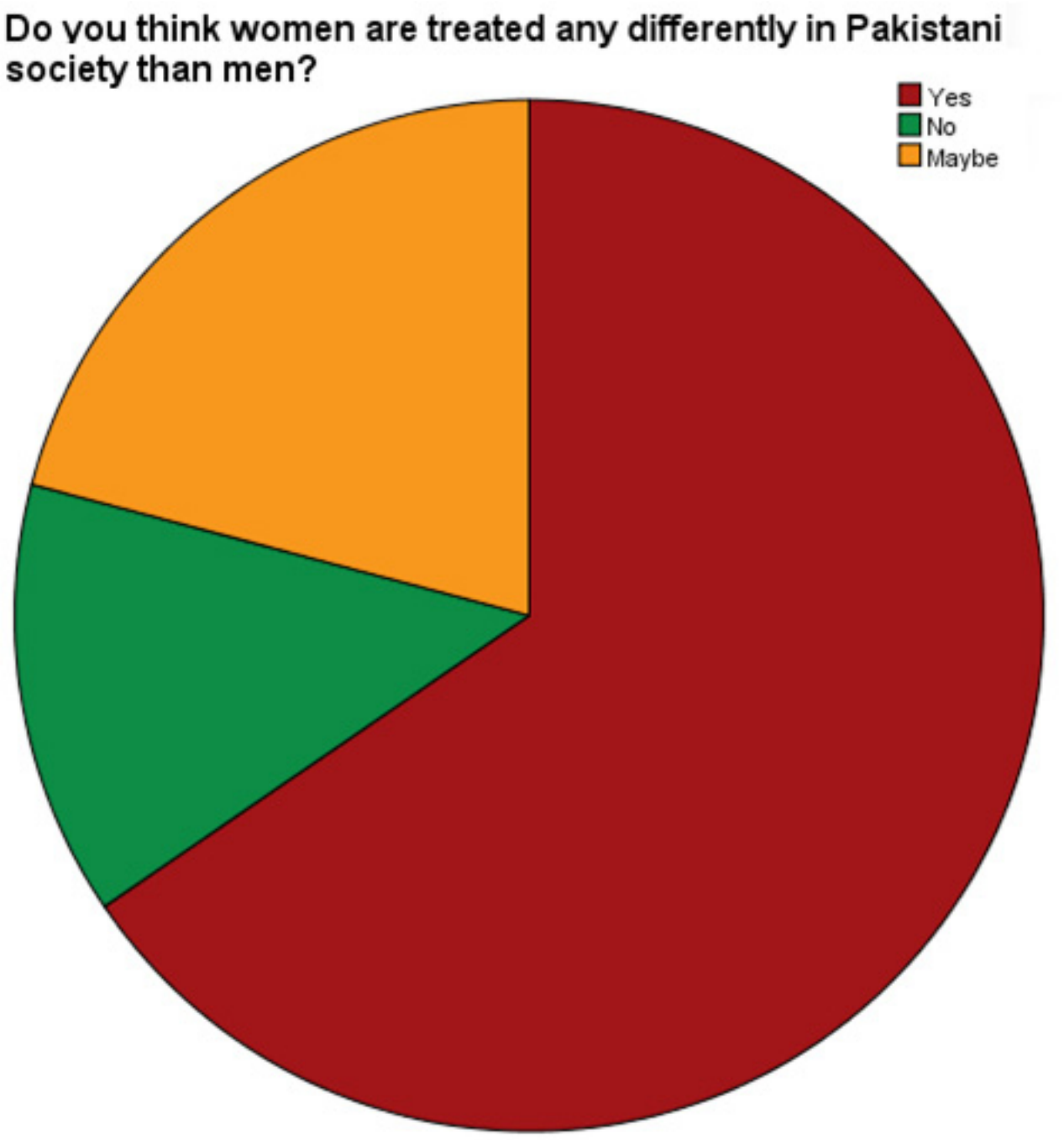


Figure 3 shows that 89.1% of our audience believes that mostly in Pakistani society today, mothers of sons get more respect in family matters and decision making than mothers of daughters.

Figure 3

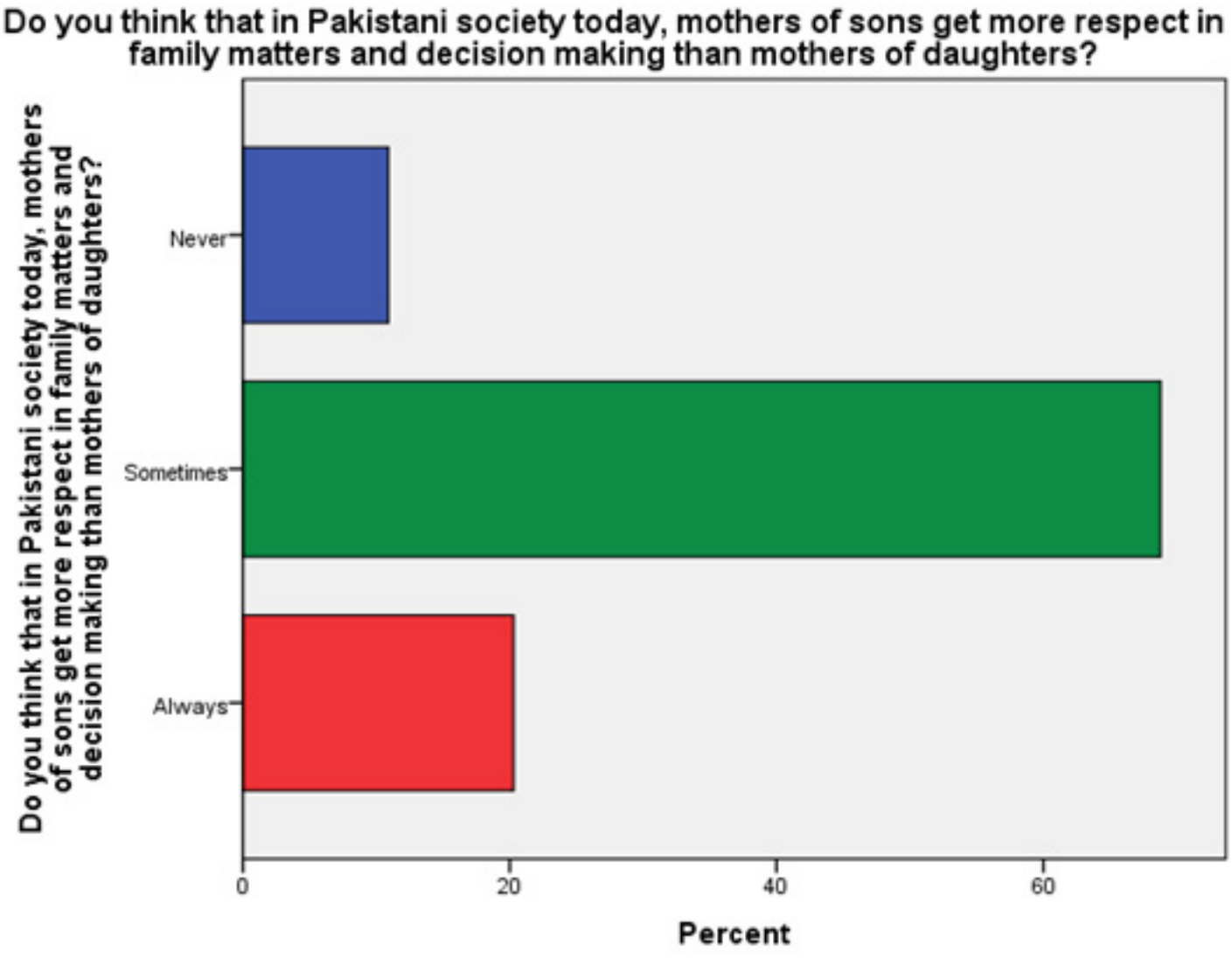


Figure 4 shows that 85.2% of the participants believe women in Pakistan get treated differently if they become pregnant with daughters as compared to sons.

Figure 4

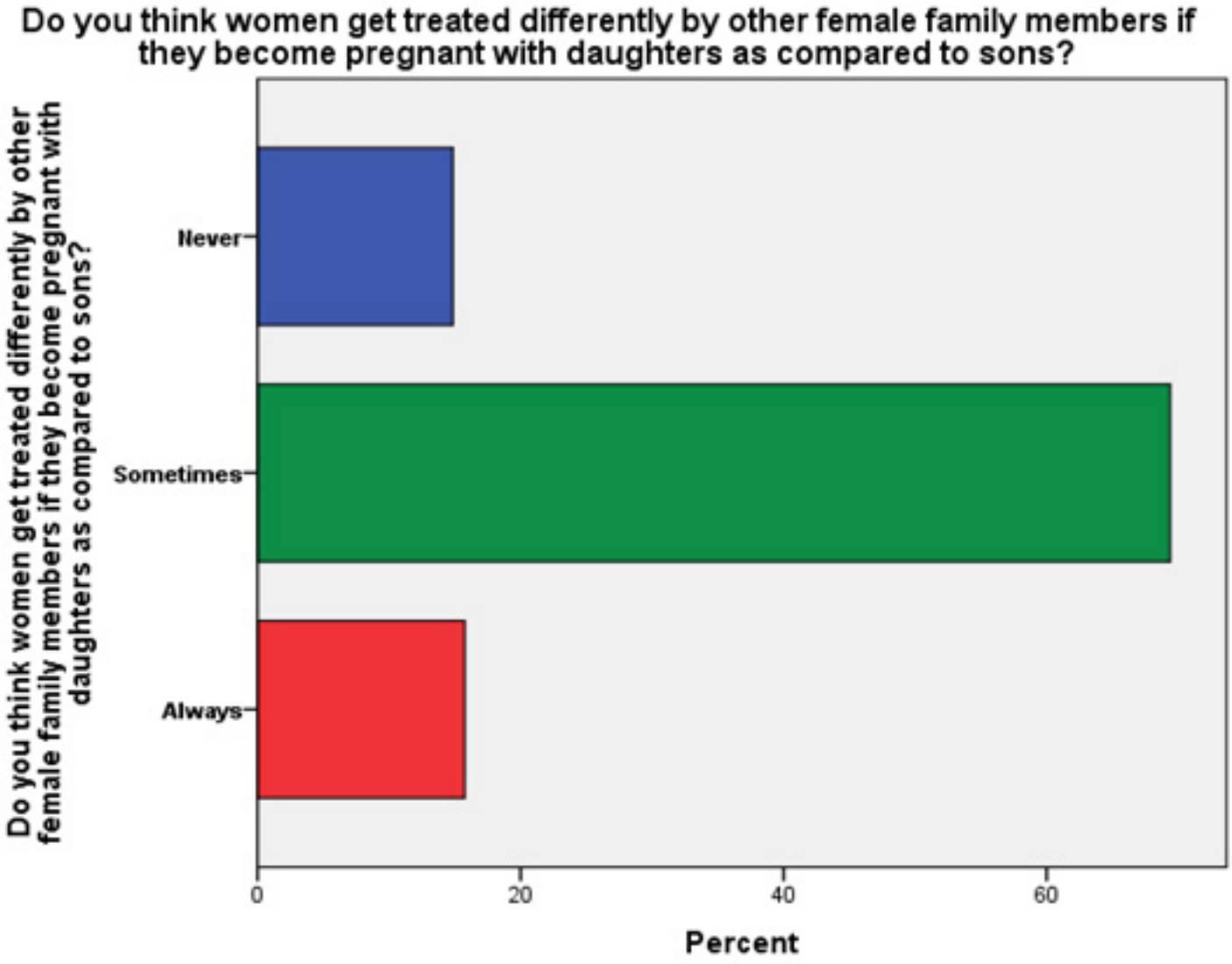


Figure 5 shows that 74.2% of the participants believe that women get treated badly if they become pregnant with daughters.

Figure 5

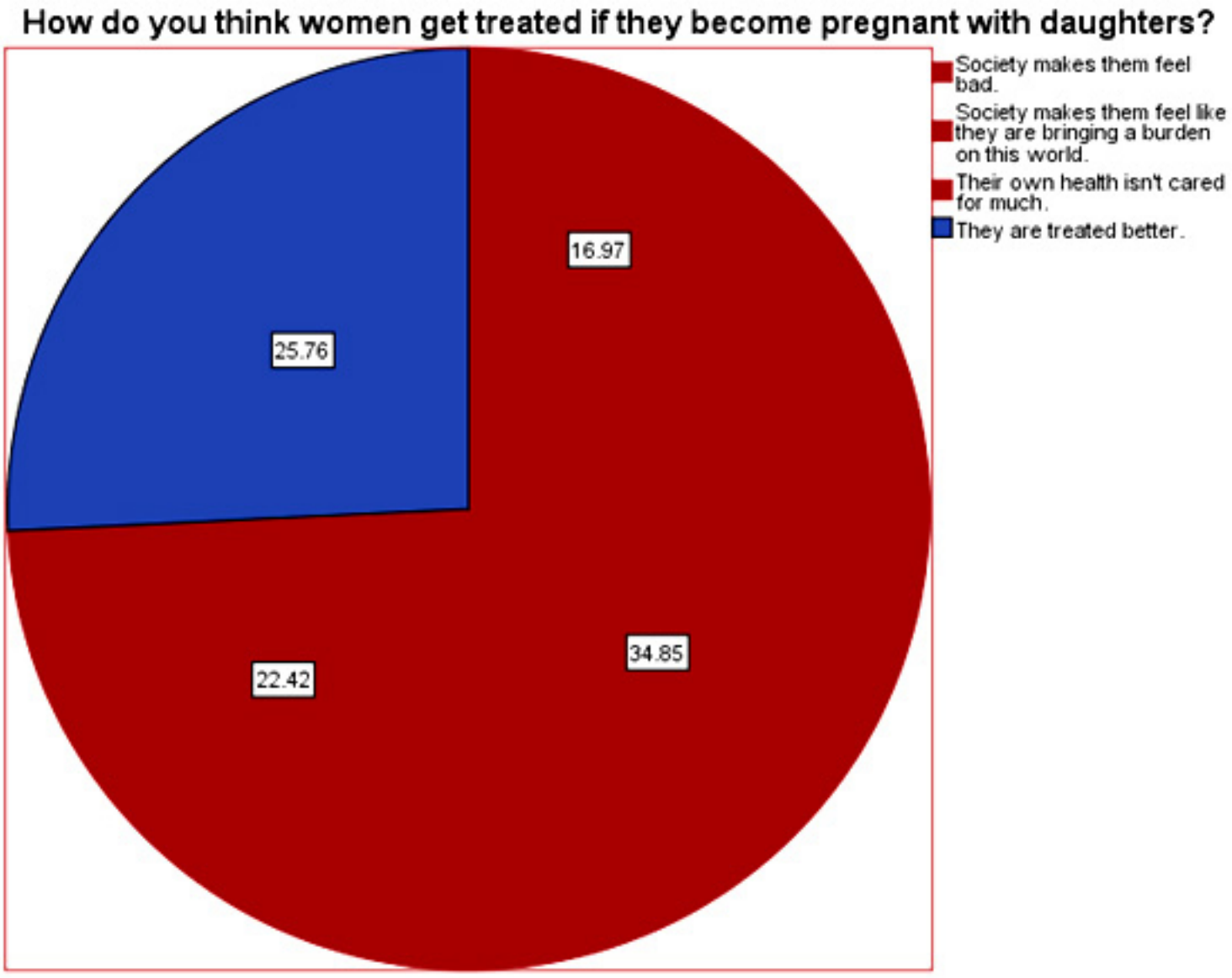


Figure 6 shows that 3.6% of participants said that they would have a softer spot for a woman if she were having a boy.

Figure 6

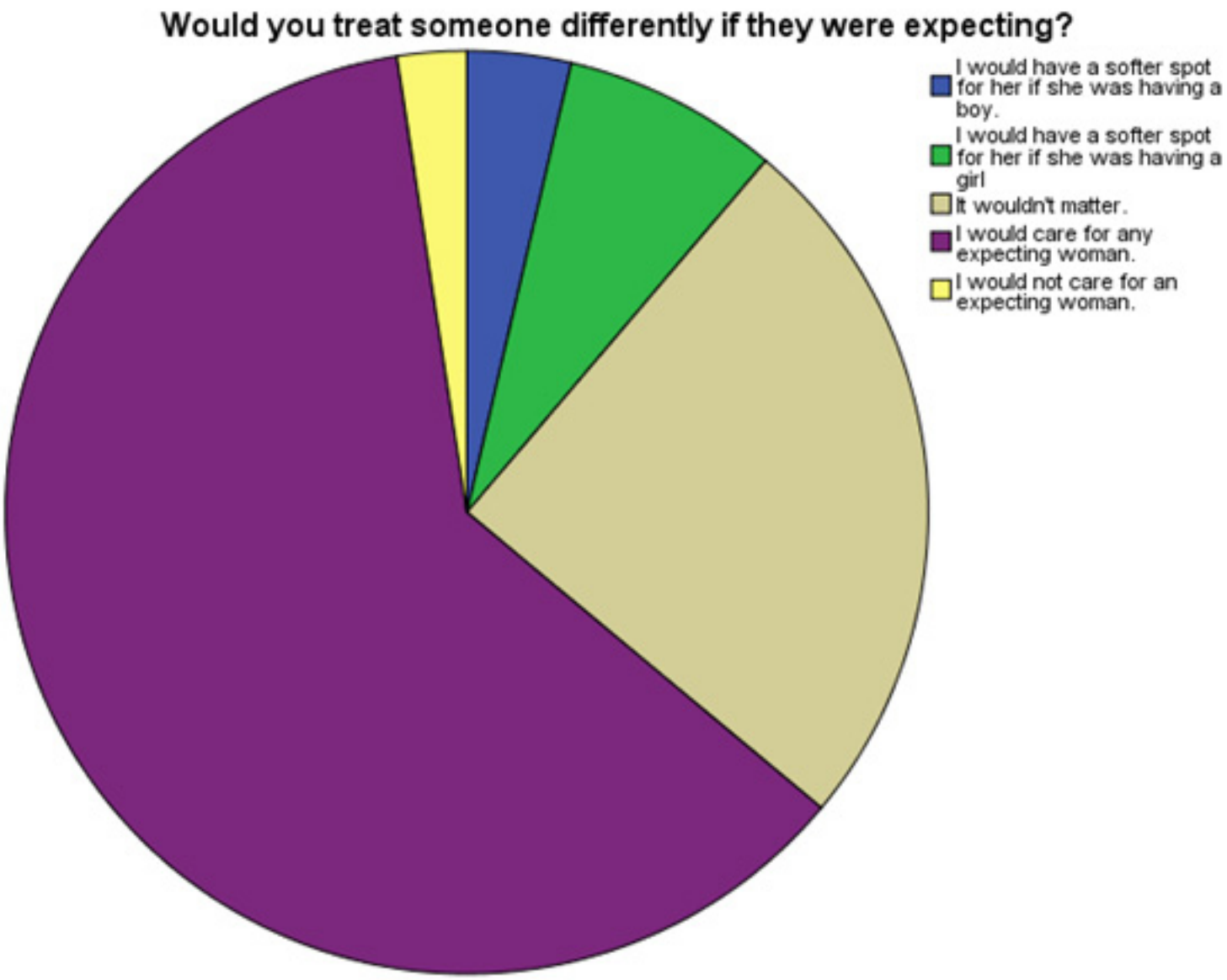


Figure 7 shows that 58% of our targeted audience has misconceptions about basic human genetics.

Figure 7

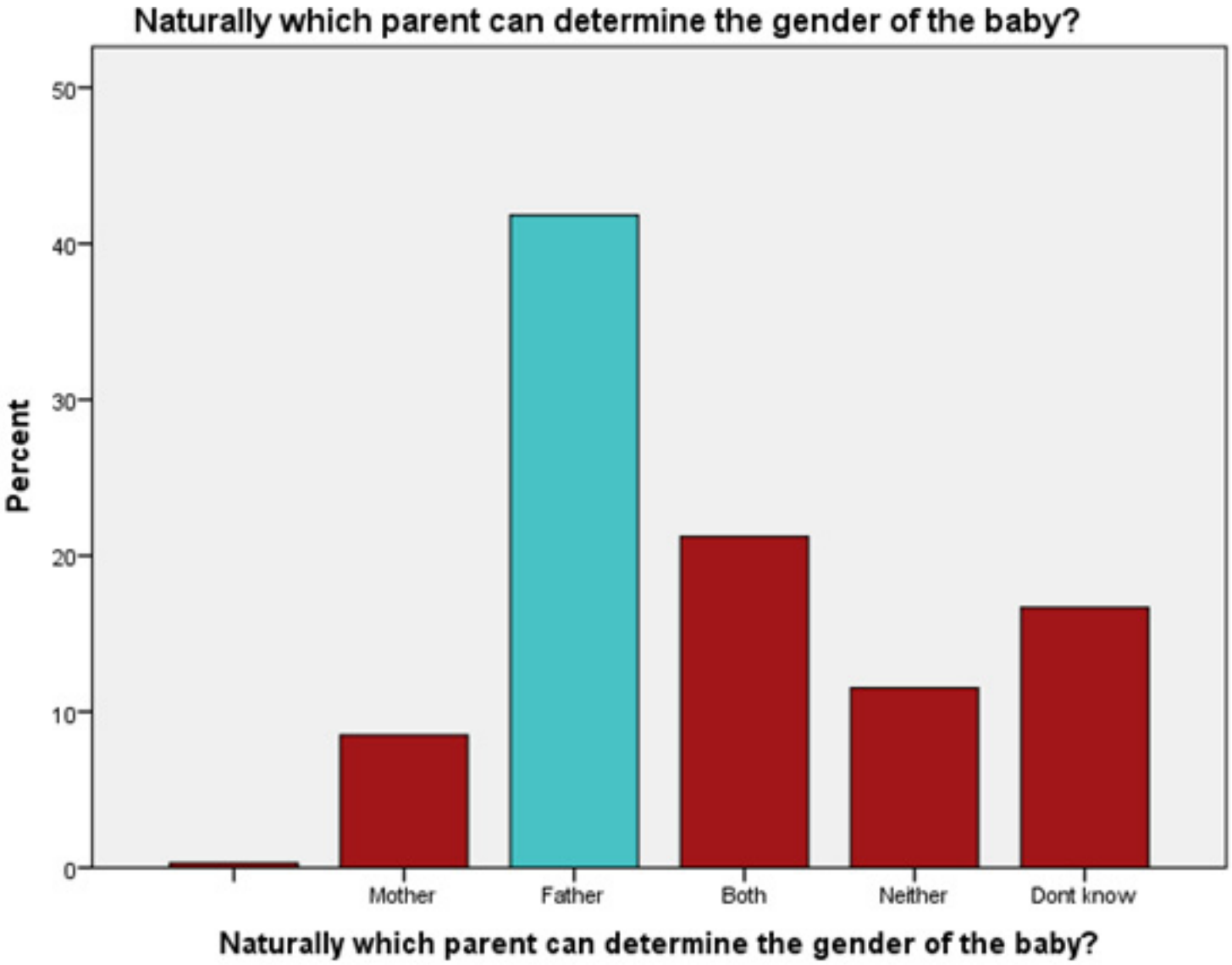


Figure 8 shows more than 4% of our participants still think a man should re-marry in hopes of having a son, if he is only having daughters from his first wife.

Figure 8

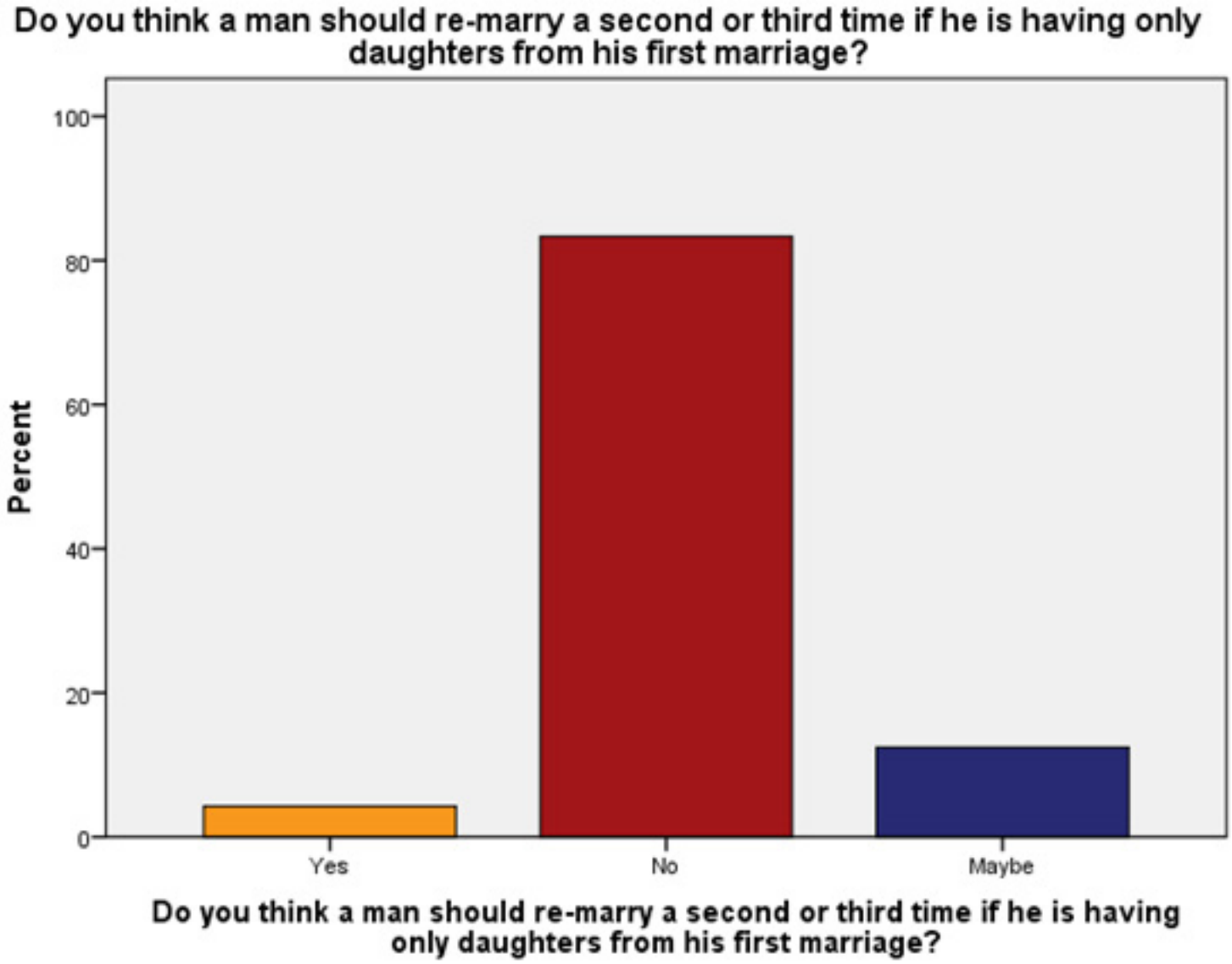
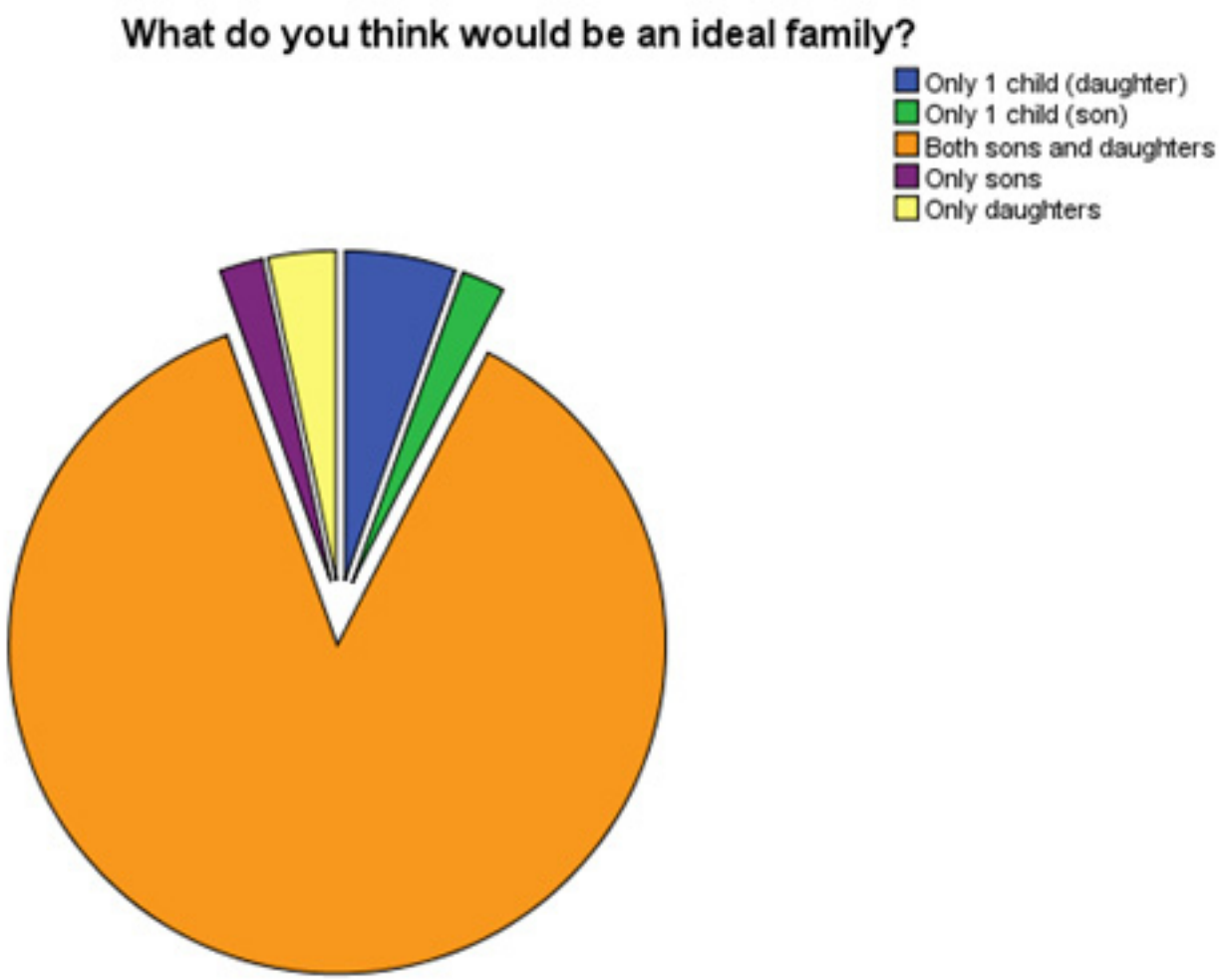


Figure 9 shows that when asked about their ideal family, 5.5% said only 1 child (daughter), 2.1% said only 1 child (son), 87% said both sons and daughters, 2.1% said only sons and 3.3% said they would ideally want only daughters.

Figure 9



Discussion

According to our study, more than 4% of our participants still think a man should re-marry in hopes of having a son, if he is only having daughters from his first wife.
Similar results were found in 2004, when an article published in The National Bureau of Economic Research stated that, " We document that parents with girls are significantly more likely to be divorced, that divorced fathers are more likely to have custody of their sons," [11] Another study conducted in Punjab, Pakistan in 2013 also shows disheartening results where a couple is simply stated infertile if they fail to bare sons, and the idea of men remarrying in hopes of children is deeply embedded in the Indo-Pak culture. The study states, "Infertility, which is perceived as no children, or not having the right number and type of children (sons), therefore weakens the woman's marital ties with her husband. The consequences of the weakening of the marital bonds can be catastrophic for women. This includes emotional and physical abuse, threat of remarriage," [12].

According to our study, 61.5% of the candidates said they would care for any expecting woman, 3.6% said they would have a softer spot for her if she were having a boy while 7.6% said they would care more for her if she was expecting a girl whereas for 24.8% the gender of the foetus did not matter.

These results contradicted greatly those of a study conducted in 2011 in Jordan which states"The prevalence of violence (of any type) during pregnancy was 40.9%. Physical violence was the highest (34.7 %), followed by psychological violence (28.1%) and sexual violence (15.5%). Women who had four or more female children (OR 4.03, 95% CI 1.3- 11.9) and were under pressure to have a male child (OR 1.82, 95% CI 1.07- 3.08) were more likely to be exposed to violence during pregnancy" [13].

According to our study, only 3.3% of our candidates consider an ideal family consisting of just daughters, and only 5.5% were content with just 1 child and that too being a daughter whereas 87% considered an ideal family to consist of both sons and daughters, regardless of the number of children. These results coincided with the results of a few more articles published worldwide. An article published in 2004 in The National Bureau of Economic Research stated that, "families with at least two children, the probability of having another child is higher

for all-girl families than all-boy families. This preference for sons seems to be largely driven by fathers, with men reporting they would rather have a boy by more than a two to one margin" [11] .

It is sad that the same results were found in an empirical study in Korea in 1983 where "The observed frequency of all-girl families is especially small in comparison with the expected value" [14] which just goes to show that in the past three and a half decades, while on one hand the world has developed in every field, our mentalities have stayed perfectly preserved.

Another study conducted in 1990 in Pakistan found results very similar to the ones we found in our study in 2019 which state that, "all workers with an ideal of 1 child wanted a son. 90% of those wanting an ideal of 2 children desired 1 son and 1 daughter 95% with an ideal of 3 children wanted 2 sons and 1 daughter" [15] .

Conclusion

This study concludes that even in today's time and age, university students from reputable Institutes of Pakistan feel that married women of our society are only respected if they have sons. 70-80% of our audience felt that women bearing just daughters are not respected in their homes. They face prejudice since pregnancy which continues till later in life where they are not taken into consideration during decision making as opposed to other women from the same household that are bearing sons; a critical argument, in a society where the joint family system prevails and nuclear families are looked down upon.

References

1) Puri P, Adams V, Ivey S and Nachtigall RD. There is such a thing as too many daughters, but not too many sons": A qualitative study of son preference and fetal sex selection among Indian immigrants in the United States: Social Sci & Med , 2011 April: 72(7):1169-1176
2) Hesketh T. Selecting sex: The effect of preferring sons: 2011 November: 87(11):759-761
3) Qadir F, Khan MM, Medhin G and Prince M. Male gender preference, female gender disadvantage as risk factors for psychological morbidity in Pakistani women of childbearing age - a life course perspective" : BMC Public Health , 2011 September : 11(745):
4) Kumar N., Darshan BB., et al. Awareness and Attitudes Regarding Prenatal Sex Determination, Pre-Conception and Pre-Natal Diagnostic Techniques Act (PCPNDTA) among Pregnant Women in Southern India: J Clin Diagn Res. 2014 Oct: 8(10):09–11
5) R Kansal, Khan AM, Bansal R, Parashar P. A hospital-based study on knowledge, attitude and practice of pregnant women on gender preference, prenatal sex determination and female feticide. Indian Journal Of Public Health. 2010 ; 54 (4) : 209-212
6) Srivastav S, Kariwal P, Kapilashrami MC. A community based study on Awareness And Perception on Gender Discrimination and Sex preference in rural areas of district Bareilly. Natl J Community Med . 2011;(2):273-276.
7) Waqas A., Raza N., Lodhi H.W., Muhammad Z., Jamal M., and Rehman A. Psychosocial Factors of Antenatal Anxiety and Depression in Pakistan: Is Social Support a Mediator? PLOS One .2015 January; 10(1) https://doi.org/10.1371/journal.pone.0116510
8) Delavande A, Zafar B,.Gender Discrimination and Social Identity: Experimental Evidence from Urban Pakistan. FRB of New York Staff Report. 2013 Jan;593 ; 1-37
Available at SSRN: https://ssrn.com/abstract=2198386 or http://dx.doi.org/10.2139/ssrn.21983866)
9) Sathar ZA, Wazir A, Sadiq M. Struggling against the Odds of Poverty, Access, and Gender: Secondary Schooling for Girls in Pakistan. The Lahore Journal of Economics. 2013 Sep;18 : 67–927)
10) Biswas S, Bose K,. Sex differences in the effect of birth order and parents' educational status on stunting: A study on Bengalee preschool children from eastern India. HOMO. 2010 Aug; 61(4):271-2768)
11) Shipp T.D., Sheahan R. et al. What Factors Are Associated with Parents' Desire To Know the Sex of Their Unborn Child? Birth Issues in Prenatal care. 2004 December: 31(4): 272-279
12) Mumtaz Z, et al. Understanding the impact of gendered roles on the experiences of infertility amongst men and women in Punjab. Reproductive Health. January 2013; 10: https://link.springer.com/article/10.1186/1742-4755-10-3
13) Okour AM, Badarneh R. Spousal Violence Against Pregnant Women from a Bedouin Community in Jordan; J of Women's Health. December 2011; 20 (12) 1853-1859.
14) Park CB. Preference for Sons, Family Size, and Sex Ratio: An Empirical Study in Korea; Demography. August 1983; 20:333–352
15) Farooqui MN. Son preference, fertility desire and contraceptive use in two largest cities of Pakistan; Pak Popul Rev. Autumn 1990; 1(1):54-64.

What a high prevalence of rheumatic heart disease in sickle cell patients

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Abstract

Background: We tried to understand whether or not there is a higher prevalence of rheumatic heart disease (RHD) in the sickle cell diseases (SCDs).
Methods: All patients with the SCDs and controls were studied.

Results: The study included 428 patients with the SCDs (208 females) and 2,855 controls (1,620 females). Mean ages of the SCDs patients were similar in males and females (30.6 versus 30.1 years, respectively, p>0.05). Mean ages of the controls were 40.8 versus 41.8 years, respectively (p<0.001 for both). Although the higher mean ages and female predominance (56.7% versus 48.5%, p<0.001) of the control cases, RHD was detected just in 0.3% of them (eight females and one male). Whereas this ratio was 6.5% (13 females and 15 males) in the SCDs (p<0.001). The mean ages of RHD were 48.2 and 32.2 years in the control and SCDs groups, respectively (p=0.012). The female ratios of RHD were 88.8% and 46.4% in the control and SCDs groups, respectively. Mitral valve was involved in 58.8%, aortic valve was involved in 32.3%, and tricuspid valve was involved in 8.8% of cases with the SCDs. Interestingly, the tricuspid valve was never involved alone instead together with mitral valve in all of the cases.

Conclusion: SCDs induce severe and chronic inflammatory processes on vascular endothelium all over the body, and terminate with end-organ insufficiencies in early years of life. Beside that SCDs cause a moderate to severe immunosuppression by several mechanisms that may be the cause of higher prevalence of RHD in them.

Key words: Rheumatic heart disease,
sickle cell diseases, chronic endothelial damage,
immunosuppression

Introduction

Chronic endothelial damage may be the major cause of aging by inducing disseminated tissue hypoxia all over the body. Much higher blood pressure (BP) of the afferent vasculature may be the major underlying cause, and probably whole afferent vasculature including capillaries are mainly involved in the process. Some of the well-known accelerators of the inflammatory process are physical inactivity, excess weight, smoking, and alcohol for the development of irreversible consequences including obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary heart disease (CHD), mesenteric ischemia, osteoporosis, and stroke. They were researched under the title of metabolic syndrome in the literature, extensively (1, 2). Similarly, sickle cell diseases (SCDs) are severe and chronic inflammatory processes on vascular endothelium, terminating with end-organ insufficiencies in early years of life. Hemoglobin S (HbS) causes loss of elasticity and biconcave disc shaped structures of red blood cells (RBCs). Probably loss of elasticity instead of shape is the main problem since sickling is rare in peripheric blood samples of the SCDs with associated thalassemia minors, and human survival is not so affected in hereditary spherocytosis or elliptocytosis. Loss of elasticity is present during whole lifespan, but exaggerated with various stresses of the body. The hard RBCs induced severe and chronic vascular endothelial damage, inflammation, edema, and fibrosis terminate with tissue hypoxia all over the body (3, 4). Capillary systems may mainly be involved in the process due to their distribution function for the hard bodies. In another definition, metabolic syndrome is an accelerated atherosclerotic process, and SCDs are an accelerated metabolic syndrome. We tried to understand whether or not there is a higher prevalence of rheumatic heart disease (RHD) in the SCDs.

Material and Methods

The study was performed in Internal Medicine Units of the Dumlupinar and Mustafa Kemal Universities between August 2005 and April 2016. All patients with the SCDs and cases who had applied for the check up procedure were included. The SCDs were diagnosed with hemoglobin electrophoresis performed via high performance liquid chromatography (HPLC). Medical histories of SCDs patients including smoking habit, regular alcohol consumption, painful crises per year, transfused units of RBCs in their lives, surgical operations, leg ulcers, and stroke were learnt. Due to their cumulative atherosclerotic effects together with the SCDs, patients with a history of one pack-year were accepted as smokers, and one drink-year were accepted as drinkers. A complete physical examination of all study cases was performed by the Same Internist. Cases with acute painful crisis or another inflammatory event were treated at first, and the laboratory tests and clinical measurements were performed on the silent phase. A check up procedure including fasting plasma glucose, creatinine, hepatic function tests, markers of hepatitis viruses A, B, C and human immunodeficiency virus, a posterior-anterior chest x-ray film, an electrocardiogram, and a Doppler echocardiogram both to evaluate cardiac walls and valves and to measure systolic BP of pulmonary artery was performed for all cases. An additional abdominal ultrasonography, a venous Doppler ultrasonography of the lower limbs, a computed tomography of brain, and a magnetic resonance imaging (MRI) of hips was performed just for the SCDs cases. Other bones were scanned for avascular necrosis according to complaints of the SCDs patients. Associated thalassemia minors were detected with serum iron, iron binding capacity, ferritin, and hemoglobin electrophoresis performed via HPLC. The criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in one second/forced vital capacity of less than 70% (5). An x-ray film of abdomen in upright position was taken just in patients with abdominal distention or discomfort, vomiting, obstipation, or lack of bowel movement, and ileus was diagnosed with gaseous distention of isolated segments of bowel, vomiting, obstipation, cramps, and with the absence of peristaltic activity on the abdomen. Systolic BP of the pulmonary artery of 40 mmHg or higher is accepted as pulmonary hypertension (6). CRD is diagnosed with a persistent serum creatinine level of 1.3 mg/dL in males and 1.2 mg/dL in females. Cirrhosis is diagnosed with physical examination, liver function tests, ultrasonographic evaluation, and tissue samples in case of indication. Digital clubbing is diagnosed with the ratio of distal phalangeal diameter to interphalangeal diameter which is greater than 1.0, and with the presence of Schamroth's sign (7, 8). An exercise electrocardiogram is performed just in cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is taken just for the exercise electrocardiogram positive cases. So CHD was diagnosed either angiographically or with the Doppler echocardiographic findings as the movement disorders in the cardiac walls. RHD is diagnosed with the echocardiographic findings, too. Avascular necrosis of bone is diagnosed by means of MRI (9). Stroke is diagnosed by the computed tomography of brain. Sickle cell retinopathy is diagnosed with ophthalmologic examination in patients with visual complaints. Eventually, prevalence of RHD was detected both in the SCDs and control groups, and compared in between. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 428 patients with the SCDs (208 females) and 2,855 control cases (1,620 females), totally. Mean ages of the SCDs patients were similar in males and females (30.6 versus 30.1 years, respectively, $p>0.05$). Mean ages of the control cases were 40.8 versus 41.8 years, respectively ($p<0.001$ for both) (Table 1). Although the significantly higher mean ages and female predominance (56.7% versus 48.5%, $p<0.001$) of the control cases, RHD was detected just in 0.3% of them (eight females and one male). Whereas this ratio was 6.5%

(13 females and 15 males) in the SCDs group (p<0.001) (Table 2). The mean ages of RHD cases were 48.2 ± 16.6 (22-69) and 32.2 ± 8.4 (20-49) years in the control and SCDs groups, respectively (p=0.012). The female ratios of RHD were 88.8% and 46.4% in the control and SCDs groups, respectively. Mitral valve was involved in 58.8%, aortic valve was involved in 32.3%, and tricuspid valve was involved in 8.8% of cases with the SCDs. Interestingly, tricuspid valve was never involved alone instead together with mitral valve in all of the cases. On the other hand, smoking (24.0% versus 6.2%, p<0.001), alcohol (5.0% versus 0.4%, p<0.001), transfused RBCs in their lives (47.6 versus 28.4 units, p=0.000), COPD (25.4% versus 7.2%, p<0.001), ileus (7.2% versus 1.4%, p<0.001), cirrhosis (7.2% versus 1.9%, p<0.001), leg ulcers (20.0% versus 7.2%, p<0.001), digital clubbing (14.0% versus 6.2%, p<0.001), CHD (18.1% versus 12.9%, p<0.05), CRD (10.4% versus 6.2%, p<0.05), and stroke (12.2% versus 7.6%, p<0.05) were all higher in males with the SCDs, significantly. There were 30 mortality cases (16 males) during the ten-year follow-up period (Table 3). The mean ages of mortality were 30.8 ± 8.3 years (range 19-50) in males and 33.3 ± 9.2 years (range 19-47) in females (p>0.05). Beside that there were four patients with HBsAg positivity (0.9%) but HBV DNA was positive in none of them by polymerase chain reaction (PCR). Although antiHCV was positive in 5.8% (25 cases), HCV RNA was positive just in three cases (0.7%) by PCR.

Discussion

Chronic endothelial damage may be the leading cause of aging in human beings. It may be the most common type of vasculitis all over the world at the moment. Whole afferent vasculature including capillaries may chiefly be involved in the process. Much higher BP of the afferent vasculature may be the major underlying cause by inducing recurrent injuries on endothelium. Therefore the term of venosclerosis is not as famous as atherosclerosis in the medical literature. Physical inactivity, excess weight, smoking, alcohol, chronic inflammations, prolonged infections, and cancers probably accelerate the process. Secondary to the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls become thickened, their lumens are narrowed, and they lose their elastic nature which reduces blood flow and increases systolic BP further. Although early withdrawal of underlying factors may delay terminal consequences, after development of cirrhosis, COPD, CRD, CHD, PAD, or stroke, endothelial changes cannot be reversed completely due to their fibrotic nature (10).

SCDs are life-threatening hereditary disorders affecting around 100.000 individuals in the United States (11). As a difference from other causes of chronic endothelial damage, the SCDs may keep vascular endothelium particularly at the capillary level (12), because the capillary system is the main distributor of the hard RBCs into the tissues. The hard cells induced severe and chronic endothelial damage, inflammation, edema, and fibrosis terminate with end-organ insufficiencies in early years of life. As a result, mean lifespans of the patients were 48 years in females and 42 years in males in the literature (13), whereas they were 33.3 and 30.8 years, respectively in the present study. Unfortunately, the great differences may be secondary to delayed diagnosis, delayed initiation of hydroxyurea therapy, and inadequate RBCs supports during medical and surgical emergencies in Turkey. Actually, RBCs supports must be given in all medical and surgical emergencies in which there is evidence of clinical deterioration in the SCDs (14, 15). RBCs supports decrease sickle cell concentration in the circulation, and suppress bone marrow for the production of abnormal RBCs. So it decreases sickling induced endothelial damage all over the body. According to our 20-year experiences, simple RBCs transfusions are superior to the exchange. First of all, preparation of one or two units of RBCs suspensions at each time rather than preparation of six units or more provides time for clinicians to prepare more units by preventing sudden death of such patients. Secondly, transfusion of one or two units of RBCs suspensions at each time decreases the severity of pain, and relaxes anxiety of the patients and surroundings in a short period of time. Thirdly, transfusions of lesser units of RBCs suspensions at each time decreases transfusion-related complications in the future. Fourthly, transfusions of RBCs suspensions in the secondary health centers prevent some deaths developed during transport to the tertiary centers for the exchange. Fifthly, transfusions of RBCs suspensions in the secondary health centers prevent some extra costs on the health system developed during the exchange in the tertiary centers. On the other hand, longer survival of females in the SCDs (13) and longer overall survival of females in the world (16) cannot be explained by the atherosclerotic effects of smoking and alcohol alone; instead it may be explained by stronger physical efforts of male sex in life that may terminate with an exaggerated sickling and an exaggerated chronic endothelial damage in their bodies (17).

RHD is caused by an autoimmune reaction against Group A β-hemolytic streptococci. The majority of morbidity and mortality associated with rheumatic fever is caused by its destructive effects on cardiac valves. It is characterized by repeated inflammation with fibrinous repair. Fibrosis and scarring of valve leaflets, commissures, and cusps leads to abnormalities that can result in valvular stenosis or regurgitation. The valvular endothelium is a prominent site of lymphocyte-induced damage. Normally, T cell activation is triggered by presentation of the bacterial antigens. In RHD, molecular mimicry results in incorrect T cell activation, and these T lymphocytes can go on to activate B cells, which will start to produce self-antigen-specific antibodies. This leads to an immune response attack mounted against tissues in the heart that are misidentified as pathogens. RHD usually occurs after repeated attacks. Rheumatic fever primarily affects children between the ages of 5 and 17 years. In one third of cases, the underlying Streptococcal infection develops without any symptom. On the other hand, some patients develop significant carditis that manifests as congestive heart failure. Unlike typical heart failure, rheumatic heart

Table 1: Characteristics of the sickle cell patients

Variables	Males with SCDs*	*p*-value	Females with SCDs
Prevalence	51.4% (220)	Ns†	48.5% (208)
Mean age (year)	30.6 ± 10.1 (5-58)	Ns	30.1 ± 9.9 (8-59)
Thalassemia minors	72.2% (159)	Ns	67.7% (141)
Smoking	***24.0% (53)***	***<0.001***	***6.2% (13)***
Alcohol	***5.0% (11)***	***<0.001***	***0.4% (1)***

*Sickle cell diseases †Nonsignificant (p>0.05)

Table 2: Comparison of the sickle cell patients and control cases

Variables	Patients with SCDs*	*p*-value	Control cases
Number	428		2855
Female ratio	48.5% (208)	***<0.001***	56.7% (1620)
Mean age of males	30.6 ± 10.1 (5-58)	***<0.001***	40.8 ± 16.5 (9-85)
Mean age of females	30.1 ± 9.9 (8-59)	***<0.001***	41.8 ± 16.3 (11-88)
Prevalence of RHD†	***6.5% (28)***	***<0.001***	***0.3% (9)***

*Sickle cell diseases †Rheumatic heart disease

Table 3: Frequent pathologies of the sickle cell patients

Variables	Males with SCDs*	*p*-value	Females with SCDs
Painful crises per year	5.0 ± 7.1 (0-36)	Ns†	4.9 ± 8.6 (0-52)
Transfused units of RBCs‡	***47.6 ± 61.6 (0-434)***	***0.000***	***28.4 ± 35.8 (0-206)***
COPD§	***25.4% (56)***	***<0.001***	***7.2% (15)***
Ileus	***7.2% (16)***	***<0.001***	***1.4% (3)***
Cirrhosis	***7.2% (16)***	***<0.001***	***1.9% (4)***
Leg ulcers	***20.0% (44)***	***<0.001***	***7.2% (15)***
Digital clubbing	***14.0% (31)***	***<0.001***	***6.2% (13)***
CHD¶	***18.1% (40)***	***<0.05***	***12.9% (27)***
CRD*	***10.4% (23)***	***<0.05***	***6.2% (13)***
Stroke	***12.2% (27)***	***<0.05***	***7.6% (16)***
Pulmonary hypertension	12.7% (28)	Ns	12.5% (26)
Varices	8.6% (19)	Ns	5.7% (12)
RHD***	6.8% (15)	Ns	6.2% (13)
Avascular necrosis of bone	25.0% (55)	Ns	25.0% (52)
Sickle cell retinopathy	0.9% (2)	Ns	0.4% (1)
Mortality	7.2% (16)	Ns	6.7% (14)

*Sickle cell diseases †Nonsignificant (p>0.05) ‡Red blood cells §Chronic obstructive pulmonary diseases ¶Coronary heart disease **Chronic renal disease ***Rheumatic heart disease

rheumatic heart failure responds well to corticosteroids, probably due to its autoimmune nature. In Western countries, rheumatic fever has become fairly rare, probably due to the widespread use of antibiotics. Although RHD disproportionately affects women of reproductive age (18), it was detected with a female ratio of 46.4% in the SCDs in the present study. Rheumatic tricuspid valve dysfunction is the rarest of all valvular diseases, and is often associated with left-sided valvular diseases (19). The prevalence of rheumatic tricuspid dysfunction was 8.4% in a previous study (19). In another study, rheumatic tricuspid valve disease was detected with a ratio of 7.7%, and associated mitral valve disease was present in 99.3% of them (20). Similarly, tricuspid valve was involved in 8.8% of cases with the SCDs, and it was never involved alone, instead together with mitral valve in all of the cases in the present study. Mitral valve is involved in 97% of cases with the RHD (21), and mitral stenosis is classically caused by it (22). Whereas mitral and aortic valves were involved in 58.8% and 32.3% of cases, respectively in the present study.

SCDs are severe inflammatory processes terminating with end-organ insufficiencies in early years of life (23). First of all, the SCDs are chronic hemolytic anemias in which the normal lifespan of RBCs decreased from the normal 120 to 15-25 days. Secondly, the severe and chronic endothelial inflammation all over the body causes an overlapping chronic disease anemia in them. Thirdly, the chronic hemolytic process may even cause folate and vitamin B12 deficiencies. Furthermore, end-organ insufficiencies can suppress the immune system of the patients. Frequent acute sinusitis, tonsillitis, and urinary tract infections are the common causes of painful crises and hospitalizations, and they can rapidly progress into the severe and life-threatening infections including pneumonia, meningitis, and sepsis due to the moderate to severe immunosuppression in such patients (24). For example, tonsillary hypertrophy is a common physical examination finding that may be the result of a prolonged infectious process due to the moderate to severe immunosuppression in them (25). Severe and prolonged endothelial inflammation induced prominent weight loss and cachexia are also frequent findings in the SCDs (4). As a result, menarche is retarded in females with the SCDs (26). Moderate to severe anemias, autosplenectomy, frequent painful crises, hospitalizations, invasive procedures, RBC supports, medications, prevented normal daily activities, and a suppressed mood of the body may just be some of the possible reasons of immunosuppression in the SCDs (27-29). As a result, the significantly higher prevalence of RHD due to repeated bacterial infections should not be an amazing finding in the SCDs.

As a conclusion, SCDs induce a severe and chronic inflammatory process on vascular endothelium all over the body, and terminate with end-organ insufficiencies in early years of life. Beside that SCDs cause a moderate to severe immunosuppression by several mechanisms that may be the cause of higher prevalence of RHD in them.

References

1. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005; 365(9468): 1415-1428.
2. Helvaci MR, Kaya H, Sevinc A, Camci C. Body weight and white coat hypertension. Pak J Med Sci 2009; 25(6): 916-921.
3. Helvaci MR, Gokce C, Davran R, Akkucuk S, Ugur M, Oruc C. Mortal qu ntet of sickle cell diseases. Int J Clin Exp Med 2015; 8(7): 11442-11448.
4. Helvaci MR, Kaya H. Effect of sickle cell diseases on height and weight. Pak J Med Sci 2011; 27(2): 361-364.
5. Vestbo J, Hurd S, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013; 187(4): 347-65.
6. Fisher MR, Forfia PR, Chamera E, Housten-Harris T, Champion HC, Girgis RE, et al. Accuracy of Doppler echocardiography in the hemodynamic assessment of pulmonary hypertension. Am J Respir Crit Care Med 2009; 179(7): 615-621.
7. Vandemergel X, Renneboog B. Prevalence, aetiologies and significance of clubbing in a department of general internal medicine. Eur J Intern Med 2008; 19(5): 325-329.
8. Schamroth L. Personal experience. S Afr Med J 1976; 50(9): 297-300.
9. Mankad VN, Williams JP, Harpen MD, Manci E, Longenecker G, Moore RB, et al. Magnetic resonance imaging of bone marrow in sickle cell disease: clinical, hematologic, and pathologic correlations. Blood 1990; 75(1): 274-283.
10. Helvaci MR, Aydin LY, Aydin Y. Digital clubbing may be an indicator of systemic atherosclerosis even at microvascular level. HealthMED 2012; 6(12): 3977-3981.
11. Yawn BP, Buchanan GR, Afenyi-Annan AN, Ballas SK, Hassell KL, James AH, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA 2014; 312(10): 1033-1048.
12. Helvaci MR, Aydin Y, Ayyildiz O. Hydroxyurea may prolong survival of sickle cell patients by decreasing frequency of painful crises. HealthMED 2013; 7(8): 2327-2332.
13. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Mortality in sickle cell disease. Life expectancy and risk factors for early death. N Engl J Med 1994; 330(23): 1639-1644.
14. Charache S, Scott JC, Charache P. "Acute chest syndrome" in adults with sickle cell anemia. Microbiology, treatment, and prevention. Arch Intern Med 1979; 139(1): 67-69.
15. Davies SC, Luce PJ, Win AA, Riordan JF, Brozovic M. Acute chest syndrome in sickle-cell disease. Lancet 1984; 1(8367): 36-38.
16. Mathers CD, Sadana R, Salomon JA, Murray CJ, Lopez AD. Healthy life expectancy in 191 countries, 1999. Lancet 2001; 357(9269): 1685-1691.
17. Helvaci MR, Ayyildiz O, Gundogdu M. Gender differences in severity of sickle cell diseases in non-smokers. Pak J Med Sci 2013; 29(4): 1050-1054.

18. Chang AY, Nabbaale J, Okello E, Ssinabulya I, Barry M, Beaton AZ, et al. Outcomes and care quality metrics for women of reproductive age living with rheumatic heart disease in Uganda. J Am Heart Assoc 2020 Apr 21; 9(8): e015562.
19. Ben Ameur Y, Zairi I, Kamoun K, Ben Sassi M, Longo S, Battikh K, et al. Tricuspid dysfunction as a result of rheumatic disease. Tunis Med 2010; 88(11): 820-828.
20. Sultan FA, Moustafa SE, Tajik J, Warsame T, Emani U, Alharthi M, et al. Rheumatic tricuspid valve disease: an evidence-based systematic overview. J Heart Valve Dis 2010; 19(3): 374-382.
21. Kanagasingam A, Francis GR, Komagarajah B, Ladchumanan D, Sivapramyan A, Packiyarajah P, et al. Pattern of rheumatic valvular involvement and its contribution towards valvular malfunction in young adults. Ceylon Med J 2019; 64(3): 91-97.
22. Pressman GS, Ranjan R, Park DH, Shim CY, Hong GR. Degenerative mitral stenosis versus rheumatic mitral stenosis. Am J Cardiol 2020 Mar 5. pii: S0002-9149(20)30190-9
23. Helvaci MR, Yaprak M, Abyad A, Pocock L. Atherosclerotic background of hepatosteatosis in sickle cell diseases. World Family Med 2018; 16(3): 12-18.
24. Helvaci MR, Acipayam C, Aydogan A, Akkucuk S, Oruc C, Gokce C. Acute chest syndrome in severity of sickle cell diseases. Int J Clin Exp Med 2014; 7(12): 5790-5795.
25. Helvaci MR, Gokce C, Davran R, Acipayam C, Akkucuk S, Ugur M. Tonsilectomy in sickle cell diseases. Int J Clin Exp Med 2015; 8(3): 4586-4590.
26. Helvaci MR, Davarci M, Inci M, Yaprak M, Abyad A, Pocock L. Chronic endothelial inflammation and priapism in sickle cell diseases. World Family Med 2018; 16(4): 6-11.
27. Helvaci MR, Acipayam C, Davran R. Autosplenectomy in severity of sickle cell diseases. Int J Clin Exp Med 2014; 7(5): 1404-1409.
28. Helvaci MR, Aydogan A, Akkucuk S, Oruc C, Ugur M. Sickle cell diseases and ileus. Int J Clin Exp Med 2014; 7(9): 2871-2876.
29. Helvaci MR, Albayrak M, Balcik OS, Celebi H, Abyad A, Pocock L. Moderate iron deficiency anemia in the treatment of metabolic syndrome. Middle East J Intern Med 2017; 10 (3): 23-26.

Clinical Characteristics and Treatment of Cryptorchidism in Adults: Our Experience in Alsaidi hospital, in Aden, Yemen

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Abstract

Background: Undescended testes are a condition when one or both of the testes have not descended into the scrotum at birth, but stay in the abdomen or only move part way down into the scrotum.

The aim of the study was to describe the pattern of clinical presentation, the ultrasound and intra-operative findings, and the outcome.

Materials and method: This is a retrospective study involving 120 medical files of adult patients with undescended testes.

Results: The mean age was 25.1 ± 4.7 years. Patients of age group 18 – 22 years were predominant (35.0%). Sixty eight (56.7%) presented to the hospital complaining of empty scrotum. another 33(27.5%) were complaining of infertility.

Undescended testes were (40.8%) in the left side, (32.5%) in the right side and bilateral (26.7%).

The sites of testes were (42.1%) not seen, inguinal (17.1%) and abdominal low (11.2%).

The operative options were one stage laparoscopic orchiopexy (35.5%), open orchiopexy (32.9%), first stage Fowler Stephen Procedure (18.4%), and (8.6%) orchiectomy.

Postoperative findings (52.7%) were alive, in their positions and normal. First Stage Fowler Stephen procedure were found in (18.4%), alive + small in their positions (23.0%) and atrophy (5.9%).

Conclusion: The best result of treatment of cryptorchidism is preferably in the childhood age, therefore careful physical examination of the baby at birth, regular follow-up of the infant and advice for early corrective surgery in cases of persistent undescended testis will go a long way in reducing the morbidity due to cryptorchidism.

Key words: cryptorchidism, adult,
clinical characteristics, treatment, Aden

Introduction

Cryptorchidism is a pathological condition defined as the failure of the testis to descend into the scrotum [1].
It is a congenital condition in which one or both testicles are not appropriately positioned in the scrotum at birth and cannot be moved into the proper position manually. The term “cryptorchidism” literally means “hidden testicle” and is often used interchangeably with the term “undescended testicle”[2].

It affects an estimated 3 percent of full-term male neonates and up to 30 percent of premature male infants, making it the most common male genital anomaly identified at birth [3,4].

The treatment of cryptorchidism in infants and children is well known. A surgical approach such as orchiopexy is recommended for testes that remain undescended after 6 months of age [5,6]. In addition, fertility disorders may occur, and are commonly ascribed to the harmful effects of the undescended testis on the contralateral one, or to related immunologic reactions [7].

The aims of this study are to determine the occurrence of cryptorchidism related to age, side of cryptorchidism, location, treatment procedures, outcome and complications.

Materials and Method

This study was designed as a retrospective study. It was conducted at Alsaidi Hospital in Aden, Yemen.

We retrieved the patients’ records of adults with undescended testes and we found 120 cases of the age group ≥ 18 years who were seen and treated by the author during a period of six years, from January 2012 to December 2017.

The data extracted from the files included patient’s demographics, side affected, clinical presentation, associated anomaly, place of residence, location and size of testis as measured by ultrasound and intra-operatively, surgical treatment given, and post-operative complications.

The data obtained were analyzed using SPSS 17 and presented as count, frequency and percentage. Data were analyzed using Chi-square test, where necessary P -values less than 0.05 were regarded as statistical significant.

Results

Table 1 (next page) shows that the age group 18 – 22 years is represented with 42 (35.0%) followed by the age group 23 – 26 years with 34 (28.3%) and the last age group is 31 – 34 years with 21 (17.3%). The mean age of the patients is 25.1 ± 4.7 years and the age ranged between 18 – 34 years. Most of the patients 66 (55.0%) were from rural areas. Empty scrotums were predominant with 68 (56.7%) followed by infertility 33 (27.5%) and the last clinical presentation was inguinal pain with 1 (0.8%).

Table 2 reveals that 49 (40.8%) of UDT occurred in the left side and 39 (32.5%) occurred in the right side while 32 (26.7%) were bilateral.

The table also, shows association with other anomalies in which 67 (55.9%) were inguinal hernia of same side UDT followed by Inguinal hernia of both sides 4 (3.3%) then attenuated vas deferens 2 (1.6%) and the last one was absent of vas deferens 1 (0.8%). Table 2 reveals the mean hospital stay which was 1.02 ± 0.14 days.

Table 3 shows the sites of testes were distributed as follows: not seen 64 (42.1%), inguinal 26 (17.1%), abdominal low 17 (11.2%), peeping 15 (9.8%), abdominal high 14 (9.2%), deep inguinal ring 13 (8.6%) and ectopic 3 (2.0%).
The distribution of testis size by ultrasound were 47 (30.9%) normal, 43 (28.3%) small and 62(40.8%) not seen. Also, table 3 reveals the distribution of intraoperative size of testis as follows: 88 (57.9%) normal, 44 (28.9%) small, 13 (8.6%) atrophy, 5 (3.3%) vanished and 2 (1.3%) torsion.
Table 3 also, reveals the operative options which were applied for the study patients. They were distributed as follows: One stage laparoscopic orchiopexy 54 (35.5%), open orchiopexy 50 (32.9%), first stage Fowler Stephen Procedure 28 (18.4%), orchiectomy 13 (8.6%), nothing done - vanished testis 6 (3.9%) and second stage of Fowler Stephen Orchiopexy 1 (0.7%).

Table 4 represents the follow up results after one month of the surgical procedure. We found 80 (52.7%) of testes were alive, in their positions and normal. First Stage Fowler Stephen procedure were found in 28 (18.4%), alive + small in their positions 35 (23.0%) and atrophy 9 (5.9%).

Table 1: Variables of age groups, residency and clinical presentation (n=120)

Variable	No	%
Age group (years):		
18 – 22	42	35.0
23 – 26	34	28.3
27 – 30	23	19.2
31 - 34	21	17.5
Mean age (years)	25.1 ±4.7	
Age range (years)	18 – 34	
Residency:		
Urban	54	45.0
Rural	66	55.0
Clinical presentation:		
Empty scrotum	68	56.7
Infertility	33	27.5
Inguinal hernia	10	8.3
Abdominal mass	8	6.7
Inguinal pain	1	0.8

Table 2: Side variables of UDT, and associated anomalies (n=120)

Variables	No	%
Side of UDT:		
Left	49	40.8
Right	39	32.5
Bilateral	32	26.7
*Ass other anomalies by clinical exam:**		
Inguinal hernia of same side UDT	67	55.9
Inguinal hernia of both sides	4	3.3
Attenuated vas deferens	2	1.6
Absent of vas deferens	1	0.8
Nothing	78	37.6
Mean hospital stay (days):	1.02 ± 0.14	

*Ass other anomalies by clinical exam = Associated other anomalies by clinical examination

Table 3: Distribution of site and size of testes by US, intraoperative size, and operative options: (n=152)

Variables	No	%
Site of testis by US:		
Not seen	64	42.1
Inguinal	26	17.1
Abdominal low	17	11.2
Peeping	15	9.8
Abdominal high	14	9.2
Deep inguinal ring	13	8.6
Ectopic	3	2.0
Size of testis by US:		
Normal	47	30.9
Small	43	28.3
Not seen	62	40.8
Size of testis intraoperative:		
Normal	88	57.9
Small	44	28.9
Atrophy	13	8.6
Vanished	5	3.3
Torsion	2	1.3
Operative options:		
One stage laparoscopic orchiopexy	54	35.5
Open orchiopexy	50	32.9
First stage Fowler Stephen Procedure	28	18.4
Orchiectomy	13	8.6
Nothing done - vanished testis	6	3.9
Second stage of Fowler Stephen orchiopexy	1	0.7

Table 4: Results of follow up at the end of one month post hospital discharge

Variables	No	%
Alive, in its position, normal	80	52.7
Alive, in its position, small	35	23
First Stage Fowler Stephen procedure	28	18.4
Atrophy	9	5.9
Total	152	100

Discussion

The first description of undescended testis dated back to the 18th century and theories of testis migration troubles started during the 19th century [8]. Since then, the literature has been enriched in the management of this pathology, especially in children. Observation of an undescended testis in an adult is a situation whose frequency is variously reported [9].

In our study we found the mean age of the patients was 25.1 ± 4.7 years and the age ranged between 18 – 34 years.

The age group 18 – 22 years represented with 42 (35.0%) followed by the age group 23 – 26 years with 34 (28.3%) and the last age group is 31 – 34 years with 21 (17.3%).

To some extent a similar finding was reported by Avakoudjo et al [9] from Benin where the mean age was 23.3 ± 6.1 years, with extremes of 16 and 42 years. The most represented age group was 16 to 20 years of age.

Most of the patients (55.0%) were from rural areas. They presented due to empty scrotums with (56.7%) followed by infertility (27.5%) and the last clinical presentation was inguinal pain with (0.8%).

Shuaibu et al [10] reported in their study that (42.8%) of patients presented because of infertility or were detected during a work up for infertility. 50% complained of empty scrotum. One patient (3.6%) presented with sudden abdominal pain, another patient (3.6%) presented with features of metastatic testicular carcinoma.

In the current study we found that (40.8%) of cryptorchidism occurred in the left side and (32.5%) occurred in the right side while (26.7%) were bilateral.

Similar to our finding was reported by Musa et al [11] from Sudan that the side of impalpable testis was the left in (50%), and the right in (42%) while only (8%) had bilaterally impalpable testes.

Different from our results, was reported by Hadziselimovic [12] in which he mentioned that cryptorchidism may occur on one or both sides, but more commonly affects the right testicle.

Our finding also differs from that reported by Avakoudjo et al [9] right side in (36.1%), left side in (34.8%) and bilateral in (26.1%) patients.

We found in our present study UDT was associated with other anomalies in which (55.9%) were inguinal hernia of same side cryptorchidism followed by inguinal hernia of both sides (3.3%) then attenuated vas deferens (1.6%) and the last one was absent of vas deferens (0.8%).

Cryptorchidism can be associated with various anatomical anomalies, but epididymal anomalies and patency of the vaginal process are among the most frequent [13,14]. Epididymal anomalies are associated with cryptorchidism with highly variable incidence reported in the literature: from 36 to 79% [15]. The occurrence of inguinal hernias associated with cryptorchidism is due to the persistence of the vaginal process [16]. The vaginal process is a conduit that extends from the peritoneum to the scrotum and is covered by a coelomic epithelium. This conduit is usually obliterated after the end of the testicular migration [16]. In cases where the vaginal process does not close, the child may develop inguinal hernia or communicating hydrocele.

Our study revealed that the mean hospital stay was 2.1 ± 0.8 days and range 1-3 days. These findings are similar to that reported by Torricelli et al [17].

In the present study the site of testes were distributed as follows: not seen 64 (42.1%), inguinal 26 (17.1%), abdominal low 17 (11.2%), peeping 15(9.8%), abdominal high 14(9.2%), deep inguinal ring 13(8.6%) and ectopic 3(2.0%).

Shuaibu et al [10] reported that of the 54 nonpalpable testes evaluated, 34 (63%) testicles were intrabdominal, 12(22.2%) were located at the inguinal canal, 5 (9.3%) were at the internal ring or just proximal to it, 3 (5.5%) were vanishing.

Jeong et al [18] reported in their study that the location of cryptorchid testis identified during the operation was inguinal in 14 (82.4%), prepubic in 2 (11.7%), and intra-abdominal in 1 (5.9%), respectively.

In our present study we found the distribution of intraoperative size of testis as follows: 88 (57.9%) normal, 44 (28.9%) small, 13 (8.6%) atrophy, 5 (3.3%) vanished and 2 (1.3%) torsion.

In our current study the operative options which were applied for the study patients were distributed as follows: One stage laparoscopic orchiopexy (35.5%), open orchiopexy (32.9%), first stage Fowler Stephen Procedure (18.4%), orchiectomy (8.6%), nothing done - vanished testis (3.9%) and second stage of Fowler Stephen Orchiopexy (0.7%).

Laparoscopy has proved to be the best available procedure for diagnosis and management of impalpable undescended testes [19,20,21].

Sangrasi et al [22] performed the following treatment options on their patients with impalpable testes. Of 30 intraabdominal testes, single-stage laparoscopic-assisted orchiopexy was successfully performed in 16 (40%) testes, while laparoscopic orchiectomy was performed in 14 (35%) testes. Testes were atrophic and were easily retrieved through a 10-mm port. Six testes where vas and vessels entered the internal ring were diagnosed as intracanalicular testis. They were explored by inguinal incision, inguinal orchiopexy was done in 2 (5%) testes, and inguinal orchiectomy was performed in the remaining 4% of testes.

In the present study the follow up results after one month of the surgical procedure were distributed as follows: (52.7%) of testes were alive, in their positions and normal. First Stage Fowler Stephen procedure were found in (18.4%), alive + small in their positions (23.0%) and atrophy (5.9%).

Corvin et al [23] described their experience with laparoscopic management of adult cryptorchidism in 8 cases.

In just one patient, a morphologically intact abdominal testicle was found and a first-stage Fowler-Stephens orchiopexy was performed. In all others cases, atrophic or vanishing testicles were found and resected.

Vijjan et al [24] reported better results in their experience with 14 adults with a mean age of 21 years. A total of 19 undescended testes were evaluated and 94.7% of the testes were intra-abdominal. Seven patients with unilateral undescended testes underwent laparoscopic orchiectomy, and laparoscopic-assisted orchiopexy was carried out in the remaining two patients. Five patients with bilateral undescended testes underwent laparoscopic orchiectomy on one side and laparoscopic-assisted orchiopexy on the other.

Testicular preservation rate was 36.8%. The authors also concluded that laparoscopy is a safe and effective modality in the localization and management of adult undescended testes.

Conclusion

The best result of treatment of cryptorchidism is preferably in the childhood age. Therefore, careful physical examination of the baby at birth, regular follow-up of the infant and advice for early corrective surgery in cases of persistent undescended testis will go a long way in reducing the morbidity due to cryptorchidism. Delay in providing care for cryptorchid patients can be costly and dangerous; it is necessary to increase awareness and to health educate people on this problem.

References

1. Sijstermans K, Hack WW, Meijer RW, Van der Voort-Doedens LM. The frequency of undescended testis from birth to adulthood: a review. Int J Androl. 2008;31:1–11.
2. Campbell MF, Wein AJ, Kavoussi LR. Campbell-Walsh Urology. 9th ed. Philadelphia: W.B. Saunders; 2007.
3. Miller DC, Saigal CS, Litwin MS. The demographic burden of urologic diseases in America. Urol Clin North Am. 2009 Feb;36(1):11-27.
4. Barthold JS, Gonzalez R. The epidemiology of congenital cryptorchidism, testicular ascent and orchiopexy. J Urol. 2003 Dec;170(6 Pt 1):2396-401.
5. Moradi M, Karimian B, Moradi A. Adult orchidopexy: a survey on necessity of intraoperative testicular biopsy. Nephrourol Mon. 2011;3:196–200.
6. Barthold JS. Abnormalities of the testis and scrotum and their surgical management. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh Urology. 10th ed. Philadelphia: Saunders; 2012. pp. 3560–3574.
7. Lania C, Grasso M, Mantovani G, Hadjigeorgiou D, Annoni F, Rigatti P. Cryptorchidism: review and evaluation of the fertility of adult cryptorchids. J Androl. 1984:125–127.
8. Tackett LD, Patel SR, Caldamone AA. A History of Cryptorchidism: Lessons from the Eighteenth Century. Journal of Pediatric Urology. 2007; 3: 426-432. https://doi.org/10.1016/j.jpurol.2007.07.003
9. Avakoudjo J, Hodonou F, Sewa EV, Tandje Y, Sossa J, Yevi M, Gandaho I, et al. Undescended Testis in Adult: Epidemiology and Therapeutic Aspects. About 23 Cases in HKM University Teaching Hospital of Cotonou. Open Journal of Urology. 2018; 8: 206-213
10. Shuaibu SI, Gideon OC, Cletus AI, Ramyil VM, Dakum NK, et al. Bilateral NonpalpableCryptorchidism In Adults; Does Social Class Influence Presentation? IOSR Journal of Dental and Medical Sciences. 2013; 10(3): 48-51
11. Musa MT, Abdul-Rahman RZ. Empty scrotum in adults. Kharoum Medical Journal. 2008; 01(02): 69-71
12. Hadziselimovic F. On the descent of the epididymo-testicular unit, cryptorchidism, and prevention of infertility. Basic Clin Androl. 2017;27:21.
13. Lee PA, Houk CP. Cryptorchidism: Current Opinion in Endocrinology, Diabetes and Obesity. 20.13; 20(3): 210–216
14. Barthold JS, Redman JF. Association of epididymal anomalies with patent processus vaginalis in hernia, hydrocele and cryptorchidism. The Journal of Urology. 1996; 156(6): 2054–2056
15. Favorito LA, Costa WS, Sampaio FJB. Analysis of anomalies of the epididymis and processus vaginalis in human fetuses and in patients with cryptorchidism treated and untreated with human chorionic gonadotrophin. BJU International. 2006: 98(4): 854–857
16. Johansen TEB. Anatomy of the testis and epididymis in cryptorchidism. Andrologia. 1987: 19(5): 565–569
17. Torricelli FCM, Arap MA, Duarte RJ. Anuar IbrahimMitre, andMiguel Srougi. Laparoscopic Testicular Preservation in Adults with Intra-Abdominal Cryptorchidism: Is It Beneficial?. Advances in Urology. 2012; 1-4
18. Jeong SC, Lee S, Ku JY, Lee SD. Clinical Characteristics and Treatment of Cryptorchidism in Adults: A Single Center Experience. World J Mens Health. 2014; 32(2): 110-115
19. Ismail K, Ashour M, El-Afifi M, Hashish A, El-Dosouky N, Nagm M, et al. Laparoscopy in the management of impalpable testis: Series of 64 cases. World J Surg. 2009;33:1514–9.
20. Moursy EE, Gamal W, Hussein MM. Laparoscopic orchiopexy for non-palpable testes: Outcome of two techniques. J Pediatr Urol. 2011;7:178–81.
21. Park JH, Park YH, Park K, Choi H. Diagnostic laparoscopy for the management of impalpable testes. Korean J Urol. 2011;52:355–8.
22. Sangrasi AK, Laghar A, Abbasi MR, Bhatti S. Laparoscopic-Assisted Management of Impalpable Testis in Patients Older than 10 Years. JSLS. 2010; 14(2): 251–255.
23. Corvin S, Sturm W, Anastasiadis A, Kuczyk M, Stenzl A. Laparoscopic management of the adult nonpalpable testicle. Urologia Internationalis. 2005; 75(4): 337–339.
24. Vijjan VK, Malik VK, Agarwal PN. The role of laparoscopy in the localization and management of adult impalpable testes. Journal of the Society of Laparoendoscopic Surgeons. 2004; 8(1): 43–46.

Glucose- 6-phosphate dehydrogenase deficiency: A review

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Abstract

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a genetic disorder affecting people at any age and is thought to affect 400 million people worldwide. It is normally asymptomatic but can lead to significant morbidity and mortality. There are recognized factors that need to be avoided. Detection of the disorder, avoidance of provoking factors, management of the symptoms and any complications are essential to ensure that people with G6PD deficiency can remain as healthy as possible.

Key words: Glucose-6-phosphate dehydrogenase; G6PD deficiency; Red blood cells; Hemolysis; Neonatal jaundice; Fava beans; Malaria; Primaquine.

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest enzymatic disorder affecting red blood cells, estimated to affect 400 million people worldwide (1). Since complete absence of G6PD is incompatible with survival, the deficiency is incomplete (2). The deficiency can arise from a reduction in the quantity of enzyme, a qualitative change caused by a change to its structure, or both (1). It is normally asymptomatic but serious complications can occur from presentations like neonatal jaundice or through episodes of acute hemolysis.

The global distribution of the disorder reflects areas where malaria was once endemic, suggesting that the disorder provides selective advantage against that infection. The Middle East is thought to contain a high frequency of this disorder (3). Concern also exists that G6PD deficiency can increase susceptibility to COVID-19 infection (4) and the risk of acute hemolysis from using medications suggested as treatment for that infection (5).

History

Acute hemolysis was detected in some patients treated for malaria with 6-methoxy-8-aminoquinoline drugs in 1926 (6). G6PD was identified in yeast cells in the 1930s and, in 1956, researchers discovered that volunteer prisoners from Illinois State Penitentiary developing hemolytic anemia after taking primaquine had low levels of G6PD activity in their red blood cells (7). At the same time, a similarity was noted between the severe hemolytic anemia associated with ingestion of fava beans and the hemolytic anemia induced by primaquine (8).

Genetic basis

G6PD deficiency is inherited recessively as an X-linked disorder (9). The encoding gene is found on the distal arm of the X chromosome (band Xq28), near to genes that code for hemophilia A, dyskeratosis congenital and colour blindness (10). It was the first gene to be cloned in human beings (11).

Being X linked, G6PD deficiency affects the two genders differently (12). Males who inherit the mutated gene are homozygous for the disorder and all their red blood cells are G6PD deficient.

Females can be:
a. Homozygous normal, or
b. heterozygous deficient, or
c. homozygous deficient, or
d. compound heterozygous for two mutations on the G6PD gene (13).

In heterozygous females, one copy of the G6PD gene is randomly inactivated during embryogenesis through a process called lyonization. Hence, heterozygous females have one group of red blood cells with normal G6PD activity and another G6PD-deficient group (14). The relative ratio of these red blood cell groups determines the G6PD activity, and the ratio can vary, but is typically 30% to 80% of normal G6PD activity (15).

Function of G6PD

G6PD functions as a housekeeping enzyme in all cells but in varying amounts according to the tissue type (16). It is the rate-limiting enzyme in the pentose phosphate pathway maintaining the level of nicotinamide adenine dinucleotide phosphate (NADPH). NADPH enables glutathione to remain in a reduced state within cells. Reduced glutathione protects cells from oxidative damage.

Since red blood cells lack mitochondria, the only source of reducing power comes from the pentose phosphate pathway (17). In red blood cells, G6PD operates at only 1–2% of its maximum potential and, therefore, a large reserve of reductive potential exists (18). However, when the reduced glutathione store is depleted, hemoglobin becomes vulnerable to damage through oxidation and hemolysis can result.

Distribution of affected people

Over 400 variants of the G6PD enzymes have been identified and the majority are due to single amino acid substitutions (19). G6PD's stability and effectiveness are reduced to varying degrees through these mutations (10).

The most frequent G6PD variants are found in people from the Middle East and the Mediterranean region (G6PD Mediterranean type), areas of Africa (G6PD A-) and parts of India and South East Asia (17).

G6PD deficiency is common in areas where Plasmodium falciparum malaria is endemic, suggesting that G6PD deficiency confers a type of defense against malaria (18). Although the exact mechanism for that advantage is not yet known, in heterozygotic females, red blood cells with normal G6PD function were 2 - 80 times more likely to be infested than their G6PD deficient cells (20).

Severity of G6PD Deficiency

The World Health Organization has categorized the deficiency into five classes according to the degree of enzyme deficiency and hemolysis (21).

Class 1: severe enzyme deficiency (less than 10% of normal) and is associated with chronic non-spherocytic hemolytic anemia;
Class 2: severe enzyme deficiency (less than 10% of normal) and is associated with acute hemolytic anemia. G6PD Mediterranean is the classic variant.
Class 3: moderate-to-mild enzyme deficiency (10%-60% of normal). G6PD A- is the classic variant.
Class 4: very mild or no enzyme deficiency (60%-150% of normal). Typically, these variants are not clinically significant.
Class 5: increased enzyme activity (greater than 150% of normal). Typically, these variants are not clinically significant.

Presentation of G6PD Deficiency

Most people with G6PD deficiency are asymptomatic. The most frequent clinical manifestations of G6PD deficiency are neonatal jaundice and acute hemolytic anemia. G6PD-deficient variants can also cause chronic hemolysis, leading to congenital non-spherocytic anemia (1).

Neonatal jaundice
Neonatal jaundice most commonly presents 2–3 days after birth (22). It has variable severity but can lead to kernicterus and death (23). The condition is thought to result more from impairment of bilirubin conjugation and clearance by the liver than from hemolysis (10). Inheritance of the mutation of the uridine-diphosphate-glucuronosyltransferase 1 gene promoter (24) responsible for Gilbert syndrome, increases the risk of neonatal jaundice (24). The hyperbilirubinemia can require phototherapy or exchange transfusion (25).

G6PD deficiency should be considered in neonates who develop hyperbilirubinemia within the first 24 hours of life, or have a history of jaundice in a sibling, bilirubin levels greater than the 95th percentile, or are from ethnicities where the G6PD is prevalent (26).

The WHO recommends that neonatal screening be performed when G6PD deficiency affects more than 3–5% of males in a population (21). Heterozygote females are considered to have less severe clinical manifestations than G6PD deficient males (27). However, those females are also at risk of kernicterus because hemolysis of their G6PD deficient cells can result in hyperbilirubinemia (28).

Acute hemolytic anemia.
Hemolysis can occur after exposure to a variety of provoking agents. The degree of hemolysis is dependent on several factors, including the variant of G6PD deficiency (the Mediterranean variant is most frequently affected), as well as the age of the individual, dose of the provoking agent and coexisting morbidities. As such, the episode of hemolysis can range from mild to life- threatening (29). Treatment such as blood transfusions and renal dialysis may be required in serious cases. The most common provoking agents are infection, fava beans and certain medications (21). Rarer causes include exposure to naphthalene (30) and henna (31).

Clinically detectable hemolysis and jaundice typically arise within 24–72 hours of exposure. Hemoglobinuria causes characteristic dark urine. Anemia worsens until days 7–8. After exposure to the provoking agent ends, the hemoglobin concentrations start to recover from 8–10 days (1). Depending on the severity of the hemolysis, the patient may complain of a number of symptoms including lethargy, headache, lumbar pain, jaundice, and dark urine.

A normochromic, normocytic anemia with anisocytosis and reticulocytosis will appear in laboratory tests. Heinz bodies, which are denatured hemoglobin precipitates and a classic finding, may be present (1).

Fava Bean
Pythagoras is claimed to have forbidden his students from eating fava beans. He eventually preferred to be captured by his enemies who were pursuing him rather than enter a field of fava beans as he was trying to escape (32). Divicine and isouramil, chemicals present in fava beans, are thought to be responsible for acute hemolysis (termed favism) through their oxidizing actions (10).
Favism most commonly affects young children (33). After ingestion of fava beans, symptoms of favism occur within 5 to 24 and include nausea, headache, back pain and fever, followed later by jaundice and hemoglobinuria (34). It is believed that all patients with favism have G6PD deficiency, but not all G6PD-deficient individuals develop hemolysis when they eat fava beans (2) and so there may be an additional property to fava beans and their consumption that results in the risk of hemolysis. Furthermore, passive transmission, through breast feeding when mothers had ingested fava beans has been described (35).

Infection

Although the exact mechanism of susceptibility is not known, it is considered that the lack of glutathione in its reduced form results in the cells inability to withstand the oxidative damage that infections cause (36). Another suggestion is that during phagocytosis, leukocytes discharge active oxygen species that damage erythrocytes in their environment (37).

The most frequent infections causing hemolysis include Salmonella, Escherichia coli, beta-hemolytic streptococci, rickettsial infections, viral hepatitis, and influenza A (26). Hence, G6PD deficient patients need to be aware to seek medical attention promptly when they become ill.

G6PD deficiency has been found to enhance infection of cells with human coronavirus 229E (HCoV 229E). Viral gene expression was higher in G6PD deficient cells compared with control cells. G6PD-deficient cells were more susceptible to HCoV 229E–mediated cell death (38). There are suggestions that SARS-CoV-2 may have a similar effect on cells in G6PD-deficient patients although a definitive association has yet to be made (4).

Medications

A variety of medications can cause acute hemolytic crisis in people with G6PD deficiency (39). These include antimalarial medications such as primaquine or aminoquinoline drugs, and combination medication containing sulphonamide. There have also been concerns regarding the use of hydroxychloroquine as a treatment for COVID 19 without ensuring that the recipients did not have G6PD deficiency (5).

The ability of the medication to cause hemolysis is not always predictable. Inherited differences such as acetylator status or if the medication shortens the life span of the red blood cell will affect the severity of hemolysis (2).

WHO recommends testing of all patients routinely for G6PD deficiency before considering primaquine therapy (40). If the G6PD status is unknown and testing to determine it not available, patients given primaquine are recommended to receive close medical supervision and instructed to stop taking primaquine if signs or symptoms of hemolytic anemia appear (41).

Benefits of G6PD Deficiency

It is thought that G6PD deficiency, particularly the G6PD A- variant, confers a defense against malaria. In G6PD A– heterozygous females, red blood cells with normal G6PD activity had more parasitic growth than G6PD-deficient red-blood cells (20). There is some evidence that G6PD deficiency has a positive effect on longevity and can prevent cancer progression (42).

Detection of G6PD Deficiency

G6PD deficiency can be assessed using a fluorescent screening test or quantitative spectrophotometric analysis to assess the activity of the enzyme. Alternatively, DNA sequencing can be used to detect the actual gene mutation (17).

Tests for measuring G6PD activity are based on detecting the rate of reduction of NADP to NADPH. The tests rely upon certain characteristics of NADPH: (10)

1 Light absorption at 340 nm.
2 Fluoresces when subjected to long wavelength UV light (approximately 340 nm).
3 Decolorizes or leads to the precipitation of certain dyes.

Screening for G6PD deficiency, using a fluorescent spot test or dye decolorization method, are relatively easy to use and can yield results quickly, allowing them to be employed as point of care tests (17).

The British Society for Haematology (10) recently suggested criteria to undertake screening:
• Before commencing medication able to cause oxidative damage to red blood cells.
• History of non-immune hemolytic anemia or neonatal jaundice that is prolonged or severe.
• If hemolysis has occurred and is associated with infection or medication considered to oxidize red blood cells, or following haemopoietic stem cell transplantation if donor is G6PD deficient or status unknown
• History of favism
• Family history of G6PD deficiency or favism.
• Detection of red blood cell morphology suggesting oxidant damage or positive Heinz body stain
• The presence of congenital non-spherocytic hemolytic anemia, hemoglobinuria, sickle cell disease or thalassemic disorders

If the screening test yields an abnormal or equivocal result, or the subject is female, then quantitative analysis is required. Quantitative assays provide an actual measure of G6PD activity normalized for either hemoglobin concentration or red blood cell count and provide the definitive diagnosis of G6PD deficiency (44).

If a female is suspected to be heterozygous for G6PD deficiency, a cytochemical test should be undertaken even if the quantitative assay is normal. Staining allows visualization of G6PD normal and G6PD deficient red blood cell groups, thereby identifying heterozygote females (10).

Attempting to diagnose G6PD deficiency during an acute hemolytic episode is likely to lead to inaccurate results (1). During these episodes young red cells and reticulocytes have more G6PD activity than mature red cells leading to false negative results; hence, the assay should be undertaken 2 -3 months following the hemolytic episode (10).

Management of G6PD Deficiency

The most effective strategy is to avoid oxidative stress to red blood cells. Dietary restrictions need to be followed for those with G6PD deficiency. Medication considered unsafe in the presence of G6PD deficiency should be avoided.

Neonatal jaundice due to G6PD deficiency is treated in a similar fashion to neonatal jaundice from other causes. When rising concentrations of unconjugated bilirubin, phototherapy and a blood transfusion may become necessary (43).

Any agent, such as medication, provoking hemolysis should be discontinued, and supportive case instituted (44). Fortunately, most episodes of acute hemolysis are short lived, however, in severe cases, blood transfusions and renal dialysis may be required (45).

Class 1 G6PD variants, leading to congenital non-spherocytic anemia, can develop gallstones (46) and require surgical intervention. Splenomegaly can also occur although splenectomy is not considered to confer any benefit (47). Very rarely, congenital non-spherocytic hemolytic anemia is transfusion-dependent and iron-chelation treatment is required (1).

Summary

G6PD deficiency is the most common enzyme disorder affecting red blood cells. It is inherited in an X linked recessive manner and there are over 400 variants identified. It has a global distribution and includes areas where malaria has been endemic.

The disorder is considered to render red blood cells vulnerable to oxidative damage from a variety of agents, chief amongst these being infection, certain dietary factors, and medications.

The disorder is normally asymptomatic but common presentations include neonatal jaundice and acute hemolysis. Neonatal jaundice typically occurs 2 – 3 days post-partum and is worsened if there is co-existent Gilbert syndrome. Acute hemolysis can present with lethargy, back pain, jaundice, and dark urine. Chronic hemolysis, leading to gallstones and splenomegaly can also be a presentation of G6PD deficiency.

Treatment depends on the nature of the symptoms, co-existing conditions, and the degree of hemolysis. Particular caution needs to be exercised in neonatal jaundice where there is a risk of kernicterus and death.

Identification of G6PD deficiency can begin with screening tests but definitive tests are required to diagnose the condition. Once diagnosed, people with G6PD deficiency need to avoid any agent that can provoke oxidative stress upon the red blood cell and seek medical attention if symptoms develop suggesting hemolysis.

References

1. Cappellini MD, Fiorelli G. Glucose-6- phosphate dehydrogenase deficiency. Lancet 2008; 371: 64–74.
2. Beutler E. G6PD deficiency. Blood 1994; 84:3613–36.
3. Hilmi F, Al-Allawi N, Rassam M, Al-Shamma G, Al-Hashimi A. Red cell glucose-6-phosphate dehydrogenase phenotypes in Iraq. East Mediterr Health J 2002; 8:42 - 48.
4. Vick DJ. Glucose-6-Phosphate Dehydrogenase Deficiency and COVID-19 Infection. Mayo Clinic proceedings 2020, S0025-6196(20)30598-X. Advance online publication. https://doi.org/10.1016/j.mayocp.2020.05.035. Accessed 26/7/20.
5. Wodarg W. Rapid Response BMJ 2020;369:m1432. https://www.bmj.com/content/369/bmj.m1432/rr-22. Accessed 20/7/20
6. Cordes W. Experiences with plasmochin in malaria. In: Anonymous. 15th Annual Report. Boston, MA: United Fruit Co.1926: 66-71. Cited in Beutler E. Glucose-6-phosphate dehydrogenase deficiency: a historical perspective. Blood. 2008; 111(1):16-24
7. Carson PE, Flanagan CL, Ickes CE, Alving AS. Enzymatic deficiency in primaquine-sensitive erythrocytes. Science 1956; 124: 484–85.
8. Crosby WH. Favism in Sardinia (newsletter). Blood 1956; 11: 91–92. As cited in Cappellini MD, Fiorelli G. Glucose-6- phosphate dehydrogenase deficiency. Lancet 2008. 371: 64–74.
9. Adam A. Linkage between deficiency of glucose 6-phosphate dehydrogenase and colour-blindness. Nature. 1961; 189:686–688.
10. Roper D, Layton M, Rees D, Lambert C, Vulliamy T, De la Salle B et al. Laboratory diagnosis of G6PD deficiency. A British Society for Haematology Guideline. British Journal of Haematology. 2020;189(1):24-38.
11. Persico MG, Viglietto G, Martini G, Toniolo D, Paonessa G, Moscatelli C, Dono R, Vulliamy T, Luzzatto L, D'Urso M. Isolation of human glucose-6-phosphate dehydrogenase (G6PD) cDNA clones: primary structure of the protein and unusual 59 non-coding region. Nucleic Acids Res. 1986; 14:2511–2522. As cited in Cappellini MD, Fiorelli G. Glucose-6- phosphate dehydrogenase deficiency. Lancet 2008. 371: 64–74.
12. Kuwahata M, Wijesinghe R, Ho MF, et al. Population screening for glucose-6-phosphate dehydrogenase deficiencies in Isabel Province, Solomon Islands, using a modified enzyme assay on filter paper dried bloodspots. Malar J. 2010; 9:223.
13. van den Broek L, Heylen E, van den Akker M. Glucose-6-phosphate dehydrogenase deficiency: not exclusively in males. Clin Case Rep. 2016; 4(12):1135-1137.
14. Luzzatto L. Glucose 6-phosphate dehydrogenase deficiency: from genotype to phenotype. Haematologica. 2006; 91(10):1303–6.
15. Domingo GJ, Advani N, Satyagraha AW, et al. Addressing the gender-knowledge gap in glucose-6-phosphate dehydrogenase deficiency: challenges and opportunities. Int Health. 2019;11(1):7-14.
16. Battistuzzi G, D'Urso M, Toniolo D, Persico GM, Luzzatto L. Tissue specific levels of G6PD correlate with methylation at the 3´ end of the gene. Proc Natl Acad Sci U S A 1985; 82: 1465–69. As cited in Cappellini MD, Fiorelli G. Glucose-6- phosphate dehydrogenase deficiency. Lancet 2008; 371: 64–74.
17. Beutler, E. Glucose-6-phosphate dehydrogenase deficiency: a historical perspective. Blood 2008; 111:16–24.
18. Ruwende C, Hill A. Glucose-6-phosphate dehydrogenase deficiency and malaria. J Mol Med. 1998; 76:581–588.
19. Mehta A, Mason PJ, Vulliamy TJ. Glucose6-phosphate dehydrogenase deficiency. Baillieres Best Prac. Res. Clin. Haematol. 2000; 13:21–38
20. Luzzatto L, Usanga EA, Reddy S. Glucose 6-phosphate dehydrogenase deficient red cells: resistance to infection by malarial parasites. Science. 1969; 164:839-842. As cited in Beutler, E. Glucose-6-phosphate dehydrogenase deficiency: a historical perspective. Blood 2008; 111: 16–24.
21. WHO working group? Glucose-6-phosphate dehydrogenase deficiency. Bull World Health Organ 1989; 67: 601–11.
22. Luzzatto L Glucose 6-phosphate dehydrogenase deficiency. 2010. In: Oxford Textbook of Medicine (Eds by D.A. Warrell, T.M. Cox, J.D. Firth, E.J. Benz Jr), OUP, Oxford. 4474–4479. As cited in Roper D, Layton M, Rees D, Lambert C, Vulliamy T, De la Salle B et al. Laboratory diagnosis of G6PD deficiency. A British Society for Haematology Guideline. British Journal of Haematology 2020;189(1):24-38.
23. Cunningham AD, Hwang S, Mochly-Rosen D. Glucose-6-phosphate dehydrogenase deficiency and the need for a novel treatment to prevent kernicterus. Clinical Perinatology 2016;43(2):341–54.
24. Bancroft JD, Kreamer B, Gourley GR. Gilbert syndrome accelerates development of neonatal jaundice. J Pediatr. 1998;132(4):656–660.
25. Kaplan M, Abramov A. Neonatal hyperbilirubinemia associated with glucose-6-phosphate dehydrogenase deficiency in Sephardic-Jewish neonates: incidence, severity, and the effect of phototherapy. Pediatrics. 1992; 90:401–405
26. Frank JE. Diagnosis and Management of G6PD Deficiency. Am Fam Physician. 2005;72(7):1277-1282
27. Lim F, Wulliamy T, Abdalla SH. An Ashkenazi Jewish woman presenting with favism. J Clin Pathol 2005; 58: 317–19. As cited in Cappellini M D, Fiorelli G. Glucose-6- phosphate dehydrogenase deficiency. Lancet 2008; 371:64–74.
28. Algur N, Avraham I, Hammerman C, Kaplan M. Quantitative neonatal glucose-6-phosphate dehydrogenase screening: distribution, reference values, and classification by phenotype. J Pediatr. 2012;161(2):197-200.
29. Domingo GJ, Advani N, Satyagraha AW, et al. Addressing the gender-knowledge gap in glucose-6-phosphate dehydrogenase deficiency: challenges and opportunities. Int Health. 2019;11(1):7-14.
30. Sanctucci K, Shah B. Association of Naphthalene with Acute Hemolytic Anemia. Academic Emergency Medicine. 2000;7(1):42-47.
31. Raupp P, Hassan JA, Varughese M, Kristiansson B. Henna causes life threatening haemolysis in glucose-6-

phosphate dehydrogenase deficiency. Arch Dis Child. 2001; 85 (5):411–412.
32. Arie THD. Pythagoras and beans. Oxf Med School Gaz. 1959; 11:75-81. As cited in Beutler, E. Glucose-6-phosphate dehydrogenase deficiency: a historical perspective. Blood 2008; 111:16–24.
33. Hagag AA, Badraia IM, Elfarargy MS, Abd Elmageed MM, Abo-Ali EA. Study of Glucose-6-Phosphate Dehydrogenase Deficiency: 5 Years Retrospective Egyptian Study. Endocr Metab Immune Disord Drug Targets. 2018;18(2):155-162.
34. Luzzatto L, Arese P. Favism and Glucose-6-Phosphate Dehydrogenase Deficiency. New England Journal of Medicine 2018; 378:60.
35. Yeruchimovich M, Shapira B, Mimouni FB, Dollberq S. Neonatal nucleated red blood cells in G6PD deficiency. Am J Perinatol 2002;19: 215 –8. As cited in Al-Azzam SI, Al-Ajlony MJ, Al-Khateeb T, Alzoubi KH, Mhaidat N, Ayoub A. An audit of the precipitating factors for haemolytic crisis among glucose-6-phosphate dehydrogenase-deficient paediatric patients. 2009. J Med Screen, 16(4):167-169
36. Hsieh YT, Lin MH, Ho HY, Chen LC, Chen CC, Shu JC. Glucose-6-phosphate dehydrogenase (G6PD)-deficient epithelial cells are less tolerant to infection by Staphylococcus aureus. PLoS One. 2013;8(11): e79566.
37. Baehner RL, Nathan DC, Castle WB: Oxidant injury of caucasian glucose-6-phosphate dehydrogenase-deficient red blood cells by phagocytosing leukocytes during infection. J Clin Invest 50:2466, 1971, Cited in Beutler E. G6PD deficiency. Blood 1994; 84:3613–36.
38. Wu Y.H., Tseng C.P., Cheng M.L., Ho H.Y., Shih S.R., Chiu D.T.Y. Glucose-6-phosphate dehydrogenase deficiency enhances human coronavirus 229E infection. J Infect Dis. 2008;197(6):812–816. As cited in Vick DJ. Glucose-6-Phosphate Dehydrogenase Deficiency and COVID-19 Infection. Mayo Clinic proceedings 2020, S0025-6196(20)30598-X. Advance online publication. https://doi.org/10.1016/j.mayocp.2020.05.035. Accessed 26/7/20.
39. G6PD Association. https://www.g6pd.org/G6PDDeficiency/SafeUnsafe.aspx. Accessed 1/8/20 Accessed 28/7/20
40. Guidelines for the treatment of malaria, 3rd edition. Geneva: World Health Organization; 2015.
41. Guide to G6PD deficiency rapid diagnostic testing to support P. vivax radical cure. World Health Organization. 2018. file:///D:/G6PD%20WHO.pdf. Accessed 22/7/20.
42. Schwartz AG, Pashko LL. Dehydroepiandrosterone, glucose-6-phosphate dehydrogenase, and longevity. Ageing Research Reviews 2004: 3: 171–187.
43. Althomali R, Aloqayli R, Alyafi B, Nono A, Alkhalaf S, Aljomailan A, et al. Neonatal jaundice causes and management. Internal J Community Med Public Health 2018; 5:4992-4996.
44. Phillips J, Henderson AC. Hemolytic Anemia: Evaluation and Differential Diagnosis. Am Fam Physician. 2018;98(6):354-361.
45. Abid S, Khan AH. Severe hemolysis and renal failure in glucose-6-phosphate dehydrogenase deficient patients with hepatitis E. The American Journal of Gastroenterology Volume 97, Issue 6, June 2002; 97(6):1544-1547.
46. Haley K. Congenital Hemolytic Anemia. Medical Clinics of North America 2017;101(2):361-374.
47. Beutler E, Mathai CK, Smith JE. Biochemical variants of glucose-6-phosphate dehydrogenase giving rise to congenital non spherocytic hemolytic disease. Blood 1968; 31: 131–50. As cited in Cappellini MD, Fiorelli G. Glucose-6- phosphate dehydrogenase deficiency. Lancet 2008; 371: 64–74.

Thyroid disease in pregnancy and screening

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Abstract

Thyroid dysfunction in the form of hypo and hyperthyroidism are some of the most common endocrine conditions encountered in primary care. The hormone deficiency or excess can be easily diagnosed and managed yet is potentially fatal in severe cases if left untreated. Detection of thyroid dysfunction becomes even more important in pregnant women because it can lead to various complications and adverse outcomes for the mother and foetus. Clinical manifestations of thyroid dysfunction can range from life threatening to no signs or symptoms. Furthermore, often, the non-specific symptoms can be difficult to differentiate from symptoms related to normal physiological changes in pregnancy that women often experience. Primary care physicians are the first point of contact for women when they become pregnant. Therefore, it's important that clinicians are able to confidently diagnose and manage these conditions at the earliest opportunity by organising thyroid function tests and seeking specialist input where necessary. However, guidelines around the world advocate various approaches to decision making about testing pregnant women for thyroid disease. There is increasing debate about whether thyroid screening should be made universal. In this article we look at the current guidelines and latest evidence and opinion in this important area.

Key words: thyroid disease, pregnancy, screening

Introduction

There are significant changes to thyroid physiology during a normal pregnancy. Early foetal and placental growth relies on availability of adequate maternal thyroid hormone. In response to the increased metabolic demand, the size of the thyroid gland in pregnant women increases by about 10% in parts of the world with adequate dietary iodine, and 20-40% in countries where there is iodine deficiency. When there is thyroid dysfunction in pregnancy, it is classified as hypo or hyperthyroidism and further subcategorised as either overt or subclinical (Table 1). Over the last few decades, observational studies have shown that maternal thyroid dysfunction, in the form of overt, subclinical and autoimmune disease states is associated with adverse outcomes for the mother and the foetus. At the same times, studies have also shown that there is clear improvement in outcomes when overt maternal hypo and hyperthyroidism are treated. Although subclinical hypothyroidism is much more common than overt hypo or hyperthyroidism, the picture is not as clear when it comes to the benefits in its detection and subsequent treatment with levothyroxine. This has resulted in considerable debate around the world about universal thyroid screening for pregnant women.

Understanding thyroid function in pregnancy

In pregnancy in order meet the increased metabolic demands of the body, there are significant changes in thyroid physiology which can be seen in the form of altered thyroid hormones level (1). Therefore, thyroid function tests of pregnant women will be different from those of healthy non pregnant women. From conception there is an increase in serum hCG levels which peak around 10-12 weeks of gestation. During the first trimester, this maternal hCG directly stimulates the TSH receptor which increases thyroid hormones production. The total serum T4 and T3 concentrations increase with a slight increase in serum free T4 and T3 within the normal range. In response to this increased production in thyroid hormone levels, the thyroid axis negative feedback leads to decreased serum TSH concentrations (2). Pregnant women will therefore have lower serum TSH concentration compared to before pregnancy. Although widely accepted that there is a decrease in TSH concentration in early pregnancy in all populations, studies have shown that there are significant variations in terms of the extent of this reduction in different racial and ethnic groups. Due to this variation in thyroid hormone levels during different stages of pregnancy and amongst different population groups, the American Thyroid Association (ATA) for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum 2017 guidelines recommend using population based, trimester specific reference ranges for TSH and serum T4 (3). Many labs around the world do not provide trimester specific ranges, in which case ATA recommend that TFTs are interpreted as such that;

• In weeks 7-12 – reduce the lower limit of the reference range of TSH by approximately 0.4mU/L and upper limit by 0.5 mU/L (corresponding to a TSH reference range of approximately 0.1 to 4mU/L).
• In the second and third trimester – there should be a gradual return of TSH towards the non-pregnant normal range

Serum TSH remains the initial and most reliable test that is available for assessing thyroid function in pregnancy. Furthermore, its widely available and relatively inexpensive. In ATA's previous guidelines in 2011, the recommendation for upper reference limit of TSH in first trimester was 2.5mU/L and for the 2nd and 3rd Trimesters it was 3.0mU/L. If the TSH is outside the trimester specific range then FT4 and FT3 levels should also be measured. Thyroid peroxidase antibodies (TPOAb) and TSH receptor antibodies (TRAb) can also be checked to confirm autoimmunity which is the commonest cause of thyroid dysfunction.

Hyperthyroidism in pregnancy

Overt hyperthyroidism is relatively uncommon in pregnancy and is defined as serum TSH levels below the trimester specific reference range with elevated free T3, T4 or both. This occurs in approximately 0.1%-0.4% of pregnancies (4). Although hyperthyroidism from any cause can be potentially detrimental to the pregnancy, Graves' disease and hCG mediated hyperthyroidism are the 2 most common causes of hyperthyroidism in pregnant women (5). Although a definitive diagnosis may not be easy at the outset, the differential diagnosis in early pregnancy in the majority of the cases is usually between these two conditions. The primary aim should be to differentiate between the two. This is done through a combination of careful history, examination and analysis of the thyroid function test. Some of the symptoms suggestive of hyperthyroidism can be similar to the nonspecific symptoms associated with pregnancy such as; heat intolerance, increased perspiration and tachycardia. More specific symptoms can include tremor, anxiety, weight loss with normal appetite. Examination findings such as presence of goitre or eye signs could be more suggestive of Grave's disease.

When there is history of thyroid disease, risk factors or clinical suspicion in women who are trying to conceive or have become pregnant, then serum TSH level should be measured (Figure 1). If the TSH level is <0.1 mU/L then free or total T4 and T3 measurements should be obtained. The diagnosis of overt hyperthyroidism can be confirmed with a suppressed (<0.1mU/L) or undetectable TSH (<0.01 mU/L) and free T4/T3 levels that are above the normal range for pregnancy. If TRAb are measured and present then that will be indicative of Graves' disease. Further investigations such as radioiodine scans are contraindicated, therefore careful history and examination is vital in establishing the cause of hyperthyroidism. Without prior thyroid disease and absence of signs such as a goitre or thyroid eye disease hCG mediated hyperthyroidism is more likely the cause of suppressed TSH. There are couple of variants of hCG mediated hyperthyroidism which include;

Gestational transient thyrotoxicosis; which occurs towards the end of first trimester and is characterised by slightly low TSH levels and mildly elevated free T4 concentrations. This form of subclinical hyperthyroidism or mild overt hyperthyroidism is related to the peak in hCG levels around weeks 10-12. This phenomenon is transient and does not require treatment with antithyroid drugs and typically resolves as hCG production tails off after the first trimester.

Table 1 – summarises the changes in thyroid hormones in different forms of thyroid dysfunction

Type of thyroid dysfunction	Laboratory findings
Overt hypothyroidism	High TSH, low fT4
Subclinical hypothyroidism	High TSH, normal fT4
Overt hyperthyroidism	Low TSH, high fT4
Subclinical hyperthyroidism	Low TSH, normal fT4

Hyperemesis gravidarum; is a syndrome whereby the pregnant women will experience vomiting due to the presence of higher hCG and oestradiol levels compared to normal pregnant women. TSH levels will be suppressed in these women due to the thyroid stimulating effect of the hCG. Some of these women will also have higher serum free T4 concentrations resulting in overt hyperthyroidism. Vomiting with absence of other signs and symptoms of hyperthyroidism helps to distinguish this from other causes. Again, this is transient and is expected to resolve by the end of the first trimester. Only symptomatic treatment for the vomiting is required and there is no role for antithyroid drugs.

Pregnant women in whom overt hyperthyroidism (most often due to Graves' disease) is not corrected are at increased of spontaneous miscarriage, congestive heart failure, thyroid storm, preterm birth, pre-eclampsia, foetal growth restriction and increased perinatal morbidity and mortality (6-8). Treatment options include carbimazole, methiamazole or propylthiouracil. These block the thyroid hormones synthesis and reduce titre of TSH receptor antibodies. There is in indecision in literature about the choice of drugs for hyperthyroidism in pregnancy. Primary care physicians are likely to need input from specialists in the management of pregnant women with Graves' disease.

Hypothyroidism

Overt hypothyroidism in pregnancy is defined as having an elevated population and trimester specific TSH concentration with reduced free T4 concentration. According to ATA 2017 guidelines when local reference ranges are not available an upper limit of TSH can be set at 4mU/L (3). The prevalence of hypothyroidism is estimated to be around 2% whilst 0.5% of all pregnant women will have overt hypothyroidism (9,10). The most common cause of hypothyroidism in pregnancy is chronic autoimmune thyroiditis (Hashimoto's disease). Other less common causes include iodine deficiency, previous radioactive iodine therapy and thyroidectomy.

Clinical symptoms of hypothyroidism during pregnancy is similar to those that non pregnant women experience, which can include general tiredness, cold intolerance, constipation and weight gain. Some women will not have any symptoms at all whereas in others it may be mild and difficult to differentiate from physiological changes attributed to the pregnancy.

Over the last few decades observational studies have consistently shown that untreated overt hypothyroidism has been associated with increased risk for adverse pregnancy complications. As well as the classic detrimental effects on foetal neurocognitive development, some of the other complications include increased risk of miscarriage, premature births, low birth weight and gestational hypertension (11-13). Due to these well-established associations between overt hypothyroidism and risk to the mother and foetus, it is essential that this condition is detected and treated at the earliest opportunity with levothyroxine to stabilise the maternal serum TSH levels within recommended trimester specific reference range. ATA recommend that 'parallel to treatment of hypothyroidism in (the) general population, it is reasonable to target a TSH in the lower half of the trimester-specific reference range. When this not available, it is reasonable to target maternal TSH concentration below 2.5mU/L' (3).

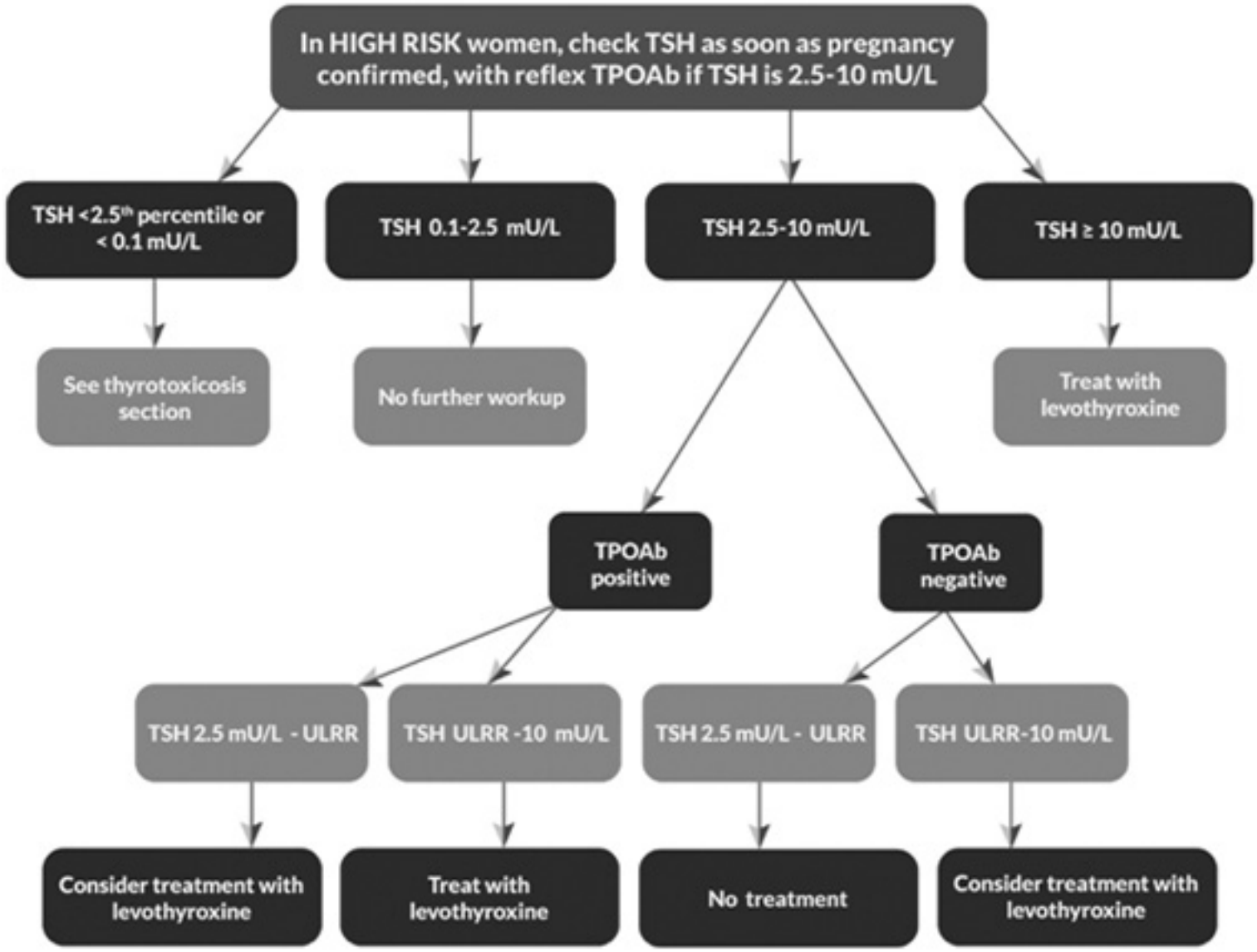
Subclinical Hypothyroidism

In the last few decades subclinical hypothyroidism has emerged as a clinical topic which has generated a great deal of attention and debate especially when considered in pregnant women. It has become a stumbling block when it comes to recommending universal screening for thyroid dysfunction in pregnancy. In context of pregnancy, its incidence is more common than overt hypothyroidism, with an estimate from 15-28% in regions where there is no iodine deficiency (14). One of the main issues has been in defining subclinical hypothyroidism because there has been a lack of agreement amongst societies around the world about what cut off values are to be applied to TSH levels. As per ATA 2017 guidelines subclinical hypothyroidism can be defined by a normal free T4 in the presence of elevated TSH concentration (3). The upper limit of normal TSH is different in each trimester and should be defined by local laboratories to reflect the population demographics. However, it is recognised that population derived trimester specific data and reference ranges will not be widely available in which case an upper limit of 4.0mU/L can be used (3). To highlight the difficulty in defining and diagnosing subclinical hypothyroidism, it is to be noted that ATA's 2017 reference ranges for TSH are higher than the previous guidelines in 2011.

In subclinical hypothyroidism the risk of complications is lower compared to pregnant women who have overt hypothyroidism. However, there have been numerous studies in which women with subclinical hypothyroidism were at higher risk of severe preeclampsia, placental abruption, preterm delivery, neonatal respiratory distress syndrome and miscarriage in comparison to euthyroid women (15-19). These risks in mildly elevated TSH become even higher in the presence of thyroid peroxidase antibodies (TPOAb). Therefore, ATA recommends testing of TPOAb in pregnant women who have a TSH level above 2.5mU/L.

Whilst there are many studies which have demonstrated the increased risks associated with subclinical hypothyroidism, only a few small studies have actually been done to investigate the impact of treatment with levothyroxine in these women. Therefore, the treatment of pregnant women who have subclinical hypothyroidism with levothyroxine is just as controversial as its diagnosis. ATA recommends consideration for treatment with levothyroxine in subclinical hypothyroidism when TSH level is greater than 2.5mU/L with the presence of TPOAb or TSH level above 10mU/L without TPOAb (Figure 1). The ATA 2017 guidelines suggest that treatment of subclinical

Figure 1: Testing for thyroid function in pregnancy with references ranges – from ATA guidelines (3)



hypothyroidism in pregnant women, especially those with TPOAb may reduce the risk of adverse outcomes (3). However, it is not clear whether the treatment with levothyroxine actually reduces the risk of complications for the mother and baby in this situation. One of the limitations of the data from some of the studies is the start of levothyroxine treatment after the first trimester, which could be too late. A metanalysis of 18 studies in 2016 acknowledged that 'subclinical hypothyroidism during pregnancy is associated with multiple adverse maternal and neonatal outcomes. The value of levothyroxine therapy in preventing these adverse outcomes remains uncertain' (20). However, ATA does acknowledge despite the limitations of data from interventional trials for treatment of subclinical hypothyroidism, the aggregate data available does suggest benefit of treatment. The task force also acknowledged the very low risk in initiating low dose treatment with levothyroxine 50 micrograms.

Screening

The issue of screening for thyroid disease either before or during pregnancy is a controversial one which experts continue to debate around the world. Screening is defined by WHO as the presumptive identification of recognised disease in an apparently healthy, asymptomatic population by means of test or examinations that can be applied rapidly and easily to the target population (21). Before universal screening can be recommended, the condition for which screening is being suggested must fulfil the WHO 10-point criteria for screening. This is based on a report called 'Principles and Practice of Screening for Disease', by James Wilson and Gunner Jungner in 1968 (Table 2).

The idea of screening for thyroid dysfunction in pregnancy is keenly debated by those for and against it. Those in favour argue that careful analysis of these 10 criteria provides a persuasive case for universal thyroid screening in pregnancy. For criteria 1, it is well established that thyroid dysfunction, particularly untreated overt thyroid disease and autoimmunity in pregnancy are associated with adverse maternal and foetal outcomes and are therefore an important health problem. Furthermore, in pregnant women with overt hypothyroidism who are not diagnosed, the majority will remain hypothyroid after pregnancy, with a mean time to diagnosis in one of the studies being 5 years (23). Treatment of both hypothyroidism and hyperthyroidism results in improved outcomes with treatment and testing being both acceptable and widely available (criteria 2, 3, 5 and 6). For hypothyroidism in particular, there is a well-recognised latent asymptomatic stage (criteria 4 and 7). Thyroid status can be accurately assessed with inexpensive and widely available measurement of TSH, fT4 Levels and TPOAb. The cost of universal thyroid screening is favourable even if only the overt disease is considered (criteria 9). Also, the nature of screening in pregnancy ensures that it will be a continuous process (criterion 10).

However, those against universal thyroid screening argue that screening struggles to meet criterion 8 as a policy on whom to treat is yet to be agreed. Whilst all societies around the world would recommend treatment of overt thyroid disease, there is much greater debate about treating subclinical hypothyroidism with levothyroxine. They argue that overt thyroid dysfunction is less common than subclinical dysfunction and can be identified by clinical assessment and subsequent testing based on risk factors. Therefore, the biggest impact of universal screening would be identification of a large proportion of patients with subclinical hypothyroidism.

The main issue in the context of screening seems to be related to the lack of consistent evidence for treatment and effectiveness amongst the population of pregnant women with subclinical hypothyroidism. Whilst retrospective studies have shown some benefit in treatment with levothyroxine, this has not been replicated in prospective trials (23,24). A RCT by Negro and colleagues investigated the benefit of universal screening of pregnant women and the subsequent treatment when they had a TSH level of >2.5mU/L. In this study they randomised 4,500 women to universal screening versus screening of women at high risk of thyroid disease. Those women who were positive for TPOAb and had a TSH>2.5 mU/L were treated with levothyroxine in the first trimester. The study showed that there was no significant difference in adverse outcomes between the universally screened cohort versus those women who underwent high risk screening (25). Furthermore, results of the TABLET trial from UK that ATA 2017 guidelines refer to, have also been published in 2019 which concluded that, 'the use of levothyroxine in euthyroid women with thyroid peroxidase antibodies did not result in higher rate of live births than placebo' (26).
One of the largest prospective studies on 22,000 women, investigated the effect of treatment with levothyroxine on maternal hypothyroidism in early pregnancy. This study provided high quality evidence that hypothyroidism was far more likely to be diagnosed during pregnancy when women were screened (measurement of TSH and/or fT4) compared to with no screening. The incidence of hypothyroidism was 4.5% in the screened population and 5% in the unscreened group who had their TSH and fT4 samples stored until after birth, at which point 5% were diagnosed with hypothyroidism. Although, higher rates of hypothyroidism were diagnosed, there were no obvious difference between the two groups in terms of preterm births, low birth weight in the new born, or any neurocognitive disability at age of 3 (27).

Another study that was ongoing at the time the ATA guidelines were published in 2017 was a multicentre, RCT conducted by the National Institute of Health in the US. This study was evaluating the effect of levothyroxine treatment in pregnant women with subclinical hypothyroidism on the children's neurocognition. The results of the study also revealed that, 'treatment for subclinical hypothyroidism or hypothyroxinaemia at the beginning, between 8 and 20 weeks of gestation, did not result in significantly better cognitive outcomes in children through 5 years of age than no treatment for those conditions' (28).

ATA 2017 guidance with regards to screening for thyroid dysfunction concluded that; 'There is insufficient evidence to recommend for or against universal screening for abnormal TSH concentrations in early pregnancy' (3). Instead, the advice is all women planning pregnancy or newly pregnant should have a clinical assessment and if they have risk factors for thyroid disease then they should be offered serum TSH test.

Both the American College of Obstetricians and Gynecologists (ACOG) (2015) and the ATA 2017 clinical practice guidelines support screening of women at high risk for thyroid dysfunction before they become pregnant, or early in pregnancy (29,3). The European Thyroid Association guidelines concur with the ATA and ACOG regarding universal screening. However, these guidelines note that while not formally recommended, most of the authors support universal screening given that a substantial number of women with thyroid dysfunction may be missed with targeted screening strategies (30, 3). This was confirmed in a survey conducted in Maine which showed that many practitioners have already implemented routine TSH testing in pregnant women (30). A European survey found similar results, with 42% of responders screening all pregnant women for thyroid dysfunction (31). In fact, some countries like Spain, China and Poland are already recommending universal thyroid screening for pregnant women (32-34).

Table 2: World Health Organisation Screening Principles (Wilson & Jungner, 1968) (22).

1	The condition sought should be an important health problem
2	There should be an accepted treatment for patients with recognised disease
3	Facilities for diagnosis and treatment should be available
4	There should be a recognisable latent or early symptomatic stage
5	There should be suitable test or examination
6	The test should be acceptable to the population
7	The natural history of the condition, including development from the latent to declared disease should be adequately understood
8	There should be agreed policy on whom to treat as patients
9	The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to the possible expenditure on medical care as a whole
10	Case findings should be a continuous process and not a "once and for all" project

Table 3: List of risk factors for thyroid dysfunction screening in pregnancy (3)

1. A history of hypothyroidism/hyperthyroidism or current symptoms/signs of thyroid dysfunction
2. Known thyroid antibody positivity or presence of a goitre
3. History of head or neck radiation or prior thyroid surgery
4. Age >30 years
5. Type 1 diabetes or other autoimmune disorders
6. History of pregnancy loss, preterm delivery, or infertility
7. Multiple prior pregnancies (≥2)
8. Family history of autoimmune thyroid disease or thyroid dysfunction
9. Morbid obesity (BMI ≥40 kg/m2)
10. Use of amiodarone or lithium, or recent administration of iodinated radiologic contrast
11. Residing in an area of known moderate to severe iodine insufficiency

Conclusion

From observational and prospective studies over the last 3 decades, it has been well established that thyroid dysfunction can significantly impact a pregnant woman and her child. Thyroid dysfunction is common in women of child-bearing age and also results in substantial adverse obstetric and child neurodevelopmental outcomes. Furthermore, thyroid dysfunction can be readily diagnosed with reliable blood tests and easily corrected with inexpensive and available treatments, resulting in decreased rates of adverse outcomes. Given the dependence of the developing foetus on adequate maternal thyroid function, especially in early pregnancy, as well as the severity of outcomes in untreated thyroid disease, it makes sense for screening to take place as early as possible so that appropriate treatment can be administered without delay.

Universal screening for thyroid disease in pregnancy can identify patients with thyroid disease requiring treatment, and ultimately decrease rates of complication. The issue, therefore forms key debate in the world of thyroidology and obstetrics. American and European guidelines recommend screening only high-risk patients, which would appear to miss the majority of cases of overt thyroid dysfunction. However, opponents of universal thyroid screening argue that, asymptomatic borderline thyroid abnormalities such as subclinical hypothyroidism form the bulk of cases of thyroid dysfunction seen in pregnancy, and that there is a lack of high-quality evidence to support their screening and treatment. Due to the absence of strong evidence showing a benefit of levothyroxine therapy for subclinical hypothyroidism in pregnancy, confusion has arisen about the utility of screening using TSH during pregnancy. Therefore, well conducted large randomised trials with levothyroxine are still needed at early stage of pregnancy or preconception to refine the available information and settle this debate.

Those in favour argue that economic models have shown compared to high-risk screening; universal screening is cost effective even if only overt hypothyroidism was assumed to have adverse obstetric effects. As a result, several countries now implement universal screening. Also an increasing number of providers are performing universal screening, contrary to society guidelines. Furthermore, various prominent contributors to this field have argued that the limited evidence concerning the impact of untreated and treated subclinical disease has become a distraction from the core rationale for universal screening,

which is the beneficial impact of detecting and treating overt thyroid disease. They point out that the evidence supporting universal screening for overt disease stands independently from that of subclinical disease. It remains to be seen whether the views and independent practises of expert contributors to the society guidelines lead to change in guidelines in the near future in this important area.

References

1 - Glinoer D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocrine reviews. 1997 Jun 1;18(3):404-33.

2- Ballabio M, Poshyachinda M, Ekins R. Pregnancy-induced changes in thyroid function: role of human chorionic gonadotropin as putative regulator of maternal thyroid. The Journal of Clinical Endocrinology & Metabolism. 1991 Oct 1;73(4):824-31.

3 - Alexander EK, Pearce EN, Brent GA et al. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. Thyroid. 2017 Mar 1;27(3):315-89.

4 - Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocrine reviews. 2010 Oct 1;31(5):702-55.

5 - Cooper D, Laurberg P. Hyperthyroidism in pregnancy. The Lancet Diabetes & Endocrinology. 2013;1(3):238-249.

6 - Davis L, Lucas M, Hankins G, Roark M, Gary Cunningham F. Thyrotoxicosis complicating pregnancy. American Journal of Obstetrics and Gynecology. 1989;160(1):63-70.

7 - Millar LK, Wing DA, Leung AS, et al. Low birth weight and preeclampsia in pregnancies complicated by hyperthyroidism. Obstetrics & Gynecology. 1994 Dec 1;84(6):946-9.

8 - Kriplani A, Buckshee K, Bhargava V, Takkar D, Ammini A. Maternal and perinatal outcome in thyrotoxicosis complicating pregnancy. European Journal of Obstetrics & Gynecology and Reproductive Biology. 1994;54(3):159-163.

9 - Taylor P, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus J, Dayan C et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nature Reviews Endocrinology. 2018;14(5):301-316.

10 - Allan W, Haddow J, Palomaki G, Williams J, Mitchell M, Hermos R et al. Maternal thyroid deficiency and pregnancy complications: implications for population screening. Journal of Medical Screening. 2000;7(3):127-130.

11- Casey BM, Dashe JS, Wells CE, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstetrics & Gynecology. 2005 Feb 1;105(2):239-45.

12- Allan WC, Haddow JE, Palomaki GE, et al. Maternal thyroid deficiency and pregnancy complications: implications for population screening. Journal of medical screening. 2000 Sep 1;7(3):127-30.

13 - Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle O. Overt and Subclinical Hypothyroidism Complicating Pregnancy. Thyroid. 2002;12(1):63-68.

14 - Wiles KS, Jarvis S, Nelson-Piercy C. Are we overtreating subclinical hypothyroidism in pregnancy? BMJ. 2015 Oct 12;351:h4726.

15 - Liu H, Shan Z, Li C, et al. Maternal subclinical hypothyroidism, thyroid autoimmunity, and the risk of miscarriage: a prospective cohort study. Thyroid. 2014 Nov 1;24(11):1642-9.

16 - Stagnaro-Green A, Chen X, Bogden JD, Davies TF, Scholl TO. The thyroid and pregnancy: a novel risk factor for very preterm delivery. Thyroid. 2005 Apr 1;15(4):351-7.

17 - Breathnach FM, Donnelly J, Cooley SM, Geary M, Malone FD. Subclinical hypothyroidism as a risk factor for placental abruption: Evidence from a low-risk primigravid population. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2013 Dec;53(6):553-60.

18 - Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A. Increased pregnancy loss rate in thyroid antibody negative women with TSH levels between 2.5 and 5.0 in the first trimester of pregnancy. The Journal of Clinical Endocrinology & Metabolism. 2010 Sep 1;95(9): E44-8.

19 - Lee SY, Cabral HJ, Aschengrau A, Pearce EN. Associations Between Maternal Thyroid Function in Pregnancy and Obstetric and Perinatal Outcomes. The Journal of Clinical Endocrinology & Metabolism. 2020 May;105(5):dgz275.

20 - Maraka S, Ospina NM, O'Keeffe DT, et al. Subclinical hypothyroidism in pregnancy: a systematic review and meta-analysis. Thyroid. 2016 Apr 1;26(4):580-90.

21 - Abu BM. A Successful Model of Cancer Screening in Low Resource Settings: Findings of an Integrated Cancer Screening Camp from a Rural Setting of North India. Asian Pacific Journal of Cancer Care. 2020 Jun 7;5(2):83-6.

22 - Wilson JM, Jungner G. World Health Organization. Principles and practice of screening for disease.

23 - Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. New England Journal of Medicine. 1999 Aug 19;341(8):549-55.

24 - Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle O. Overt and subclinical hypothyroidism complicating pregnancy. Thyroid. 2002 Jan 1;12(1):63-8.

25 - Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A. Universal screening versus case finding for detection and treatment of thyroid hormonal dysfunction during pregnancy. The Journal of Clinical Endocrinology & Metabolism. 2010 Apr 1;95(4):1699-707.

26 - Dhillon-Smith RK, Middleton LJ, Sunner KK, et al. Levothyroxine in women with thyroid peroxidase antibodies before conception. New England Journal of Medicine. 2019 Apr 4;380(14):1316-25.

27 - Lazarus JH, Bestwick JP, Channon S, et al. Antenatal thyroid screening and childhood cognitive function. New England Journal of Medicine. 2012 Feb 9;366(6):493-501.

28 - Casey BM, Thom EA. Subclinical Hypothyroidism or Hypothyroxinemia in Pregnancy. The New England Journal of Medicine. 2017 Aug 1;377(7):701-.

29 - Korevaar TI, Medici M, Visser TJ, Peeters RP. Thyroid disease in pregnancy: new insights in diagnosis and clinical management. Nature Reviews Endocrinology. 2017 Oct;13(10):610-22.
30 - Lazarus J, Brown RS, Daumerie C, Hubalewska-Dydejczyk A, Negro R, Vaidya B. 2014 European thyroid association guidelines for the management of subclinical hypothyroidism in pregnancy and in children. European thyroid journal. 2014;3(2):76-94.
31 - Lazarus J, Brown RS, Daumerie C, Hubalewska-Dydejczyk A, Negro R, Vaidya B. 2014 European thyroid association guidelines for the management of subclinical hypothyroidism in pregnancy and in children. European thyroid journal. 2014;3(2):76-94.
32 - Vila L, Velasco I, González S, et al. Detection of thyroid dysfunction in pregnant women: universal screening is justified. Endocrinología y Nutrición (English Edition). 2012 Nov 1;59(9):547-60.
33 - Zhou Q, Acharya G, Zhang S, Wang Q, Shen H, Li X. A new perspective on universal preconception care in China. Acta obstetricia et gynecologica Scandinavica. 2016 Apr;95(4):377-81.
34 - Hubalewska-Dydejczyk A, Trofimiuk-Müldner M. The development of guidelines for management of thyroid diseases in pregnancy–current status. In Thyroid Research 2015 Dec (Vol. 8, No. 1, pp. 1-3). BioMed Central.

Irritable bowel syndrome: Clinical review

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Abstract

Irritable Bowel Syndrome (IBS) is a highly prevalent gastrointestinal disorder affecting over 10% of the global population. It is a condition managed mostly in primary care but can often result in referral to secondary care. The characteristic features of IBS are abdominal pain or discomfort with a change in bowel habit or defecation. Other features include bloating and abdominal distension. There is no test for diagnosing IBS and it is largely a diagnosis of exclusion. Patients are classified based on the Rome IV criteria and categorised based on the predominant symptom. The pathogenesis of IBS is understood to be multifactorial therefore the treatment options are diverse, seeking to address the IBS patient by using a holistic approach. Subsequently, therapeutic treatments are constantly evolving in an attempt to best manage the symptoms of IBS. In this review, we will aim to put a spotlight on IBS and in particular focus on the pathophysiology of IBS and how this understanding shapes how we manage IBS based on the current medical guidelines.

Key words: Irritable bowel syndrome, pathophysiology, diagnosis, treatment

Background

Irritable Bowel Syndrome (IBS) is a gastrointestinal (GI) disorder that is characterised by altered bowel habits in conjunction with abdominal pain and/or bloating without structural or chemical abnormalities. IBS can severely impair quality of life and poses a significant health burden. As there is no single indicative test for IBS, and as it is a diagnosis of exclusion, diagnosing the condition can prove to be a challenge (1). Patients often present after a lengthy period since the initial symptoms develop typically with stress or dietary triggers. Psychological co-morbidities like depression often co-exist in patients with IBS which has produced many questions regarding the cause and true nature of IBS. The New England Journal of Medicine has in its archives dating back to the 1850s, content which alludes to the varied presentation (alternating diarrhoea and constipation) of IBS which we know now describes IBS-M (IBS-mixed variant), a mixed version of IBS. Cumming reported “The bowels are at one time constipated, another lax, in the same person. How the disease has two such different symptoms I do not profess to explain”(2).

Over time, our understanding has evolved and IBS which was once regarded an exclusively functional GI condition is now seen to be more complex. Understanding the minutiae of the possible pathophysiological theories for IBS symptoms is increasingly important because newer pharmacotherapy agents are beginning to target these previously unknown mechanisms. Altered gastrointestinal motility, visceral hypersensitivity, post infectious reactivity, brain-gut interactions, alteration in faecal micro flora, bacterial overgrowth, food sensitivity, carbohydrate malabsorption, and intestinal inflammation have been considered as possible causes in the pathophysiology of IBS (3).

Epidemiology

The prevalence of IBS differs widely across the globe. Based on meta-analysis data of numerous study populations comprising over 250,000 subjects, the global prevalence of IBS is estimated to be over 11% (95% CI 9.8%-12.5%) with different parts of the world with different prevalent rates. Initially, studies found a low prevalence of IBS in developing countries. Recent research has found an increased prevalence in the developing nations. As economies begin to prosper, lifestyles have been found to become more Western-centric, possibly explaining this change (4, 5). In a large meta-analysis study, the prevalence of IBS in women was 67% higher when compared with men and more predominantly in the working age (95% CI 1.53-1.82) (6). The increased prevalence was predominantly found in the West and women were more likely to display symptoms suggestive of IBS-C rather than IBS-D. In the US, it is said that 3 in 10 people with IBS consult a primary care physician. This adheres to the trend of IBS in the western world. Therefore it is widely accepted that the majority of people with IBS remain undiagnosed in the community (7).

Pathophysiology

The cause of IBS is not fully understood however many theories have been proposed over time which have guided the approaches to managing the condition. Earlier research stipulated that IBS has traditionally been regarded as a condition exclusively associated with abnormal colonic motility. This did not fully explain the spectrum of clinical presentations of IBS and this concept has developed over time in response to new evidence and ongoing research (8).

The pathophysiology of IBS is not fully understood, but certain pathogenic factors have been identified that could explain the onset or development of IBS. Growing evidence has suggested that IBS is not solely a functional disorder as once believed.

Altered gastrointestinal motility

Early evidence from manometric and colonic transit studies revealed that patients with IBS were found to have contractions in dense clusters in the small intestine associated with symptoms like abdominal pain. Secondly, patients were found to have altered gastric transit, either too fast or too slow, resulting in diarrhoea and constipation respectively. In one study, postprandial subjects demonstrated high amplitude colonic contractions coinciding with abdominal pain suggesting a relationship with food ingestion (9).

Visceral hypersensitivity

There is sufficient evidence to suggest that many differences exist in IBS. Experimental studies revealed that patients with IBS have been found to have increased sensitivity to balloon distension in both the upper and lower GI tracts. Further to this, IBS patients have also been found to have a heightened sensitivity to intestinal contractions when compared with normal subjects. The exact mechanisms are not fully understood but it has been proposed that patients with IBS may exhibit a heightened pain response to visceral stimulation (10).

Impaired gut microbiota

Several trillion microbes reside in our bowel and make up over a thousand different species. The most recognisable bacteria are Lactobacillui and Bifidobacteria (11). Such bacteria, also known as beneficial bacteria are known to have anti-inflammatory properties via an immune mediated response. Also, microbiota is thought to be essential in ensuring the homeostasis of the gut-brain axis which is regarded as a key element in the pathophysiology of IBS (12). The current assumption is that IBS patients have altered microbiota in their intestine. A study involving over one hundred IBS patients demonstrated that IBS patients had a different composition of gut microbiota. IBS patients were found to have less variety of bacteria and fewer beneficial bacteria such as Lactobacillus and Bacteroids species whilst the number of pathogenic bacteria were found to be increased (13). In IBS certain gut bacteria can generate chemicals which produce gas leading to abdominal distension. It has been suggested that an overpopulation of gas-producing bacteria in the intestine, an alteration in the gut microbiota, may account for abdominal distension in IBS patients.

Gut-brain axis

IBS is a condition in which there is a disruption in the gut-brain axis. This axis is made up the central nervous system (CNS), the hypothalamic pituitary axis (HPA) and the enteric nervous system (ENS). Neural impulses are propagated from the gut via the vagus nerve, the spinal and the enteric nerves. The vagus nerve plays the most pivotal role in the communication between the gut and the brain. The hypothalamic pituitary axis (HPA) is also integral in this communication link because it modulates adaptive responses against stress through the production of corticosteroids alongside regulating important processes such as digestion and the immune system. Signals from CNS are transmitted by neuroendocrine neurotransmitters like serotonin to the gut to alter the behaviour of gut microbiota (14).Various neuroimaging studies on IBS patients have supported the gut-brain axis dysregulation hypothesis. Stress is thought to act on the emotional limbic system, resulting in a release of adrenocorticotropic hormone and cortisol which then engages with the ENS resulting in symptoms like abdominal pain and loose motions (due to the induction of colonic dysmotility and visceral sensitivity). Several immune mediators are thought to be involved (e.g. IL-6) in this process (15).

Dietary intolerance

One of the commonest contributing factors for troublesome symptoms in IBS is food intolerance. Patients with IBS typically report that certain foods trigger symptoms. An overwhelming majority of IBS patients report some form of food intolerance. A specific category of food known as FODMAPS (Table 1) are thought to be partly

Table 1: Dietary FODMAPs (18).

	Word that corresponds to letter in acronym	Compounds in this category	Foods that contain these compounds
F	Fermentable		
O	Oligosaccharides	Fructans, galacto-oligosaccharides	Wheat, barley, rye, onion, leek, white part of spring onion, garlic, shallots, artichokes, beetroot, fennel, peas, chicory, pistachio, cashews, legumes, lentils, and chickpeas
D	Disaccharides	Lactose	Milk, custard, ice cream, and yogurt
M	Monosaccharides	"Free fructose" (fructose in excess of glucose)	Apples, pears, mangoes, cherries, watermelon, asparagus, sugar snap peas, honey, high-fructose corn syrup
A	And		
P	Polyols	Sorbitol, mannitol, maltitol, and xylitol	Apples, pears, apricots, cherries, nectarines, peaches, plums, watermelon, mushrooms, cauliflower, artificially sweetened chewing gum and confectionery

responsible for these symptoms. These are foods that contain fermentable oligosaccharides, disaccharides, monosaccharides and polyols (16). FODMAPs cause IBS symptoms because they are fermented by gut bacteria and due to their osmotic effects. Meta-analysis data has demonstrated an improvement in symptoms and a 70% improvement in quality of life in patients who adopt a low FODMAP diet (17). Lactose containing foods and gluten rich diets have also been found to have a possible link to the pathogenesis of IBS symptoms but the evidence is not robust enough to substantiate this up to now.

Post-infectious IBS

Acute GI infections are a predisposing factor for development of IBS. It is thought that approximately 10% of patients with IBS had a preceding infectious illness. Prospective data has shown that 3-36% of GI infections can lead to IBS symptoms (19). The cause of persistent or new bowel symptoms after an acute GI infection is uncertain, but several mechanisms have been highlighted. Enteritis may increase the risk of IBS via one of many mechanisms which include disruption of the mucosal nerves leading to irritability, bile acid dysfunction and malabsorption, and distortion of colonic flora (20). One study looked at 19,000 patients who consumed contaminated drinking water which contained Giardia lamblia, norovirus and Campylobacter jejuni (21). The researchers noted that the risk for IBS symptoms was more profound in those with a background of anxiety and depression. This reinforces the concept of the gut-brain interaction in IBS and reaffirms the hypothesis that the pathophysiology of IBS is multifactorial.

Genetics

Growing evidence shows that there may be genetic link to IBS. 5CN5A is a sodium channel gene mutation which is associated with abdominal pain in IBS and is thought to be a common denominator in 2% of IBS patients (22). A link between congenial sucrose isomaltase deficiency and IBS has also been considered highlighting the possibility of genes in the predisposition of IBS (23). These associations require further research but further demonstrate the ever changing understanding of the pathophysiology of IBS.

Serotonin dysregulation

There is evidence to suggest that serotonin (5HT) is an important neurotransmitter involved in the stimulation of gut peristalsis. A function of 5HT is to enable gut motility and secretion of intestinal matter. 5HT is also thought to be pivotal in visceral sensitivity and blood flow (24). Abnormalities in the serotonin reuptake transport system have been discovered in patients with IBS. 5-HT2A receptor polymorphisms may be associated with the development of IBS. A significant association has also been found between the SS genotype of serotonin re-uptake transporter polymorphism (SERT-P) and IBS-C (25). Research has also found that patients with IBS-C have an increased serotonin concentration in the colonic mucosa compared with IBS-D sufferers. Therefore there is a possible link between the impaired release of serotonin and the development IBS symptoms (26).

Diagnosis and Assessment

Without the presence of a specific disease marker, several diagnostic criteria have been developed to standardise the diagnosis of IBS. The diagnostic criteria have developed over many years from Manning et al in 1979, to the Rome I criteria in 1994, and most notably, Rome IV criteria (2006). The current and widely used Rome IV criteria (Table 2) is the foundation upon which The National Institute for Health and Care Excellence (NICE) offers clinical recommendations in diagnosing IBS in the UK (27).

Routine diagnostic testing is not recommended in IBS as it is a diagnosis of exclusion and no spe cific test is available to confirm a diagnosis. It is important for clinicians to perform a detailed history and examination of patients with IBS to exclude other important differential diagnoses. Specific attention ought to be made to exclude key alarm features (Table 2) or red flags for GI malignancies.

Table 2 (1, 28)

ROME IV CRITERIA FOR IRRITABLE BOWEL SYNDROME

Patient has recurrent abdominal pain (≥ 1 day per week, on average in the previous 3 months), with an onset ≥ 6 months prior to diagnosis
Abdominal pain is associated with at least two of the following three symptoms: - Pain related to defecation - Change in frequency of stool - Change in form (appearance) of stool
Patient has none of the following warning signs (alarm features): - Age ≥ 50yr, no previous colon cancer screening, and presence of symptoms - Recent change in bowel habit - Evidence of overt GI bleeding (melaena or haematochezia) - Nocturnal pain or passage of stools - Unintentional weight loss - Family history of colorectal cancer of inflammatory bowel disease - Palpable abdominal mass or lymphadenopathy - Evidence of iron deficiency on blood testing - Positive test for faecal occult blood

Where indicated, testing should include a complete blood count, coeliac antibodies, comprehensive metabolic profile, inflammatory markers, erythrocyte sedimentation rate or C-reactive protein, thyroid function tests and if suspected, imaging and cancer tumour markers. Stool sampling should be offered on a case by case basis paying attention to possible infective and inflammatory pathologies (28).

Treatments

Effective counselling and patient education are important initial tools in managing IBS. Such measures can often alleviate the common anxieties and misconceptions about IBS which often act as underlying triggers for symptom relapse. This was highlighted in a study, where 52% of the enrolled patients with IBS assumed that the condition was caused by digestive enzyme deficiency, 34% assumed it required surgical intervention, and over one fifth of patients thought IBS was a precursor to cancer (29).

Patient education should be followed by practice dietary and lifestyle modification advice and evidence based medical therapies. Moderate to severer forms of IBS can be managed simultaneously with psychological therapies where considered appropriate. For some patients, a multidisciplinary approach is likely to achieve better outcomes typically involving primary care physicians, dieticians, nurse practitioners and psychologists or psychiatrists (30).

Medical treatments for IBS are currently symptomatic and there are a wide variety of approaches to management. Initial medications include antispasmodics, prokinetics and bulk-forming agents. If little clinical benefit is found, further symptomatic treatments are available. The variety of treatments available reflects the convoluted and multifaceted pathophysiology involved in the manifestation of IBS symptoms. Therefore it comes as little surprise that there is no single treatment plan that can be used for all IBS patients (31).

Dietary and lifestyle modification

Dietary modifications have heralded successful outcomes anecdotally in the past, however new data has shown positive outcomes in study groups. The low FODMAP diet has for many patients been a beneficial dietary modification resulting in improvement and for some, resolution of IBS symptoms.

Dietary FODMAPs resulted in prolonged hydrogen production and subsequent methane production which lead to typical symptoms of IBS such as excessive gas and bloating. The combination of altered pH levels coinciding with changes to the gut microbiota are thought to contribute to changes in colonic function (32). Two studies compared the low-FODMAP diet to commonly recommended IBS diets (modified NICE guidelines). NICE and low-FODMAP diets were reported to be effective however, one study showed significantly better results in the low-FODMAP diet group, particularly with regard to pain and bloating (33).

There is insufficient evidence on the long term efficacy of FODMAP diets, however in a retrospective study, Maagaard et al highlighted the beneficial effects of the low FODMAP diet on IBS symptoms. In the study, the mean follow up time was 16 months and the majority of IBS patients in the study experienced relief of abdominal pain and bloating following adherence to low FODMAPs (34). Whilst low FODMAP diets have yielded success in patients, the underlying mechanism is not fully understood and perhaps in time with further understanding, diets may become more refined.

The challenges with low FODMAP lie in its compliance as it can be difficult to implement as routine and often requires detailed and time consuming patient education which is dependent on resource availability. Secondly, any elimination diet may be associated with nutritional deficiencies however some studies have shown little detrimental effects on nutritional status (35).

Gluten free diet

Gluten free diets have demonstrated clinical benefit in patients without coeliac disease. A number of published studies have investigated the role of gluten in patients with IBS in recent years. Biesiekierski et al focused on patients in a double-blind, placebo-controlled, re-challenge dietary study. The significant outcome was that those patients exposed to gluten reported uncontrolled symptoms (68%), compared with patients exposed to placebo (40%) (36). Gluten reduction may be helpful in IBS, particularly if a low FODMAP diet did not provide adequate benefit.

Fibre

There is no consensus on whether fibre intake has a favourable effect on IBS sufferers. However, given its benign nature with few side effects, it has been found to be of benefit in patients with IBS-C. Moderate efficacy was seen with constipation but studies found that pain relief was not associated with increased fibre intake (37). Fibre intake should be constantly reviewed in IBS patients, and when indicated, soluble fibre such as psyllium powder or foods high in soluble fibre such as oats are preferred (38).

Lactose intolerance

It is important to consider lactose intolerance in patients with IBS symptoms. There is no evidence to suggest that the incidence of lactose malabsorption is higher in patients with IBS but patients with IBS and lactose intolerance have significantly more noticeable GI symptoms in response to lactose ingestion. Lactose intolerance can be diagnosed via a breath test, however a negative test does not exclude intolerance to cow's milk protein and alternative sources of milk, e.g. other mammals or soy, should be considered (39).

Exercise

There are likely to be many processes involved for symptom relief in response to exercise. Both the physical and psychological benefits are likely to play a key role. Changes in gas transit and colonic transit due to exercise

have provided a rationale for the improved symptoms in IBS. This is supported in a paper by Villoria et al who highlighted that exercise increases gas clearance and reduced the frequency of abdominal bloating (40). Studies have demonstrated a correlation between physical activity and IBS symptom relief. Aerobic activity such as cycling has demonstrated a reduction in intestinal gas production in several studies and protects against the development of IBS according to several studies (41). Engaging in yoga as part of a study has also shown a reduction in IBS symptoms which is thought to be related to increase in sympathetic tone, which is typically reduced in IBS-D (42). Due to the increasing link between IBS and mental health conditions, exercise naturally comes under the spotlight as it has found to benefit or prevent mental health conditions. There is evidence to suggest physical activity has a positive impact on mental health, and in turn, it is assumed that this has a positive impact on IBS symptoms because of the increasingly recognisable gut-brain connection in IBS.

Pharmacological treatment

Antispasmodics

Antispasmodic agents can be used on an 'as required' basis when managing IBS. They offer short term relief for troublesome symptoms associated with IBS such as abdominal pain and/or bloating.

Antispasmodics work by inhibiting smooth muscle contractions in the GI tract such as mebeverine and pinaverine. There are also those that work by utilising anticholinergic or antimuscarinic properties such as those found in hyoscine and dicyclomene (43). A systemic review found that peppermint oil also helps in reducing IBS symptoms and is thought to be a calcium channel antagonist, resulting in relaxation of GI smooth muscle (44).

Despite the fact that antispasmodic medications have not shown significant clinical efficacy based on robust evidence, they are still commonly used in clinical practice. The anticholinergic side effect profile typically consisting of constipation, dry mouth and urinary retention are the most common reasons for early cessation of drug therapy (45).

Probiotics

Probiotics are not routinely recommended in IBS however there is some evidence that probiotics improve symptoms in IBS. Preparations of the lactobacillus species are commercially available and widely consumed by patients with IBS. Trials for lactobacilli have yet to definitively prove its clinical benefit and more research is required in this field to present a stronger argument for its efficacy. Recent evidence based on studies observing the use of multi-strain probiotics (as opposed to mono-strain) has yielded improvement in symptoms for IBS patients (46).
NICE guidelines have not recommended specific bacteria or named probiotic products, however 2017 guidelines summarised that they are a useful self-management option for people with IBS with little adverse effects (27).

Medical management of IBS

Medical treatments in IBS-C

Initial management of constipation in IBS differs in no way to conventional constipation management. The focus centres around dietary and lifestyle modification and adequate oral hydration. Dietary fibre is plentiful in a variety of foods that are also low-FODMAP such as fruits like bananas, vegetables like broccoli and seeds e.g. flaxseeds and pulses (dried seeds of legumes). Soluble fibre such as psyllium is widely available and is an inexpensive adjunct to dietary modifications. Lactulose is a typical over the counter osmotic laxative, which should be avoided in IBS due to its gas-producing and bloating effects (47). Relatively recent randomised controlled trial data has supported the role of soluble fibre in managing IBS. Analysis revealed that wheat bran, a source of insoluble fibre was found not to be of benefit. Methylcellulose is an option for patients who are unable to maintain adequate dietary fibre and it is better tolerated than bran (48). For patients with IBS-C, after a trial of soluble fibre and/or alternative constipation remedies as previously discussed, it is recommended that clinicians should consider treatment with PEG (polyethylene glycol) such as Linaclotide. Linaclotide is a synthetic guanylate cyclase C (GCC) agonist and has shown success in studies for improving IBS symptoms. It is supported strongly by the American Gastroenterological Association in the US and NICE in the UK (49).

A randomised trial involving 139 adults with IBS-C were assigned to PEG or placebo for 1 month. Patients treated with PEG compared with placebo had significantly more frequent bowel movements, improved stool consistency and less severe straining on defecation. There was little change noted with respect to the severity of bloating or abdominal pain however. Diarrhoea is the most common side effect experienced with Linaclotide which can be bothersome to most patients and is typically the cause for withdrawal of treatment (50, 51).

Medical treatments in IBS-D

In IBS patients prone to diarrhoea, there is a typical increase in stool frequency but of normal overall volume. Loperamide, a common antidiarrhoeal can be the initial treatment of choice to be used when required. The evidence for loperamide is lacking in quality but due to its low cost and availability, it can be a useful adjunct to other therapies in countering IBS symptoms (43). An alternative to loperamide albeit with limited evidence is the use of bile acid sequestrants such as cholestyramine. The basis upon this recommendation is that in patients with IBS-D up to half of patients with functional diarrhoea and IBS-D are thought to have bile acid malabsorption (52).

Alosetron is a 5-hydroxytryptamine-3 receptor (5HT-3) antagonist. It is approved in the US for severe IBS-D in female patients in whom symptoms persist for longer than 6 months and who in those who have failed to respond to conventional treatment. Side effects of ischaemic

colitis and complications of severe constipation led to its temporary withdrawal by the Food and Drug Administration (FDA). Following a review, it was reapproved in the US under restricted conditions and starting at low dose regimes (53).

Rifaximin

Rifaximin is an antibiotic approved by FDA that has been found to combat symptoms associated with IBS-D. It is recommended for patients who exhibit moderate/severe IBS symptoms (especially bloating) without constipation and those who fail to respond to conventional therapies. In two large RCT's, 1,260 patients with IBS received rifaximin 550mg three times a day vs placebo for 2 weeks duration and were followed up for 10 weeks. During the initial 1-month follow up phase, patients who received Rifaximin reported relief of IBS symptoms compared with placebo (41% v 32 %) (54). Rifaximin should be used in caution in patients and for an appropriate duration of time. This is because of the risk of bacterial or fungal superinfection such as Clostridioides-difficile associated diarrhoea and pseudomembranous colitis.

Antidepressants in IBS

Antidepressants have been shown to relieve symptoms of IBS. Many antidepressants have analgesic properties and appear to work via their anticholinergic properties by targeting visceral hypersensitivity and central pain sensitisation (55). Tricyclic antidepressants (TCA's) and selective serotonin reuptake inhibitors (SSRI's) have both displayed some benefits in IBS patients according to studies. TCA's typically slow GI transit time, hence are used infrequently and with caution in those with IBS-C. SSRI's have been touted as a better option for IBS-C due to their recognised prokinetic effect on the small intestine. If abdominal pain persists despite initial medical treatment, NICE recommends an off-license indication of low dose TCA such as amitriptyline followed by monthly reviews to determine dose reduction. SSRI's e.g. citalopram or fluoxetine are alternatives if TCA's are not tolerated or contraindicated. TCA's and SSRI's are typically prescribed in patients who have depression. Therefore it is important to counsel patients with IBS that these drugs are used for their analgesic benefits in neuropathic pain and not for depression (56).

Psychological therapies

Psychological therapies have been found to improve patients with IBS symptoms. Studies have indicated a correlation between psychological conditions like anxiety and depression with GI irritability leading to IBS symptoms. As the exact underlying aetiological mechanism for IBS is not fully understood but thought to involve processes within the brain and the gut, psychological therapies attempt to address the former. Therapies include cognitive behavioural therapy, relaxation training, hypnotherapy and dynamic psychotherapy (56).

Many patients report a clear pattern of GI symptoms coinciding with stress or anxiety hence it is reasonable to attempt such therapies. The majority of the trials are limited to small sample sizes with little information on long term follow up. Despite this, many health care practitioners see it as an effective management option for patients.

Novel treatments

There are many exciting developments in the treatment of IBS which often runs parallel to the advances made in our understanding of the pathophysiology of IBS.

Faecal microbiota transplantation (FMT) involves the transfer of faecal matter from a healthy individual into another person (via endoscope into the intestine) with the aim of treating IBS symptoms. It is based on the same premise that probiotics are used but its apparent advantages are that it allows the maturation of a greater number of bacteria and more diverse strains of bacteria in the gut. FMT has been successful in the treatment of recurrent Clostridium difficile infection but the exact mechanism is not fully understood. A number of studies highlight the FMT success is dependent on the characteristics of the stool donor so exciting research into seeking super donors that meet favourable profiles is a growing area of research. It is assumed that microbial diversity is a positive indicator of faecal microbiota transplant success (57, 58).

There is emerging evidence suggesting the possibility of intestinal permeability in IBS. This raises the issue of the leaky gut and some patients have been found to show elevated markers of increased immune activation and raised cytokine levels and mast cells raising the question about a different pathophysiological mechanism. This has raised the potential role of mast cell stabilisers in IBS amongst other theories. Insufficient evidence exists about this concept but this may point to newer therapeutic agents in the future (59).

Conclusion

The role of primary care physicians in reducing the burden of IBS in the community is essential and managing patients with an individualised approach is encouraged. There are promising new developments which may present an exciting future in managing IBS. We have highlighted the growing need to understand the pathophysiological concepts in IBS so that we may understand better not only the treatments that currently exist, but also those that may arise in the future.

References

1) Drossman DA, Corazziari E, Delvaux M, Spiller RC, Talley NJ, Thompson WG, Whitehead WE. Rome III: The Functional Gastrointestinal Disorders, Degnon Associates. Inc., McLean, VA. 2006:1-29.
2) Brenda J, Horwitz BJ, Fisher RS. The irritable bowel syndrome. New Eng J Med. 2001;344:1846-50.
2012 Mar;25(1):46.
3) Occhipinti K, Smith JW. Irritable bowel syndrome: a review and update. Clinics in colon and rectal surgery. 2012 Mar;25(1):46.

4) Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. Clinical gastroenterology and hepatology. 2012 Jul 1;10(7):712-21.
5) Lacy BE, Mearin F, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel disorders. Gastroenterology. 2016 May 1;150(6):1393-407.
6) Lovell RM, Ford AC. Effect of gender on prevalence of irritable bowel syndrome in the community: systematic review and meta-analysis. American Journal of Gastroenterology. 2012 Jul 1;107(7):991-1000.
7) Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. Clinical epidemiology. 2014;6:71.
8) Talley NJ, Spiller R. Irritable bowel syndrome: a little understood organic bowel disease? The Lancet. 2002 Aug 17;360(9332):555-64.
9) Kellow JE, Eckersley GM, Jones M. Enteric and central contributions to intestinal dysmotility in irritable bowel syndrome. Digestive diseases and sciences. 1992 Feb 1;37(2):168-74.
10) Azpiroz F, Bouin M, Camilleri M, Mayer EA, Poitras P, Serra J, Spiller RC. Mechanisms of hypersensitivity in IBS and functional disorders. Neurogastroenterology & Motility. 2007 Jan;19:62-88.
11) Clemente JC, Ursell LK, Parfrey LW, Knight R. The impact of the gut microbiota on human health: an integrative view. Cell. 2012 Mar 16;148(6):1258-70.
12) Casen C, Vebø HC, Sekelja M, Hegge FT, Karlsson MK, Ciemniejewska E, Dzankovic S, Frøyland C, Nestestog R, Engstrand L, Munkholm P. Deviations in human gut microbiota: a novel diagnostic test for determining dysbiosis in patients with IBS or IBD. Alimentary pharmacology & therapeutics. 2015 Jul;42(1):71-83.
13) Parkes GC, Rayment NB, Hudspith BN, Petrovska L, Lomer MC, Brostoff J, Whelan K, Sanderson JD. Distinct microbial populations exist in the mucosa-associated microbiota of sub-groups of irritable bowel syndrome. Neurogastroenterology & Motility. 2012 Jan;24(1):31-9.
14) Raskov H, Burcharth J, Pommergaard HC, Rosenberg J. Irritable bowel syndrome, the microbiota and the gut-brain axis. Gut microbes. 2016 Sep 2;7(5):365-83.
15) Mertz H, Morgan V, Tanner G, Pickens D, Price R, Shyr Y, Kessler R. Regional cerebral activation in irritable bowel syndrome and control subjects with painful and nonpainful rectal distention. Gastroenterology. 2000 May 1;118(5):842-8.
16) Shepherd SJ, Parker FC, Muir JG, Gibson PR. Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. Clinical Gastroenterology and Hepatology. 2008 Jul 1;6(7):765-71.
17) Marsh A, Eslick EM, Eslick GD. Does a diet low in FODMAPs reduce symptoms associated with functional gastrointestinal disorders? A comprehensive systematic review and meta-analysis. European journal of nutrition. 2016 Apr 1;55(3):897-906.
18) Shepherd SJ, Lomer MC, Gibson PR. Short-chain carbohydrates and functional gastrointestinal disorders. American journal of gastroenterology. 2013 May 1;108(5):707-17.
19) Spiller RC. Postinfectious irritable bowel syndrome. Gastroenterology. 2003 May 1;124(6):1662-71.
20) Spiller RC, Jenkins D, Thornley JP, Hebden JM, Wright T, Skinner M, Neal KR. Increased rectal mucosal enteroendocrine cells, T lymphocytes, and increased gut permeability following acute Campylobacter enteritis and in post-dysenteric irritable bowel syndrome. Gut. 2000 Dec 1;47(6):804-11.
21) Wouters MM, Van Wanrooy S, Nguyen A, Dooley J, Aguilera-Lizarraga J, Van Brabant W, Garcia-Perez JE, Van Oudenhove L, Van Ranst M, Verhaegen J, Liston A. Psychological comorbidity increases the risk for postinfectious IBS partly by enhanced susceptibility to develop infectious gastroenteritis. Gut. 2016 Aug 1;65(8):1279-88.
22) Beyder A, Mazzone A, Strege PR, Tester DJ, Saito YA, Bernard CE, Enders FT, Ek WE, Schmidt PT, Dlugosz A, Lindberg G. Loss-of-function of the voltage-gated sodium channel NaV1. 5 (channelopathies) in patients with irritable bowel syndrome. Gastroenterology. 2014 Jun 1;146(7):1659-68.
23) Henström M, Diekmann L, Bonfiglio F, Hadizadeh F, Kuech EM, von Köckritz-Blickwede M, Thingholm LB, Zheng T, Assadi G, Dierks C, Heine M. Functional variants in the sucrase–isomaltase gene associate with increased risk of irritable bowel syndrome. Gut. 2018 Feb 1;67(2):263-70.
24) Kim DY, Camilleri M. Serotonin: a mediator of the brain-gut connection. The American journal of gastroenterology. 2000 Oct 1;95(10):2698.
25) Sikander A, Rana SV, Sinha SK, Prasad KK, Arora SK, Sharma SK, Singh K. Serotonin trans-porter promoter variant: Analysis in Indian IBS patients and control population. Journal of clinical gastroenterology. 2009 Nov 1;43(10):957-61.
26) Miwa J, Echizen H, Matsueda K, Umeda N. Patients with constipation-predominant irritable bowel syndrome (IBS) may have elevated serotonin concentrations in colonic mucosa as compared with diarrhea-predominant patients and subjects with normal bowel habits. Digestion. 2001;63(3):188-94.
27) The National Institute for Health and Care Excellence (NICE) guideline. Irritable Bowel Syndrome in adults: diagnosis and management. Available at https://www.nice.org.uk/guidance/cg61/. Updated April 2017.
28) Ford AC, Lacy BE, Talley NJ. Irritable Bowel Syndrome. N Engl J Med. 2017;376(26):2566-2578. doi:10.1056/NEJMra1607547
29) Halpert A, Dalton CB, Palsson O, Morris C, Hu Y, Bangdiwala S, Hankins J, Norton N, Drossman D. What patients know about irritable bowel syndrome (IBS) and what they would like to know. National Survey on Patient Educational Needs in IBS and development and validation of the Patient Educational Needs Questionnaire (PEQ). American Journal of Gastroenterology. 2007 Sep 1;102(9):1972-82.
30) Ballou S, Keefer L. Psychological interventions for irritable bowel syndrome and inflammatory bowel diseases. Clinical and translational gastroenterology. 2017 Jan;8(1):e214.
31)Mudyanadzo TA, Hauzaree C, Yerokhina O, Architha NN, Ashqar HM. Irritable Bowel Syndrome and Depression: A Shared Pathogenesis. Cureus. 2018 Aug;10(8).

32) Ong DK, Mitchell SB, Barrett JS, Shepherd SJ, Irving PM, Biesiekierski JR, Smith S, Gibson PR, Muir JG. Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. Journal of gastroenterology and hepatology. 2010 Aug;25(8):1366-73.
33) Eswaran SL, Chey WD, Han-Markey T, Ball S, Jackson K. A randomized controlled trial comparing the low FODMAP diet vs. modified NICE guidelines in US adults with IBS-D. American Journal of Gastroenterology. 2016 Dec 1;111(12):1824-32.
34) Maagaard L, Ankersen DV, Végh Z, et al. Follow-up of patients with functional bowel symptoms treated with a low FODMAP diet. World J Gastroenterol. 2016;22(15):4009-4019.
35) Bellini M, Gambaccini D, Bazzichi LA, Bassotti G, Mumolo MG, Fani B, Costa F, Ricchiuti A, De Bortoli N, Mosca M, Marchi S. Bioelectrical impedance vector analysis in patients with irritable bowel syndrome on a low FODMAP diet: a pilot study. Techniques in coloproctology. 2017 Jun 1;21(6):451-9.
36) Biesiekierski JR, Newnham ED, Irving PM, Barrett JS, Haines M, Doecke JD, Shepherd SJ, Muir JG, Gibson PR. Gluten causes gastrointestinal symptoms in subjects without celiac disease: a double-blind randomized placebo-controlled trial. American Journal of Gastroenterology. 2011 Mar 1;106(3):508-14.
37) Bijkerk CJ, Muris JW, Knottnerus JA, Hoes AW, De Wit NJ. Systematic review: the role of different types of fibre in the treatment of irritable bowel syndrome. Alimentary pharmacology & therapeutics. 2004 Feb;19(3):245-51.
38) Hookway C, Buckner S, Crosland P, Longson D. Irritable bowel syndrome in adults in primary care: summary of updated NICE guidance. Bmj. 2015 Feb 25;350:h701.
39) Yang J, Deng Y, Chu H, Cong Y, Zhao J, Pohl D, Misselwitz B, Fried M, Dai N, Fox M. Prev-alence and presentation of lactose intolerance and effects on dairy product intake in healthy subjects and patients with irritable bowel syndrome. Clinical gastroenterology and hepatology. 2013 Mar 1;11(3):262-8.
40) Villoria A, Serra J, Azpiroz F, Malagelada JR. Physical activity and intestinal gas clearance in patients with bloating. American Journal of Gastroenterology. 2006 Nov 1;101(11):2552-7.
41) Lustyk KM, Jarrett ME, Bennett JC, Heitkemper MM. Does a physically active lifestyle improve symptoms in women with irritable bowel syndrome? Gastroenterology Nursing. 2001 May 1;24(3):129-37.
42) Kim YJ, Ban DJ. Prevalence of irritable bowel syndrome, influence of lifestyle factors and bowel habits in Korean college students. International journal of nursing studies. 2005 Mar 1;42(3):247-54.
43) Brandt LJ, Chey WD, Foxx-Orenstein AE, Schiller LR, Schoenfeld PS, Spiegel BM, Talley NJ, Quigley EM. American college of gastroenterology task force on irritable bowel syndrome. Am J Gastroenterol. 2009;104(Suppl 1): S1-35.
44) Khanna R, MacDonald JK, Levesque BG. Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. Journal of clinical gastroenterology. 2014 Jul 1;48(6):505-12.
45) Drossman DA. Camilleri M, Mayer EA, Whitehead WE. AGA technical review on irritable bowel syndrome. Gastroenterology. 2002;123:2108-31.
46) Dale HF, Rasmussen SH, Asiller ÖÖ, Lied GA. Probiotics in irritable bowel syndrome: An up-to-date systematic review. Nutrients. 2019 Sep;11(9):2048.
47) Jailwala J, Imperiale TF, Kroenke K. Pharmacologic treatment of the irritable bowel syndrome: a systematic review of randomized, controlled trials. Annals of Internal medicine. 2000 Jul 18;133(2):136-47.
48) Moayyedi P, Quigley EM, Lacy BE, Lembo AJ, Saito YA, Schiller LR, Soffer EE, Spiegel BM, Ford AC. The effect of fiber supplementation on irritable bowel syndrome: a systematic review and meta-analysis. American Journal of Gastroenterology. 2014 Sep 1;109(9):1367-74.
49) Weinberg DS, Smalley W, Heidelbaugh JJ, Sultan S, American Gastroenterological Association. American Gastroenterological Association Institute guideline on the pharmacological management of irritable bowel syndrome. Gastroenterology. 2014 Nov;147(5):1146.
50) Chapman RW, Stanghellini V, Geraint M, Halphen M. Randomized clinical trial: macrogol/PEG 3350 plus electrolytes for treatment of patients with constipation associated with irritable bowel syndrome. American Journal of Gastroenterology. 2013 Sep 1;108(9):1508-15.
51) Chandar AK. Diagnosis and treatment of irritable bowel syndrome with predominant constipation in the primary-care setting: focus on linaclotide. International journal of general medicine. 2017;10:385.
52) Wedlake L, A'hern R, Russell D, Thomas K, Walters JR, Andreyev HJ. Systematic review: the prevalence of idiopathic bile acid malabsorption as diagnosed by SeHCAT scanning in patients with diarrhoea-predominant irritable bowel syndrome. Alimentary pharmacology & therapeutics. 2009 Oct;30(7):707-17.
53) Lacy BE, Nicandro JP, Chuang E, Earnest DL. Alosetron use in clinical practice: significant improvement in irritable bowel syndrome symptoms evaluated using the US Food and Drug Administration composite endpoint. Therapeutic advances in gastroenterology. 2018 May 8;11:1756284818771674.
54) Schey R, Rao SS. The role of rifaximin therapy in patients with irritable bowel syndrome without constipation. Expert Review of Gastroenterology & Hepatology. 2011 Jul 1;5(4):461-4.
55) Camilleri M, Boeckxstaens G. Dietary and pharmacological treatment of abdominal pain in IBS. Gut 2017;66:966-74. https://doi.org/10.1136/gutjnl-2016-313425
56) Ford AC, Quigley EM, Lacy BE, Lembo AJ, Saito YA, Schiller LR, Soffer EE, Spiegel BM, Moayyedi P. Effect of antidepressants and psychological therapies, including hypnotherapy, in irritable bowel syndrome: systematic review and meta-analysis. American Journal of Gastroenterology. 2014 Sep 1;109(9):1350-65.
57) Wilson BC, Vatanen T, Cutfield WS, O'Sullivan JM. The super-donor phenomenon in fecal microbiota transplantation. Frontiers in cellular and infection microbiology. 2019 Jan 21;9:2.
58) Vermeire S, Joossens M, Verbeke K, Wang J, Machiels K, Sabino J, Ferrante M, Van Assche G, Rutgeerts P, Raes J. Donor species richness determines faecal microbiota transplantation success in inflammatory bowel disease. Journal of Crohn's and Colitis. 2016 Apr 1;10(4):387-94.
59) Padhy SK, Sahoo S, Mahajan S, Sinha SK. Irritable bowel syndrome: is it "irritable brain" or "irritable bowel"? Journal of neurosciences in rural practice. 2015 Oct;6(4):568.

Early effects of smoking and environmental pollution on lung function, respiratory symptoms and allergic disorders

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Abstract

Background: Smoking and exposure to workplace environmental pollutants could be associated with adverse effects on respiratory health and occurrence of allergic disorders.

Objectives: To explore the early effects of exposure to cement dust in the workplace and smoking, on the occurrence of respiratory and allergic disorders in young adults.

Design: It is a cross-sectional study, where a convenient non-probability sample was selected.

Setting: The sstudy was conducted in a cement manufacturing factory at the North of Jeddah city and at a medical college.

Sample size: One hundred subjects were studied (50 workers exposed to cement dust, and 50 subjects, not exposed to any noxious substances).

Method: Each subject was asked to fill out a personal questionnaire (to collect socio-demographic, and health data), an occupational questionnaire, and the MRC questionnaire on respiratory symptoms and smoking habit, and ISAAC core questionnaire on asthma and allergy. Anthropometric measurements and forced spirometry (before and after administration of the bronchodilator), were conducted on each subject. Multi-nominal Logistic regression and multiple linear regression were used. Odds ratio (OR) and 95% confidence intervals (95% CI) were calculated. The level of significance for the study was 0.05.

Results: Smoking was significantly associated with chronic cough (OR=3.68; 95% CI: 0.99, 15.11 and $p < 0.05$), chronic phlegm production (OR=8.83; 95% CI: 2.33, 33.51, and $p < 0.001$), shortness of breath on exertion (OR=4.18; 95% CI: 1.49, 11.66, and $p < 0.006$), and eczema (OR=6.43; 95% CI: 1.33, 31.14, and $p < 0.021$). After allowing for age, height, weight and cement dust exposure, smoking subjects had significantly lower FEV1% compared to nonsmokers (Beta= -3.45%, $p < 0.05$). Cement dust exposure was not significantly associated with ill health.

Conclusions: Early effects of smoking are increased chronic respiratory symptoms and occurrence of eczema. FEV1% is the early affected lung function index in smokers, denoting airflow limitation. Cement exposure under the current environmental factory conditions seems to be safe.

Key words: Smoking, cement exposure, forced spirometry, allergic disorders

Introduction

Environmental pollution is a determinant of increased respiratory symptoms and impaired lung function [1-6]. It has been shown to be associated with occurrence and worsening of several respiratory disorders, such as bronchial asthma, and chronic obstructive pulmonary disease (COPD) [2-3]. Tobacco smoke is recognized as the most important risk factor for the development and the progression of COPD. Although tobacco smoke and combustion-related air pollution emit a range of pollutants in common, the role of ambient air pollution on the underlying chronic disease processes that ultimately lead to COPD are not well investigated. [7-9]. The cement industry provides building material for land-based and off-shore installations. Cement is typically produced by heating a homogenous blend of limestone and clay, which is then adjusted to a suitable content of calcium, silicon, aluminum and iron, in a kiln. During its heating to 1,450°C, clinker is formed, which contains calcium silicates, calcium aluminates and calcium ferrites. Clinker is subsequently ground with gypsum and other additives, resulting in a fine particulate powder called cement. In contact with water, clinker partly dissolves and forms an aqueous slurry of high alkalinity, giving clinker and cement strong irritant properties [1]. Cement production workers are exposed to airborne particles of raw materials, clinker, additives and to the final cement product, and their work has been linked to changes in lung function and airway symptoms [11]. Early studies on adverse respiratory effects of cement dust exposure include both non-positive studies and studies connecting cement production work with chronic airway inflammation and reduction of dynamic lung volumes [12, 13]. Other studies indicate a reduced forced vital capacity (FVC) or forced expiratory volume in 1 s (FEV1) [14–18], and a higher prevalence of chronic respiratory symptoms [16–19], and chronic obstructive pulmonary disease (COPD) [2], in cement production workers. Several other studies of lung function in cement production workers were non-positive [19, 21–23]. The literature is conflicting and conclusions about exposure–response relationships or safe levels of exposure cannot be drawn [11]. Thus the aim of the present study was to explore the impact of smoking, and exposure to cement dust on the occurrence of respiratory symptoms and allergic disorders; and to study its early effects on the forced flow-volume curve indices.

Methods

A cross sectional study was undertaken during January to April, 2020, in a cement factory at North of Jeddah and at a medical college at South of Jeddah, KSA.

The total number of studied subjects was 100; 50% male workers from a cement factory in North of Jeddah, and 50% male subjects not exposed to any noxious materials that can affect the chest or the skin. The total number of cases and controls was more than the necessary minimum number needed for this study (74 subjects, as assessed by G*power software [24], for $\alpha = 0.05$, $\beta = 0.95$, effect size is 0.3, and 2-tail-t-test).

Data was collected on each subject, after we obtained written consent to participate in the study. Data were collected through: 1-Interview questionnaire which provided information on personal and socio-demographic characteristics of the subject; 2- Occupational questionnaire which provided information on nature of exposure, duration of employment in years, duration of exposure per day, and use of personal protective equipment; 3- MRC questionnaire on respiratory symptoms and smoking habit which is a standardized questionnaire that provides information on chronic respiratory symptoms and smoking habit [25-26]; 4-ISAAC core questionnaire on asthma and allergy which was used to diagnose bronchial asthma, allergic rhinitis and atopic eczema [27]; 5- Anthropometric measurements: weight and height of the subject, were measured using standard techniques and equipment [28]; 6- Lung function testing according to the standardization of procedure and maneuver cited by the ATS [28] Forced spirometry was measured where indices from flow volume curve and time volume curve were obtained, namely:

FVC = forced vital capacity; FEV1 = forced expiratory volume in one second; FEV1% = (FEV1 / FVC) * 100; PEFR = Peak expiratory flow rate; FEF25 – 75%= Flow rate between 25% and 75% of the FVC; FEF75% = Forced expiratory flow at 75% of FVC expired; FEF50% = Forced expiratory flow at 50% of FVC expired; FEF25% = Forced expiratory flow at 25% of FVC expired. Lung function was assessed before and 10 minutes after administration of Salbutamol (Ventolin) inhalation. Data analysis and statistical tests: Data was analyzed using the Statistical Package for Social Sciences (IBM SPSS, version 22, Armonk, NY: IBM Corp.). Multi-nominal logistic regression method was used where respiratory symptoms and allergic disorders were used as the dependent dichotomous variables; other variables were used as independent variables, where Odds ratios, 95% confidence interval (95% CI), and p values were calculated. Linear Multiple Regression Analysis was used to study continuous variables that could significantly predict lung function indices. The significance of the differences was calculated at 95% CI; $P < 0.05$ was considered as statistically significant.

Ethical considerations

Ethical clearance was obtained from the institutional review board (IRB) of the College of Ibn Sina (IEC Ref No: H-09-12092019). Permission was obtained from the director and foremen of the factory. Informed consent was obtained from the subjects, after providing information about the purpose of the study. In order to keep confidentiality of any information provided by study participants, the data collection procedure was anonymous.

Results

The mean age of the exposed group was 34.24 years (7.88), while mean age of non-exposed group was 37.08 years (13.16). This difference was not statistically significant (t = -1.31, and p < 0.19). Mean duration of exposure to cement dust among cement exposed groups was 7.38 years (5.02). Among the whole subjects, 24% were smokers and mean duration of smoking was 13.12 years (10.25), while 76% were non-smokers. Chronic cough was encountered among 10% of the whole subjects, while chronic phlegm production was encountered among 14%, and shortness of breath on exertion was found in 23% of the subjects. Bronchial asthma was encountered among 7% of the subjects, and hay fever in 19%; while eczema was found in 8% of the subjects.

Table 1 reveals the multi-nominal logistic regression for respiratory symptoms and allergic disorders, in relation to age, exposure to cement dust and smoking habit. Chronic cough was 4 times more likely to be encountered among smoking subjects compared to non-smokers (OR=3.68; 95% CI: 0.99, 15.11' and p < 0.05). Neither advancing age nor exposure to cement dust were significantly associated with occurrence of chronic cough.

Chronic phlegm production, was about 9 times more likely to occur in smoking subjects compared to those who do not smoke (OR=8.83; 95% CI: 2.33, 33.51, and p < 0.001). Cement exposed workers were less likely to suffer from chronic phlegm production compared to the non-exposed subjects (OR=0.20; 95%CI: 0.05, 0.83; p value < 0.027). Shortness of breath on exertion, was about 4 times more likely to occur among smoking subjects compared to those who do not smoke (OR=4.18; 95% CI: 1.49, 11.66, and p < 0.006).

Eczema, was about 6 times more likely to occur among smoking subjects compared to those who do not smoke (OR=6.43; 95% CI: 1.33, 31.14, and p < 0.021). Neither bronchial asthma nor hay fever, were significantly associated with smoking habit or with exposure to cement dust (p >0.05).

Table 2 shows the comparison of mean values of forced spirometric tests (pre and post bronchodilator administration) between cement exposed workers and non-exposed subjects. The mean values of forced flow volume curve indices and time-volume curve indices were similar for both cement exposed workers and non-exposed subjects except for Pre-FEF75%, where mean value was higher in the cement exposed workers (1.78 L/S (0.81)) compared to non-exposed subjects (1.35L/S (0.53) where t = -2.19 and p < 0.03.

Table 3 reveals the comparison of mean values of forced spirometric tests (pre and post bronchodilator administration) between smokers and non-smoking subjects. The mean values of Forced flow volume curve indices and time-volume curve indices were similar in both smokers and nonsmokers (p>0.05).

Table 4 shows correlation/regression relationship between lung function tests and age, height, weight, smoking habit, and exposure to cement dust. It was found that after allowing for confounding factors such as age, height weight and smoking habit the mean values of the cement exposed workers and non-exposed subjects were similar, and no significant difference was found (p > 0.05). After allowing for age, height, weight and cement dust exposure, smoking subjects had significantly lower FEV1% compared to nonsmokers (Beta= -3.45%, p < 0.05). Other lung function indices were not significantly different for smokers compared to non-smokers (p> 0.05).

Duration of exposure to cement dust was, also, not associated with significant changes in the lung function indices (Table 5).

Table 1: Multi-nominal Logistic regression between health conditions and age, smoking habit and exposure to cement dust

Independent variables	B	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
				Lower Bound	Upper Bound
Chronic cough					
Intercept	0.899	.468			
Age in years	0.015	.642	1.015	.952	1.083
Exposure to cement	-0.235	.735	.790	.202	3.086
Smoking habit	1.352	.052	3.863	.988	15.108
Chronic phlegm production					
Intercept	1.239	.256			
Age in years	.004	.883	1.004	.952	1.059
Exposure to cement	-1.596	.027	.203	.049	.834
Smoking habit	2.178	.001	8.827	2.325	33.509
Shortness of breath on exertion					
Intercept	.069	.942			
Age in years	-.004	.858	.996	.949	1.044
Exposure to cement	.684	.189	1.981	.714	5.498
Smoking habit	1.430	.006	4.179	1.498	11.663
Doctor diagnosed Bronchial asthma					
Intercept	.715	.695			
Age in years	.038	.460	1.039	.939	1.150
Exposure to cement	1.865	.092	6.454	.736	56.627
Smoking habit	.003	.998	1.003	.173	5.804
Doctor diagnosed Hay fever					
Intercept	-.068	.946			
Age in years	.035	.184	1.035	.984	1.089
Exposure to cement	-.589	.273	.555	.193	1.591
Smoking habit	.885	.120	2.423	.795	7.389
Doctor diagnosed eczema					
Intercept	3.199	.022			
Age in years	-.056	.110	.946	.883	1.013
Exposure to cement	.577	.500	1.781	.332	9.540
Smoking habit	1.861	.021	6.429	1.327	31.136

Table 2 shows comparison of forced spirometric tests (pre and post bronchodilators) between cement exposed workers and non-exposed subjects

LFT	Exposure	Mean	Standard Deviation	t-test	p-value
Pre-FVC	not exposed	3.5528	.76210	-,.52	.582
	exposed	3.6484	.95744		
Pre- FEV1	not exposed	3.0010	.52858	-1.322	.189
	exposed	3.1620	.67948		
Pre- FEV1%	not exposed	79.8100	8.22989	-.380	.705
	exposed	80.4042	7.39206		
Pre- PEFR	not exposed	5.9010	1.91745	.118	.907
	exposed	5.8594	1.60628		
Pre- FEF25-75%	not exposed	2.9898	.99034	-.696	.488
	exposed	3.1220	.90809		
Pre- FEF75%	not exposed	1.3518	.52925	-2.194	.031
	exposed	1.7870	1.29860		
Pre- FEF50%	not exposed	3.7826	.80514	.256	.798
	exposed	3.7386	.90992		
Pre- FEF25%	not exposed	4.9972	2.10419	-.315	.754
	exposed	5.1190	1.74936		
Post-FVC	not exposed	3.6110	.69550	-.401	.689
	exposed	3.6794	.98593		
Post-FEV1	not exposed	3.1122	.45492	-.858	.393
	exposed	3.2220	.78246		
Post-FEV1%	not exposed	81.7400	7.98419	-.633	.528
	exposed	82.7000	7.16639		
Post-PEFR	not exposed	6.9138	1.85069	..428	.670
	exposed	6.7564	1.82766		
Post-FEF25-75%	not exposed	3.7226	1.06328	.654	.515
	exposed	3.5968	.84849		
Post-FEF75%	not exposed	1.5818	.62640	-1.411	.161
	exposed	1.8474	1.17418		
Post-FEF50%	not exposed	4.2742	.86359	1.751	.083
	exposed	3.9632	.91166		
Post-FEF25%	not exposed	5.5756	2.08943	.588	558
	exposed	5.3448	1.82341		

Table 3: Comparison of forced spirometric tests (pre and post bronchodilators) between smoking and non-smoking subjects

	Smoking habit	Mean	Std. Deviation	t-test	p-value
Pre-FVC	Nonsmoker	3.5914	.84207	-.188	.851
	Smoker	3.6296	.94172	-,.77	.860
Pre- FEV1	nonsmoker	3.0905	.61486	.262	.794
	Smoker	3.0529	.61084	.263	.794
Pre- FEV1%	nonsmoker	80.7975	7.82851	1.590	.115
	Smoker	77.9208	7.39500	1.638	.109
Pre- PEFR	nonsmoker	5.8726	1.87642	-.076	.939
	Smoker	5.9042	1.35989	-.090	.929
Pre- FEF25-75%	nonsmoker	3.1014	.96669	.854	.395
	Smoker	2.9117	.88851	.893	.377
Pre- FEF75%	nonsmoker	1.5857	1.00016	.285	.776
	smoker	1.5179	1.06289	.276	.784
Pre- FEF50%	nonsmoker	3.8217	.86740	1.276	.205
	smoker	3.5671	.80138	1.330	.191
Pre- FEF25%	nonsmoker	5.1180	1.96836	.552	.582
	smoker	4.8683	1.81250	.576	.568
Post-FVC	nonsmoker	3.6495	.81803	.089	.929
	smoker	3.6317	.96136	.082	.935
Post-FEV1	nonsmoker	3.1891	.65590	.610	.543
	smoker	3.0975	.59061	.644	.523
Post-FEV1%	nonsmoker	82.6447	7.27132	.999	.320
	smoker	80.8750	8.44580	.924	.362
Post-PEFR	nonsmoker	6.8451	1.82048	.097	.923
	smoker	6.8033	1.90570	.095	.925
Post-FEF25-75%	nonsmoker	3.6647	.96099	.093	.926
	smoker	3.6438	.97355	.092	.927
Post-FEF75%	nonsmoker	1.7176	.90865	.057	.955
	smoker	1.7050	1.07584	.052	.959
Post-FEF50%	nonsmoker	4.1822	.88087	1.264	.209
	smoker	3.9175	.93750	1.223	.229
Post-FEF25%	nonsmoker	5.4889	1.98415	.261	.795
	smoker	5.3692	1.89558	.267	.791

Table 4: Correlation/regression relationship between lung function tests and age, height, weight, smoking habit, and exposure to cement dust

Independent variables	Lung function indices							
	FVC	FEV1	FEV1%	PEFR	FEF25-75	FEF75	FEF50	FEF25
Constant	3.287	3.508	57.804	4.890	4.254	3.266	5.110	5.162
Age (years	-.003	-.005	-.150**	.001	-.007	-.007	-.007	-.006
Height (Cm)	.000	-.003	.180	.003	-.007	-007	-.007	-.001
Weight	.004	.004	-.034	.005	.002	-.006	003	.004
Smoking habit	.024	-.057	-3.455*	.035	-202	-.134	-.236	-.271
Exposure to cement dust	.106	.164	.837	-.009	.132	.383	-.037	.155

Table 5: Correlation/regression relationship between lung function tests and age, height, weight, smoking habit, duration of employment in cement industry

Independent variables	Lung function indices							
	FVC	FEV1	FEV1%	PEFR	FEF25-75	FEF75	FEF50	FEF25
Constant	3.519	3.823	59,463	4.895	4.497	4.016	5.049	5.462
Duration of employment	-.007	.012	.033	-.013	.016	.021	-.008	.010
Age (years	-.003	-.007	-.158*	.003	-.010	-.011	-.006	-.008
Height (Cm)	.000	-.005	.174	.003	-.007	-.009	-.007	-.002
Weight	.003	.003	-.035	.004	.002	-.007	.003	.004
Smoking habit	.054	-.049	-3.370	056	-.206	-.103	-.229	-.262

Discussion

Chronic obstructive pulmonary diseases, characterized by long-term poorly irreversible airway limitation and persistent respiratory symptoms, are a common and preventable disease [29]. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, there are three criteria to diagnose the disease: 1- a post-bronchodilator FEV1% of less than 70%, 2- symptoms of respiratory system as shortness of breath on exertion, chronic cough, production of sputum or wheezing, and 3- significant exposure to noxious environmental stimuli such as smoking or chemical environmental hazards [30]. Therefore in the present study, as the main objective was to assess the impact of smoking and environmental pollution, particularly exposure to cement dust, on the respiratory system, lung function was assessed before and after administration of bronchodilator. MRC questionnaire was used and occupational questionnaire was asked of each subject. As this study was interested in evaluating the early effects of smoking and exposure to noxious materials on the lung and occurrence of allergic disorders, the studied subjects were relatively of young age where the mean age of the exposed group was 34.24 years (7.88), while the mean age of the non-exposed group was 37.08 years (13.16). The mean duration of exposure to cement dust and smoking were relatively low (7.38 years, and 13.12 years respectively).

A recent study, conducted by Kotaki et al in 2019, revealed that in addition to the impact of smoking, the elderly who were chronically exposed to air pollution had exacerbated respiratory symptoms and impaired respiratory function [31]. Similar findings were reported by other studies [32, 33]. In the present study most of the studied subjects were relatively young, and only 2 subjects, who were nonsmokers and not exposed to cement dust, fulfilled the criteria of COPD. However, in line with previous studies (31-33), smoking was significantly associated with chronic cough (OR=3.68; 95% CI: 0.99, 15.11), chronic phlegm production (OR=8.83; 95% CI: 2.33, 33.51), and shortness of breath on exertion (OR=4.18; 95% CI: 1.49, 11.66). These findings from the present study, support the incrimination of smoking in the genesis of chronic inflammatory diseases of the lung airways and COPD. Several studies have assessed the association between smoking exposure and allergic diseases. In each of the allergic conditions, results were conflicting and alternated between the harmful effects of smoking, [34, 35, 36] and protection [37–39], while some studies could not find evidence of any effect [40–42]. In the present study smoking was only significantly associated with occurrence of eczema (OR=6.43; 95% CI: 1.33, 31.14, and $p < 0.021$). In the present study exposure to cement dust in the studied factory was not significantly associated with increased occurrence of chronic respiratory symptoms or allergic disorders. This is contradictory to the results of some studies [43-46]. This could be due to the relatively young age of the exposed workers or due to the control measures applied in this factory compared to work place exposures in other studied factories. Forced spirometric indices, also, in the present study were, similar in cement exposed workers and non-exposed subjects. Some lung function indices were better in the cement exposed workers e.g. FEF75% which reflects airflow in the small airways, compared to the employee in the medical college, and this seems to be due to the exercise effect of working as a blue collar worker in a factory compared to the sedentary life style adopted by the control subjects.

As for smokers, the early lung function index affected was FEV1% (Beta = -3.45%, $p < 0.03$) which was decreased in the smokers compared to non-smokers, which denotes the beginning of airflow limitation at this relatively young age, and before development of COPD.

Conclusions

Early effects of smoking are increased chronic respiratory manifestations and reduced FEV1%, which indicated obstructive impairment. Cement exposure under the current environmental factory conditions seems to be safe. Smoking cessation programs should be implemented among workers in industries, and to the population in the community to combat the major risk of COPD.

Strengths and limitations of this study

In this study flow volume curve indices which are sensitive to early changes in the small airways were used, in addition to time volume curve indices which, mainly, measure late effect on large airways. Lung function was measured before and after administration of bronchodilator to categorize subjects with COPD whose post bronchodilator FEV1% were less than 70%, to meet GOLD criteria.

ISAAC questionnaire used in this study has been validated worldwide. Multifactorial statistical tests were, also, employed to allow for the confounders during assessing the different associations. However, among the limitations of this study were that the questionnaire data depended on the recall of the subjects. It was also based on workers from only one factory; thus we can't exclude self-selection bias.

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Competing interests
All authors declare that they have no competing interests.

References

[1] Saskia C. van der Zee, Paul H. Fischer b, Gerard Hoek c. Air pollution and subclinical interstitial lung disease: the Multi-Ethnic Study of Atherosclerosis (MESA) air–lung study. Environmental Research 2016; 148: 475-469.
[2] Guarnieri M, Balmes JR. Outdoor air pollution and asthma. Lancet 2014; 383: 1581–1592.
[3] Adar SD, Kaufman JD, Diez-Roux AV, et al. Air pollution and percent emphysema identified by computed tomography in the multi-ethnic study of atherosclerosis. Environ Health Perspect 2015; 123: 144–151.
[4] EL-Gamal, F. M; Kordy, M. N; Ibrahim, M. A Study of respiratory symptoms and lung function in polyvinyl chloride fabrication workers. Saudi medical journal. 1995, 16,(1): 36-41..
[5] Rice MB, Rifas-Shiman SL, Oken E, et al. Exposure to traffic and early life respiratory infection: a cohort study .Pediatr Pulmonol 2015; 50: 252–259.
[6] Chinn DJ, Cotes JE, El-Gamal FM, Wollaston JF. Respiratory health of young shipyard welders and other tradesmen studied cross sectionally and longitudinally. Occup Environ Med. 1995;52:33–42.
[7] Ku nzli N, Perez L, Rapp R. Air Quality and Health. Lausanne, European Respiratory Society, 2010.
[8] Zanobetti A, Bind MA, Schwartz J. Particulate air pollution and survival in a COPD cohort. Environ Health 2008; 7: 48.
[9] Schikowski T, Mills IC, Anderson HR, et al. Ambient air pollution: a cause of COPD? Eur Respir J 2014; 43: 250–263.
[10] Ahmadi H, Durrant CAT, Sarraf KM, et al . Chemical burns: a review. Curr Anaesth Crit Care 2008; 19: 282–286.
[11] Health and Safety Executive. Portland cement dust – hazard assessment document EH75/7. Watch committee. Merseyside, Health and Safety Executive, 2004.
[12] Bazas T. Effects of occupational exposure to dust on the respiratory system of cement workers. J Soc Occup Med 1980; 30: 31–36.
[13] Fell AK, Sikkeland LI, Svendsen MV, et al. Airway inflammation in cement production workers. Occup Environ Med 2010; 67: 395–400.
[14] Meo SA. Health hazards of cement dust. Saudi Med J 2004; 25: 1153–1159.
[15] Mwaiselage J, Bratveit M, Moen B, et al. Cement dust exposure and ventilatory function impairment: an exposure-response study. J Occup Environ Med 2004; 46: 658–667.
[16] Yang CY, Huang CC, Chiu HF, et al. Effects of occupational dust exposure on the respiratory health of Portland cement workers. J Toxicol Environ Health 1996; 49: 581–588.
[17] Noor H, Yap CL, Zolkepli O, et al. Effect of exposure to dust on lung function of cement factory workers. Med J Malaysia 2000; 55: 51–57.
[18] Al-Neaimi YI, Gomes J, Lloyd OL. Respiratory illnesses and ventilatory function among workers at a cement factory in a rapidly developing country. Occup Med 2001; 51: 367– 373.
[19] Abrons HL, Petersen MR, Sanderson WT, et al. Symptoms, ventilatory function, and environmental exposures in Portland cement workers. Br J Ind Med 1988; 45: 368–375.
[20] Vestbo J, Rasmussen FV. Long-term exposure to cement dust and later hospitalization due to respiratory disease. Int Arch Occup Environ Health 1990; 62: 217–220.
[21] Catenacci G, Tringali S, Brunetti G, et al. Decrement of respiratory function indices in a case series of workers exposed to cement dust: a longitudinal study. G Ital Med Lav 1988; 10: 123–129.
[22] Fell AK, Thomassen TR, Kristensen P, et al. Respiratory symptoms and ventilatory function in workers exposed to Portland cement dust. J Occup Environ Med 2003; 45: 1008–1014.
[23] Abu Dhaise BA, Rabi AZ, al Zwairy MA, et al. Pulmonary manifestations in cement workers in Jordan. Int J Occup Med Environ Health 1997; 10: 417–428.
[24] Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods 2007; 39, 175-191.
[25] Medical Research Council on the Aetiology of Chronic Bronchitis. Standardised questionnaire on respiratory symptoms. Br Med J 1960; 2: 1665.
[26] Cotes JE, Chinn DJ. MRC questionnaire (MRCQ) on respiratory symptoms
Occupational Medicine 2007; 57 (5): 388, https://doi.org/10.1093/occmed/kqm051
[27] Mitchell R, Beasley B, Björkstén J, Crane L, García Marcos U, Keil G. The association between BMI, vigorous physical activity and television viewing and the risk of symptoms of asthma, rhino-conjunctivitis and eczema in children and adolescents: ISAAC Phase Three. Clinical & experimental Allergy 2013; 43 (1): 73 -84.
[28] Cotes JE, Chinn DJ, Miller MR. Lung Function. 6th ed. Chichester, United Kingdom:
Wiley-Blackwell 2006. ISBN13: 0632064939.
[29] Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention

of chronic obstructive lung disease 2017 report. GOLD executive summary. Am J Respir Crit Care Med. 2017;195(5):557–582.
[30] Mirza S, Clay RD, Koslow MA, Scanlon PD. COPD guidelines: a review of the 2018 GOLD report. Mayo Clinic Proc. 2018;93(10):1488–1502.
[31] Kotaki K, Ikeda H, Fukuda T, Yuhei K, Yuki F, Kawasaki M, et al. Trends in the prevalence of COPD in elderly individuals in an air-polluted city in Japan: a cross-sectional study. International Journal of COPD 2019; 14:791–798
[32] Schikowski T, Sugiri D, Ranft U, et al. Long-term air pollution exposure and living close to busy roads are associated with COPD in women. Respir Res. 2005;6:152.
[33] Li J, Sun S, Tang R, et al. Major air pollutants and risk of COPD exacerbations: a systematic review and meta-analysis. Int J Chron Obstruct Pulmon Dis. 2016; 11: 3079–3091.
[34]. Lannerö E, Wickman M, van Hage M, Bergström A, Pershagen G, et al. Exposure to environmental tobacco smoke and sensitisation in children. Thorax 2008; 63: 172–176.
[35] Cakir E, Ersu R, Uyan ZS, Oktem S, Varol N, et al. The prevalence and risk factors of asthma and allergic diseases among working adolescents. Asian Pac J Allergy Immunol 2010; 28: 122–129.
[36]. Lee CH, Chuang HY, Hong CH, Huang SK, Chang YC, et al. Lifetime exposure to cigarette smoking and the development of adult-onset atopic dermatitis. Br J Dermatol 2011; 164: 483–489.
[37] Bendtsen P, Grønbaek M, Kjaer SK, Munk C, Linneberg A, et al. Alcohol consumption and the risk of self-reported perennial and seasonal allergic rhinitis in young adult women in a population-based cohort study. Clin Exp Allergy 2010; 38: 1179–1185.
[38] Ludvigsson JF, Mostrom M, Ludvigsson J, Duchen K. Exclusive breastfeeding and risk of atopic dermatitis in some 8300 infants. Pediatr Allergy Immunol 2005; 16: 201–208.
[39] Metsälä J, Lundqvist A, Kaila M, Gissler M, Klaukka T, et al. Maternal and perinatal characteristics and the risk of cow's milk allergy in infants up to 2 years of age: a case-control study nested in the Finnish population. Am J Epidemiol 2010; 171: 1310–1316.
[40] McKeever TM, Lewis SA, Smith C, Collins J, Heatlie H, et al. Siblings, multiple births, and the incidence of allergic disease: a birth cohort study using the West Midlands general practice research database. Thorax 2001; 56: 758–762.
[41] Wang IJ, Guo YL, Lin TJ, Chen PC, Wu YN. GSTM1, GSTP1, prenatal smoke exposure, and atopic dermatitis. Ann Allergy Asthma Immunol 2010; 105: 124–129.
[42] Tariq SM, Matthews SM, Hakim EA, et al. The prevalence of and risk factors for atopy in early childhood: a whole population birth cohort study. J Allergy Clin Immunol 1998; 101: 587–593.
[43] Gizaw, Z., Yifred, B. & Tadesse, T. Chronic respiratory symptoms and associated factors among cement factory workers in Dejen town, Amhara regional state, Ethiopia, 2015. Multidiscip Respir Med 2016; 11: 13. https://doi.org/10.1186/s40248-016-0043-6
[44] Erhabor O, Kebbe BI, Zama II, Abdullahi N, Marafa Y, Okwesili AN, et al. Effect of occupational exposure of cement dust on some haematological parameters of workers in a cement company in Sokoto, Nigeria. Int J Med Sci Health Care. 2013; 1(7): 21–25.
[45] Rodríguez E, Ferrer J, Martí S, Zock JP, Plana E, Morell F. Impact of occupational exposure on severity of chronic obstructive pulmonary disease. Chest 2008; 134: 1237–43.
[46] Kakooei H, Gholami A, Ghasemkhani M, et al. Dust exposure and respiratory health effects in cement production. Acta Medica Iranica 2012; 50 (2): 122-6.

Alopecia Syphilitica: a case report involving hairloss on scalp and eyebrow

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Abstract

Alopecia syphilitica (AS) is an uncommon presentation and has been reported in up to 7% of cases with syphilis. This case report discusses the presentation and management of a 17-year-old male patient from South Asia who presented with patchy hair loss on the scalp and eyebrow.

Key words: alopecia syphilitica, primary syphilis, secondary syphilis, latent syphilis, tertiary syphilis

Introduction

Alopecia syphilitica (AS) is an uncommon presentation of secondary syphilis and is observed in up to 7% of cases according to the literature(1–3). The first sign of primary syphilis is a chancre, a painless sore on the oral or anogenital region (4). After a mean duration of 6 weeks (range: 2–16 weeks) of the primary chancre, secondary syphilis develops with a rash (5). The rash appears as a reddish-brown papula or plaque which becomes generalized, involving trunk and even the palms and soles of the patient(6). Other symptoms of secondary syphilis include a flu-like illness, muscle aches, sore throat, fatigue, fever, swollen lymph nodes, and hair loss (7). If alopecia is the only sign of secondary syphilis, it is referred to as essential syphilitic alopecia (ESA). There are three types of ESA: the classic patchy “moth-eaten” alopecia, a generalized thinning of the hair, and a combination of both(2). Among these, the “patchy moth-eaten” type of alopecia occurs most frequently and is characteristic of syphilis(8–10). The scalp hair is the most common area affected, though it can also affect the eyebrows, beard, and legs(11).

Syphilis is known to have a great mimicking ability due to its various forms of manifestation that copy those of other medical conditions(12). Other forms of alopecia, which can resemble AS, include alopecia areata, trichotillomania, planopilaris, traction alopecia, and tinea capitis (13). Untreated patients will enter into a latent period (latent syphilis), during which time, they are asymptomatic, which can last for up to 25 years before the condition progresses to tertiary syphilis(14). Tertiary syphilis may lead to death due to its complications, such as cardiovascular syphilis, neurosyphilis, and gummatous syphilis.(5).

In a recent literature review, there appears to be a paucity of reports of syphilitic alopecia involving hair loss on the eyebrow. The other important aspect in our case was the need to obtain a correct sexual history in a place where the law, culture, and religion strictly prohibit nonmarital sex.

Case Report

Patient information

A 17-year-old male south Asian Muslim patient presented with his father to a Primary Health Care Centre in Qatar with reports of an itchy scalp, severe scalp dandruff, and gradual hair loss during the preceding three months. He also showed a patch of hair loss on his left eyebrow. He had tried various types of shampoos but had noticed no improvement in his symptoms. The patient denied any symptoms of penile or mouth ulcers, rash anywhere on the body, or swelling of glands. He was fit and healthy, with no significant past medical history of note. At the time of presentation, he was attending high school for education.

Clinical findings

On examination, he had patchy hair loss of the scalp (Figure 1A - next page). He also had a small patch of hair loss at the medial aspect of the left eyebrow (Figure 1B). His scalp had widespread generalized scaling. There were no vesicles or pustules on the scalp. He categorically denied any history of sexual contact when asked alone confidentially.

Diagnostic assessments

The findings of routine blood tests, including complete blood count, ferritin, urea, electrolytes, and thyroid function tests, were all normal. The culture of the scalp skin scrapings was negative for fungal elements. Given the patchy hair loss, syphilis screening, i.e., screening for Treponema pallidum antibodies and rapid plasma regain, was requested. Both of the tests turned out to be positive, confirming the diagnosis of syphilis. Serological tests (both treponemal and nontreponemal) are routinely used to diagnose syphilis, while, more rarely, direct detection methods are employed, depending upon resources and availability(15). Despite the diagnosis, given the patient's reluctance to discuss past sexual contact, no partner notification was possible.

Therapeutic intervention

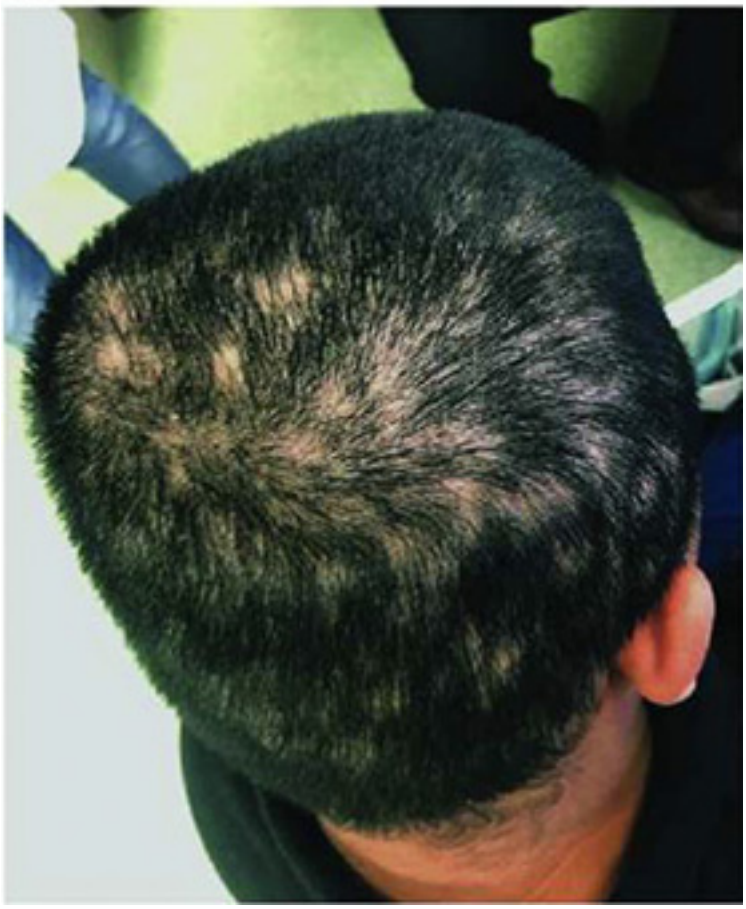
The patient was urgently referred to the Venereal Disease Clinic, part of the Infectious Disease Department at Hamad General Hospital in Qatar, where he was given his first dose of benzathine penicillin 2.4 gm Intramuscular (IM) stat. In accordance with guidelines from the United States (16) , United Kingdom (17), and Canada (18), the treatment of primary, secondary, and early latent syphilis involves a single dose of 2.4 gm of benzathine penicillin G. For late latent syphilis, the same dose of benzathine penicillin is given once weekly intramuscularly for 3 weeks.

Follow-up and outcomes

Within 24 hours of the benzathine penicillin being given, the patient developed a mild Jarisch–Hexheimer reaction with symptoms of fever, malaise, headache, and lymphadenopathy. These symptoms were managed conservatively. Unfortunately, the patient had to leave Qatar 4 weeks after the treatment for further education back to his home country. Luckily, the patient's father has remained a regular patient at the same health center and was kind enough to provide regular updates and more recent photos (of the scalp and eyebrow) taken 4 months after the treatment. A review of the photos indicated full recovery of the scalp hair (Figure 2A) and left eyebrow (Figure 2B).

Figure 1: A and B Patchy scalp hair and left eyebrow hair loss before treatment

A



B

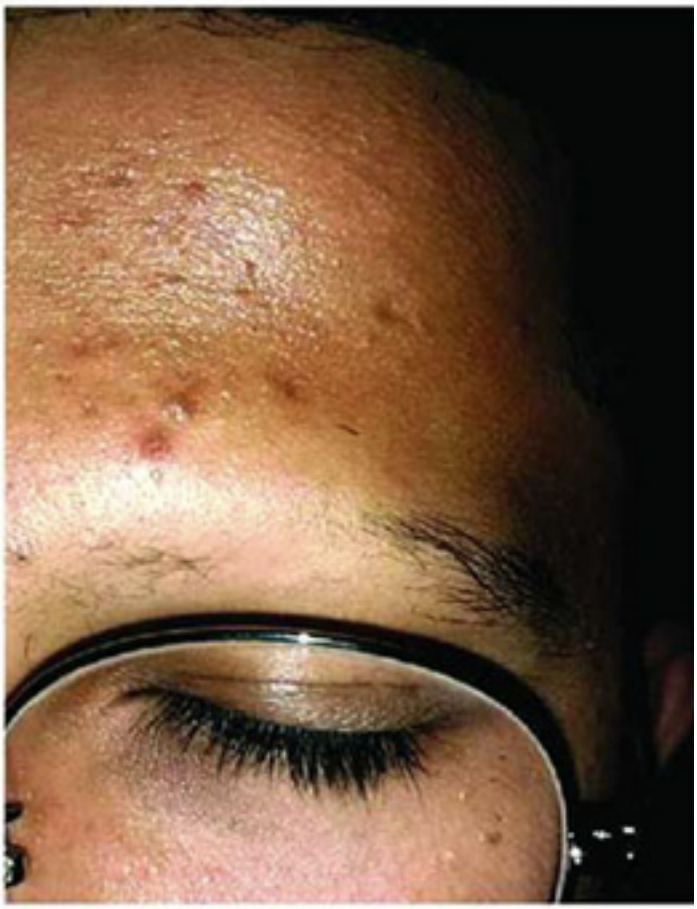
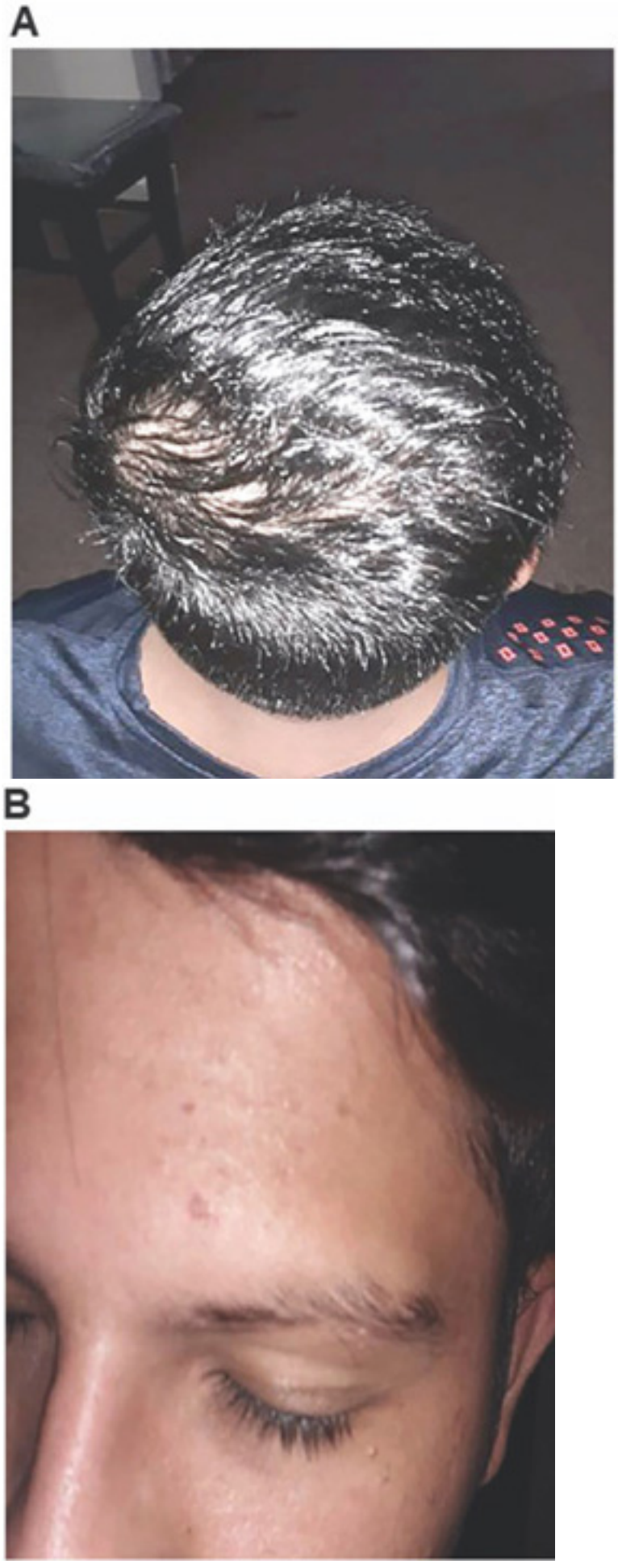


Figure 2: A and B Growth of scalp and left eyebrow hair 4 months after treatment with benzathine penicillin 2.4 gm IM



Discussion

This case of essential AS is an interesting and rare diagnosis in itself, but of particular interest is that there are no other case reports of this nature cited in the literature for Qatar. Aside from the diagnostic challenge, the ethical dimensions of this case, including maintaining confidentiality, gathering consent, and collecting a sexual history, added to the learning values. It is important to ensure the confidentiality of the patient and aim to obtain the most accurate history and establish contact tracing. In view of the typical "moth-eaten" alopecia pattern, it would be reasonable to arrange for a syphilis screening. The possibility of young patients presenting with secondary syphilis should not be ignored, as early treatment can prevent devastating complications of tertiary syphilis (19). Especially in a culture where positive syphilis results can cause stigma, members of the medical staff need to be sensitive about the diagnosis and its implications and to appropriately discuss with the patient or their parents (if the patient is considered minor as per law of the country) about their condition.

Ethical Considerations

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Since, this is a case report ethics committee approval was not needed.

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Consent

Written informed consent for case report preparation and publication was obtained.

Conflicts of Interest and Source of Funding

The authors declare that there is no conflict of interest.

References

1. Bi MY, Cohen PR, Robinson FW, et al. Alopecia syphilitica - report of a patient with secondary syphilis presenting as moth-eaten alopecia and a review of its common mimickers. Dermatol Online J 2009; 15(10): 6.
2. Hernández-Bel P, Unamuno B, Sánchez-Carazo JL, et al. Syphilitic alopecia: a report of 5 cases and a review of the literature. Actas dermo-sifiliograficas 2013; 104(6): 512-517.
3. Chapel TA. The signs and symptoms of secondary syphilis. Sex Transm Dis 1980; 7(4): 161-164.
4. Baughn RE, Musher DM. Secondary syphilitic lesions. Clin Microbiol Rev 2005; 18(1): 205-216.
5. Radolf JD, Tramont EC, Salazar JC. Syphilis (Treponema pallidum). 8th ed. In: Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas and Bennett's Principles and Practice of Infectious Disease. Philadelphia: Churchill Livington Elsevier (2014). p. 2684–709.
6. Tabasi ST. Skin rashes that involve palms and soles: an internist's view. Ann Nurs Primary Care 2018; 1(2): 1012.
7. Read PJ, Donovan B. Clinical aspects of adult syphilis. Intern Med J. 2012; 42(6): 614-620.
8. Friedli A, Chavaz P, Harms M. Alopecia syphilitica: report of two cases in Geneva. Dermatology 2001; 202(4): 376-377.
9. Bi MY, Cohen PR, Robinson FW, et al. Alopecia syphilitica – report of patient with secondary syphilis presenting as moth-eaten alopecia and a review of its common mimickers. Dermatol Online J 2009; 15(10): 6.
10. Vafaie J, Weinberg JM, Smith B, et al. Alopecia in association with sexually transmitted disease: a review. Cutis 2005; 76(6): 361-366.
11. Pareek SS. Unusual location of syphilitic alopecia: a case report. Sex Transm Dis 1982; 9(1): 43-44.
12. Klausner JD. The great imitator revealed: syphilis. Top Antivir Med 2019; 27(2): 71-74.
13. De Sousa ICVD. Simultaneous primary and secondary syphilis associated with syphilitic alopecia and folliculitis in an HIV positive patient. Hair Ther Transplant 2013; 3: 108.
14. Read PJ, Donovan B. Clinical aspects of adult syphilis. Intern Med J. 2012; 42(6): 614-620.
15. Henao-Martínez AF, Steven C. Johnson. 2014 diagnostic tests for syphilis: New tests and new algorithms. Neurol Clin Pract 2014; 4(2): 114-122.
16. Centers of disease control and prevention. 2015 sexually transmitted diseases treatment guidelines–Syphilis. Available at: https://www.cdc.gov/mmwr/pdf/rr/rr6403.pdf. Accessed March 25, 2020.
17. Kingston M, French P, Higgins S, et al. UK national guidelines on the management of syphilis 2015. Int J STD AIDS 2016; 27(6): 421-446.
18. Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections: management and treatment of specific infections–syphilis. Dec 2016; Section 5-10. Available at: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/sexually-transmitted-infections/canadian-guidelines-sexually-transmitted-infections-27.html. Accessed March 25, 2020.
19. Berger JR, Dean D. Neurosyphilis. Handb Clin Neurol 2014; 121: 1461-1472.

H Syndrome: A Case Report

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Abstract

H Syndrome is one of the rarest diseases in the world. It is an autosomal recessive (AR) disorder that occurs due to mutations in the solute carrier family 29.

H Syndrome is characterized by cutaneous hyperpigmentation, hearing loss, hypertrichosis, hypothyroidism, hepatomegaly, flexion contracture of the fingers and toes, short stature, hypertriglyceridemia, diabetes mellitus type one, and hypogonadism.

It was named H syndrome considering the fact that most of the clinical features start with the letter “H.”

Key words: H Syndrome, SLC29A3 gene, hypertrichosis.

Introduction

H Syndrome is an autosomal recessive disease (ARD) with systemic manifestations and pathognomonic skin lesions (1). It is due to mutations in the solute carrier family 29 (nucleoside transporter) member 3 (SLC29A3 gene), encoding human equilibrative nucleoside transporter hENT3, and leading to mononuclear cell skin infiltration and cutaneous manifestations(2). The first cases of this extremely rare syndrome were reported in consanguineous families of Arab and Bulgarian descent and described in 2008 by Molho-Pessach et al (3). The described disorders are characterized by hearing loss, hypertrichosis, hypothyroidism, hepatosplenomegaly, short stature, flexion contracture of the fingers and toes, hypertriglyceridemia, diabetes mellitus type one, and hypogonadism (4).

This report describes the case of an eight-year-old girl with H syndrome due to a SLC29A3 mutation identified utilizing a whole-exome sequencing approach. There are approximately 100 patients diagnosed with the disorder worldwide (5).

Case history

An eight-year-old girl, a product of consanguineous marriage and normal vaginal delivery, birth weight 2760-gram, uneventful pregnancy, presented to our pediatric endocrinology and diabetes clinic at Queen Rania Al-Abdullah Hospital for Children (Amman -Jordan) with a complaint of short stature. On examination, her height and weight were 115 cm (–2.2 standard deviation [SD]) and 18 kg (–3 SD) respectively, and the sex-adjusted mid parental height was 157 cm. On physical examination she had dilated vein on her face, was pale, wore hearing aids, had bilateral enlargement of cervical and inguinal lymph nodes, Pectus carinatum, hyperpigmented skin lesion on the abdomen, (Figure 1) and the upper half of both thighs, and hypertrichotic lesions mainly involving the extremities (Figure 2). Tanner's staging of the breasts was Prepubertal (stage 1), with stage 2 pubic hair. See table (1) for clinical examination findings.

Laboratory test results showed an elevated ESR value of 45, the CBC showed mild microcytic anemia, thyroid function tests showed hypothyroidism and abdominal ultrasound scan found mild hepatosplenomegaly.

Liver function tests, renal function tests, serum electrolytes, urine analysis, HbA1c, tissue Transglutaminase antibodies (IgG, IgA), chest x-ray, Echocardiography, and karyotype were normal.

Because of all of these clinical findings, our patient described here was suspected to have H Syndrome. Whole-exome sequencing confirmed the diagnosis

Table 1: Findings on examination

Examination	Findings
Anthropometric parameters	Weight, 17.7 kg; height, 117 cm; BMI, <17.7.
Skin	Hyperpigmented patches with overlying hypertrichosis, involving the right side of the abdominal and medial aspects of the thighs and extending to the anterior aspects of the legs. There is facial telangiectasia.
Head	The face looks flat; ears are of abnormal shape and size.
Eyes	Mildly exophthalmos; Ophthalmoscopic examination showed bilateral swelling of the optic disc. Visual acuity is normal.
Hearing assessment	Severe hearing loss.
Heart	Normal.
Abdomen	Hepatosplenomegaly and central echogenic fat.
Lymph nodes	Mildly enlarged cervical and inguinal lymph nodes
Genitourinary	Lack of secondary sexual signs.
Musculoskeletal	Pectus carinatum, flexion contracture of the fingers and toes.
Endocrine	Short stature, hypothyroidism.

Figure 1: Hyperpigmented skin lesion

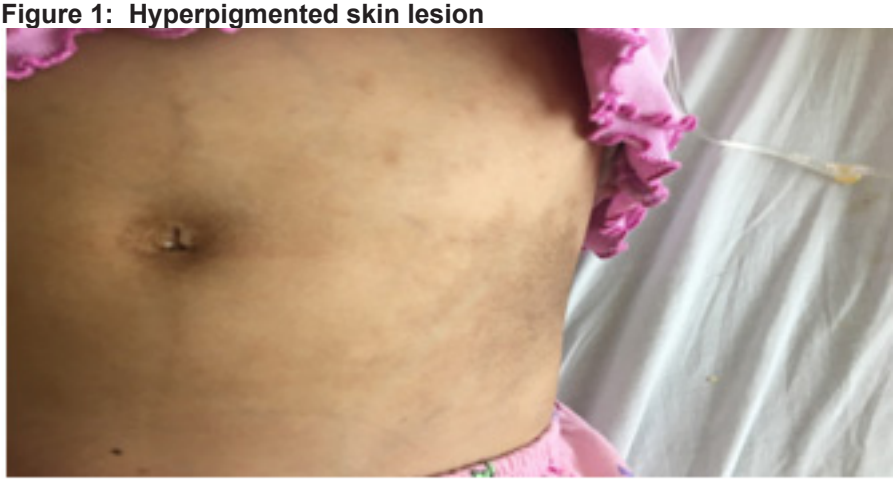
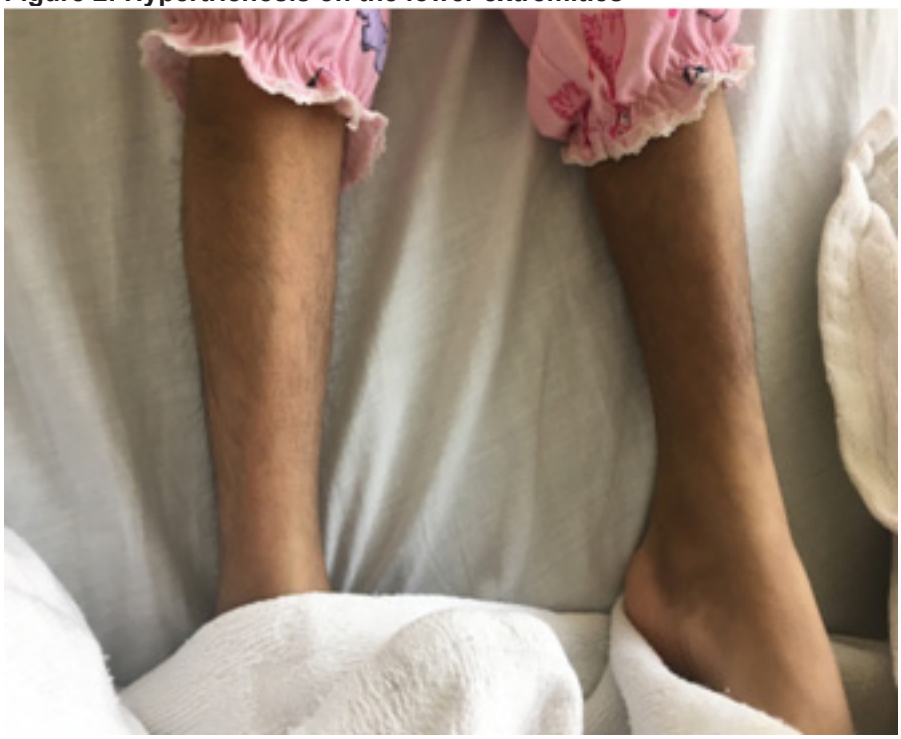


Figure 2: Hypertrichosis on the lower extremities



Discussion

We find ourselves in front of a large constellation of symptoms and signs related to different pediatric branches, including endocrinology, dermatology, gastrointestinal, ophthalmology, cardiology, and genetic diseases; so, we find that most patients are either not diagnosed or are diagnosed late by tracking and examining their history.
This syndrome is newly identified so most doctors are unaware of this syndrome, however, the pathognomonic features of H syndrome are typically the cutaneous hyperpigmentation and hypertrichosis.

In addition to the pathognomonic clinical features of H syndrome, the diagnosis should ideally be confirmed by mutation analysis of SLC29A3. Our patient had characteristic findings, including hyperpigmentation, hypertrichosis, short stature, hearing loss, hepatomegaly, hypothyroidism, and flexion contracture of the fingers and toes. Insulin-dependent diabetes mellitus and cardiac anomalies were absent in our case. We confirmed the diagnosis by whole-exome sequencing.

Molho-Pessach reported lymphadenopathy in 24% of patients with H syndrome (6). Inguinal, cervical, and axillary nodes, which were also present in our patient, are usually the most commonly affected lymph nodes. Elevated ESR, mild microcytic anemia, and bilateral optic disc swelling were present in our patient, which was also reported by Al-Hamdi KI et al (7).

Many cases reported around the world are of Arab consanguineous families with the main features of H syndrome (8).

No definitive treatment of this rare disorder exists which makes it crucial to recognize its presence, and thereby, avoid unnecessary interventions for treating cutaneous manifestations.

Genetic counseling may play an important role in management.

Conclusion

H syndrome, which seems to be more common among persons of Arab descent, has been described worldwide and should be included in the differential diagnosis of patients with short stature and systemic inflammation, particularly when accompanied by the characteristic cutaneous findings.

Despite this rare case, the cutaneous hyperpigmentation and hypertrichosis (pathognomonic feature) which are typical in H syndrome are still the key features to differentiate a multisystemic disease from others.

Moreover, recognition of the other clinical features (hypothyroidism, hepatosplenomegaly, short stature, hypertriglyceridemia, diabetes mellitus type one) of H syndrome is important for diagnosis.

Regardless, the genetic study is important not only for the diagnosis but also for genetic counseling.

Acknowledgments:
We thank Dr. Mohammad Al-raqad for participation in this study

Conclusion

1. Nasimfar A, Dashti AS, Haghbin H. A child with H syndrome. Arch Pediatr Infect Dis. 2016; 4 (2): 1–4.
2. Tekin B, Atay Z, Ergun T, Can M, Tuney D, Babay S, et al. H syndrome: A multifaceted 6 histiocytic disorder with hyperpigmentation and hypertrichosis. Acta Derm Venereol. 2015;95(8):1021–3.
3. Senniappan S, Hughes M, Shah P, et al. Pigmentary hypertrichosis and non-autoimmune insulin-dependent diabetes mellitus (PHID) syndrome is associated with severe chronic inflammation and cardiomyopathy and represents a new monogenic autoinflammatory syndrome. J Pediatr Endocrinol Metab. 2013;26:877-882
4. Molho-Pessach V, Lerer I, Abeliovich D, Agha Z, Abu Libdeh A, Broshtilova V, et al. The H Syndrome Is Caused by Mutations in the Nucleoside Transporter hENT3. Am J Hum Genet. 2008;83(4):529–34.
5. An I, Harman M, Ibiloglu I. H Syndrome - A Case Report. Indian Dermatol Online J.2019;10(3):300–2.
6. Molho-Pessach V, Ramot Y, Camille F, Doviner V, Babay S, Luis SJ, et al. H syndrome: The first 79 patients. J Am Acad Dermatol [Internet]. 2014;70 (1): 80 Available from: http://dx.doi.org/10.1016/j.jaad.2013.09.019
7. Al-Hamdi KI, Ismael DK, Qais Saadoon A. H syndrome with possible new phenotypes. JAAD Case Reports [Internet]. 2019;5(4):355–7. Available from: https://doi.org/10.1016/j.jdcr. 2019.02.003
8. Bloom JL, Lin C, Imundo L, Guthery S, Stepenaskie S, Galambos C, et al. H syndrome: 5 new cases from the United States with novel features and responses to therapy. Pediatr Rheumatol. 2017; 15 (1): 1-12.

Editorial Continued

Asif, H et al., attempted to Identify the factors responsible for students self-medicating with antibiotics in medical students at Sindh Medical College, Jinnah Sindh Medical University, Karachi. They followed a cross sectional study was conducted on a sample size of 359 students. The percentage of self-medication among students of Sindh Medical College, Jinnah Sindh Medical University, Karachi is 52.1%. Age groups were (16-18 = 14.5%, 19-21 = 58.2% and 22-24 = 27.3%). The authors concluded that students of Sindh Medical College, Jinnah Sindh Medical University, were found to self-medicate themselves with antibiotics. However, knowledge about drug resistance is required at individual level in-order to refrain from doing so. In consideration of these results, adequate measures should be taken to educate students regarding the hazardous side effects of antibiotics.

Helvaci M.R et al., tried to understand whether or not there is a higher prevalence of rheumatic heart disease (RHD) in the sickle cell diseases (SCDs). All patients with the SCDs and controls were studied. The study included 428 patients with the SCDs (208 females) and 2855 controls (1620 females). The authors concluded that SCDs induce severe and chronic inflammatory processes on vascular endothelium all over the body, and terminate with end-organ insufficiencies in early years of life. Beside that SCDs cause a moderate to severe immunosuppression by several mechanisms that may be the cause of higher prevalence of RHD in them.

Javed H et al., attempted to determine the perceptions of millennials of twenty first century regarding position of women in Pakistani society in Karachi. They followed a cross-sectional study on a sample of 330 participants from various universities of Karachi. The authors concluded that the youth of Pakistan is well aware of the social stigmas around them. Even our targeted audience that comprised of people living in urban areas has grown up seeing women mistreated for bearing daughters, but our study shows that this generation has realized the fault of their ancestors and there is hope that these young adults would bring a positive change in the future.

Hatroom A.A.S, did a a retrospective study involving 120 medical files of adult patients with undescended testes. He describes the pattern of clinical presentation, the ultrasound and intra-operatively findings, and the outcome of Cryptorchidism in Adults. Sixty-eight (56.7%) were presented to the hospital complaining of empty scrotum. Other 33(27.5%) were complaining of infertility. The best result of treatment of cryptorchidism is preferably in the childhood age, therefore careful physical examination of the baby at birth, regular follow-up of the infant and advice for early corrective surgery in cases of persistent undescended testis will go a long way in reducing the morbidity due to cryptorchidism.

Ahmed & Ali Raza reviewed thyroid disease in pregnancy. They stressed that Thyroid dysfunction in the form of hypo and hyperthyroidism are some of the most common endocrine conditions encountered in primary care. The hormone deficiency or excess can be easily diagnosed and managed yet potentially fatal in severe cases if left untreated. The authors stressed that guidelines around the world advocate various approaches to decision making about testing pregnant women for thyroid disease. There is increasing debate about whether thyroid screening should be made universal. In this article we look at the current guidelines and latest evidence and opinion in this important area.

Sumathipala, S., reviewed Glucose- 6-phosphate dehydrogenase deficiency. He stressed that G6PD deficiency is the most common enzyme disorder affecting red blood cells. It is inherited in an X linked recessive manner and there are over 400 variants identified. The disorder is normally asymptomatic but common presentations include neonatal jaundice and acute hemolysis. Treatment depends on the nature of the symptoms, co-existing conditions, and the degree of hemolysis. Identification of G6PD deficiency can begin with screening tests but definitive tests are required to diagnose the condition. Once diagnosed, people with G6PD deficiency need to avoid any agent that can provoke oxidative stress upon the red blood cell and seek medical attention if symptoms develop suggesting hemolysis.

Barg and Kadori, reported a rare case report of 17-year-old male patient from Pakistan with moth-eaten alopecia involving scalp hair and eyebrows. Alopecia syphilitic (AS) is an uncommon presentation and has been reported in up to 7% of cases with syphilis. This case report discusses the presentation and management of a 17-year-old male patient from Pakistan who presented with patchy hair loss on the scalp and eyebrow.

Ayyash F.F et al., reported H Syndrome case. H Syndrome is one of the rarest diseases in the world, it is an autosomal recessive (AR) disorder that occurs due to mutations in the solute carrier family 29. H Syndrome is characterized by cutaneous hyperpigmentation, hearing loss, hypertrichosis, hypothyroidism, hepatomegaly, flexion contracture of the fingers and toes, short stature, hypertriglyceridemia, diabetes mellitus type one, and hypogonadism.

It was named H syndrome considering the fact most of the clinical features start with the letter “H.”

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