World Family Medicine Journal
incorporating the Middle East Journal of Family Medicine

ISSN 1839-0188

July 2020 - Volume 18, Issue 7

Physical activity guidelines awareness and counselling practice in relation to health care providers' knowledge and behaviour in Qatar

... page 4

Table of Contents

Editorial

In this issue we have various papers from Australia, Canada, Iraq, Jordan, Lebanon, Oman, Nepal, Pakistan, Saudi Arabia, Turkey and the United Kingdom on topics of interest to primary care.

Al-Kuwari et al., tried to assess the level of health care providers' physical activity Vital sing (PAVS) and physical activity knowledge in relationships with health care providers' physical activity interventions. The study recruited 102 health care professionals from different specialties during the first Qatar physical activity guideline awareness campaign. The authors found that public health, physiotherapist, and family physicians were more active than other health care providers. The authors concluded that the healthcare providers are influenced by their physical activity vital sign (PAVS) and physical activity knowledge.

Salem et al., did a Descriptive cross-sectional study to assess patient satisfaction regard continuity care clinics in west bay health center , two hundred patients were asked to fill the short form of patient satisfaction questionnaire (PSQ 18).patients were satisfied in all domains of patient satisfaction questionnaire however the lowest scores in domains were for interpersonal manner (3.54 ± 0.74) and time spent (3.80 ± 0.78). Females have significant score (4.6 ±0.6) in general satisfaction domain while chronic patients report borderline significant score (4.1 ±0.5) in technical quality domain. The authors concluded that patient satisfaction scores were appropriate in all domains of care in continuity care clinics but more attention must be focused on training regard interpersonal communication and quality projects to improve time spent in health centers.

Al-Jadidi et al., attempted to determine the frequency of post-stroke delirium by systematically reviewing original research on this topic. They did MEDLINE, EMBASE, PsychINFO and the Cochrane Database of Systematic Reviews were searched for potentially relevant articles published from 1967 to March, 2014. The bibliographies of relevant articles were searched for additional references. Twelve studies met the inclusion criteria. There was significant heterogeneity in results of the studies of frequency of post-stroke delirium. The proportions ranged from 10% to 48%. The summary proportion was 0.24 (95% CI 0.18, 0.32). The frequency of post-stroke delirium may be related to medical co-morbidity or psycho-active drug use. The authors concluded that Post-stroke delirium may be frequent. Because of significant heterogeneity in the results of studies of frequency, the result of this review must be interpreted cautiously.

Mohammed et al., did A cross-sectional study involved 154 (88 males and 66 females) patients with psoriasis, of them 42(23males and 19 females) fulfilled the classification criteria of psoriatic arthritis from Oct. 2018 –Jan.2020. The study aimed to assess the occurrence of osteoporosis in patients with psoriasis and psoriatic arthritis. From the total sample, 154 patients, 112 patients with psoriasis 65 (58.9%) were males and 47 (41.1%) were females, 42 patients with psoriatic arthritis 23 (54.7%) were males and 19 (45.3%) were females. The authors concluded that osteoporosis frequently occurs in patients with psoriasis, in particular male patients. It is less frequently occurring in patients with psoriatic arthritis, in particular those on anti TNF treatment.

Al-Jamea et al., did A Descriptive/ Analytic cross-sectional study was performed, survey on a sample of 352 male and feminine students at random elect from 2 health programs in Medical schools in Jeddah city, Makkah region, Saudi Arabia in a period of 1 year. The aim of this study is to estimate the prevalence of self medication practice of undergraduate medical students listed at Medical schools. The current study was administered among 352 Pharm. The authors concluded that SM was quite common among undergraduate medical students, is also thanks to straightforward accessibility of medicines and data from textbook. A number of the scholars showed inadequate information and inappropriate angle toward some points concerning self-medication. Practice of SM is horrifying. Distribution of medication should be coordinated by Saudi healthcare professionals through rising precautionary and interventional policies; so, correct use of medicines is accomplished.

Alfayez et al., stressed that fundal placenta with abnormal invasion is relatively rare .

Most of fundal placenta with abnormal invasion is difficult to be diagnosed in antenatal period ,mostly diagnosed in postpartum period . Risk of uterine rupture in fundal placenta with abnormal invasion is one of the most dangerous complication which can lead to haemoragic shock and leads to death. They report a 32 years old woman presented to our obstetric emergency room ,she is G2p1by ceaserian section due to fetal disteress ,secondary infertility 9 years ,spontaneous pregnancy ,complaining of abdominal pain and history of vaginal spotting at 34 weeks gestation. During ceserian section haemperitoneum was noticed . After exploration fundal placenta percreta with omental band adhesion attached the placental site .

Dr Razaq & Saqib reviewed diabetes management in Ramadan. Fasting during Ramadan forms one of the five pillars of Islam. The fast involves abstinence from, food, drink, oral medications, smoking and sexual activity from dawn to dusk. It is obligatory for all healthy adults to fast. However, fasting is not intended to create excessive hardship and therefore exemptions exist. One such group of individuals who are exempt include those with chronic illnesses such as diabetes for whom fasting may be detrimental to their health. Despite this, many Muslims who could seek exemption choose to fast for cultural, social and religious reasons. The potential risks for diabetic patients who choose to fast in Ramadan include, hypoglycaemia, hyperglycaemia, diabetic ketoacidosis, dehydration and thrombosis. In addition to the risk of adverse events patients can also make unsafe choices regarding their diabetes management during this month. They will often not consult with clinicians for advice prior to fasting, arbitrarily change medication doses, timings, frequency and or omit them altogether. It is therefore important that healthcare professionals are proactive in identifying and engaging with diabetic patients who wish to fast during Ramadan at an early stage. An individualized Ramadan management plan should be discussed and agreed upon, with the aim of providing the best possible care and support to minimise the risk of any complications.

Sushil et al., did a cross-sectional study was conducted at Kathmandu Medical College, Nepal from August 2019 to January 2020. After obtaining an informed written consent, 81 breastfeeding and 81 non-breastfeeding mothers between two to four months postpartum were enrolled in the study through random sampling. The aim of the study is to evaluate o Postpartum Stress in Breastfeeding and Non-breastfeeding Mothers of Kathmandu, Nepal. A total of 162 mothers (81 breastfeeding and 81non-breastfeeding) were studied. The mean COHEN PSS score was 15.74(SD 2.36) for breastfeeding and 26.24(SD 3.78) for non-breastfeeding mothers. The authors concluded that the levels of perceived stress were high in non-breastfeeding mothers as compared to breastfeeding mothers.

Helvaci et al., tried to understand the most desired values of high density lipoproteins (HDL) in the metabolic syndrome. The study included 256 cases (153 females). Parallel to the highest HDL values, mean age, female ratio, body mass index (BMI), fasting plasma glucose (FPG), low density lipoproteins (LDL), white coat hypertension (WCH), hypertension (HT), and diabetes mellitus (DM) were the highest in the fourth group. The authors concluded that the highest mean age, female ratio, BMI, FPG, WCH, HT, and DM parallel to the highest HDL and LDL, and the highest CHD in contrast to the lowest HDL and LDL values may show initially positive but eventually negative acute phase proteins features of HDL and LDL. BMI, FPG, DM, and CHD were the lowest between HDL values of 40 and 46 mg/dL, and DM was only 3.1% between these values against 22.2% of the remaining.

The third part of Parkinson disease review discussed the diagnosis , symptoms, and prognosis of Parkinson's Disease. The author stressed Parkinson disease is a clinical diagnosis. For the condition, there are no laboratory biomarkers, and findings on routine magnetic resonance imaging and computed tomography scans are unremarkable. Medical diagnosis involves 2 of 3 cardinal signs: Resting tremor Bradykinesia and Rigidity. Parkinson's disease often has a multitude of non-motor symptoms; some may precede the diagnosis, while others may occur early or late after the diagnosis is made, depending on motor features. Careful attention to the history is needed in patients with Parkinsonism to exclude secondary causes such as medication, toxins, or trauma.

Tariq et al., looked at the trajectory of Covid-19 in Pakistan. The Ministry of Health, Government of Pakistan, reported its first two cases of the COVID-19 from Karachi and the capital Islamabad, on February 26th, 2020. Both had a history of recent travel from Iran. All four provinces and other territories compromising the state of Pakistan had reported their first cases by March 18th, 2020. The government of Pakistan quickly sprang into action and took many beneficial steps and implemented guidelines, which ensured that Pakistan was coping well with the pandemic, while its neighbors like Iran and China struggled amidst a rapidly developing crisis. However, effective policy making was in short supply as a couple of months later, the country's situation is quite dire, and deteriorating rapidly, due to a lack of caution and indecision on many crucial matters. In Pakistan, the total cases reported so far have been 139,000, with 2632 deaths. In there article, the authors reviewed measures implemented by the government, assess the trajectory of the disease in the country, while identifying some of the factors responsible for a recent downward trend.

Physical activity guidelines awareness and counselling practice in relation to health care providers' knowledge and behaviour in Qatar

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Mohamed Ghaith Al-Kuwari, Ahmad Muslim Al-Hamdani, Wadha Ahmad Al-Baker. Physical activity guidelines awareness and counselling practice in relation to health care providers' knowledge and behaviour in Qatar. World Family Medicine. 2020; 18(7): 5-10 DOI: 10.5742MEWFM.2020.93828

Abstract

Background: Health care providers represent a credible source to encourage their patients to be physically active. This study aims to assess the level of health care providers' Physical Activity Vital Sign (PAVS) and physical activity knowledge in relationship with health care providers' physical activity interventions.

Method: The study recruited 102 health care professionals from different specialties during the first Qatar physical activity guideline awareness campaign. The data were collected from subjects with information about their PAVS, physical activity knowledge, and counselling practice.

Result: Public health professionals, Physiotherapists, and Family physicians were more active than other health care providers. Verbal advice on physical activity was the most common intervention offered by health care providers to their patients. Health care providers with a high level of PAVS tend to prescribe more referrals of their patients to fitness coaches.

Conclusion: The healthcare providers are influenced by their physical activity vital sign (PAVS) and physical activity knowledge.

Key words: Physical activity, Health care providers, Counselling, physical activity vital sign.

Introduction

Sedentary behavior has become a significant public health threat all over the world. Ranked as the fourth leading risk factor for global mortality, physical inactivity contributes to around 3.2 million deaths worldwide(1). It is commonly known that participation in regular exercise reduces the risk of chronic diseases and premature mortality which eventually helps in reducing the burden exerted on healthcare systems and the economy(1-3).

Global physical activity guidelines and strategies were developed in order to spread awareness about the importance of physical activity; however, the prevalence of obesity and physical inactivity is still on the rise. Hence, it is essential to tackle such an issue differently and find other subsequent means to reach a larger scale of the community. Promoting physical activity has been considered as a public health priority and essential at each of the individual, family, healthcare-setting, community, and governmental levels(1,3). There is a growing literature that confirms the efficacy of promoting physical activity at the primary care settings(4-6). It is deemed that primary care physicians have an important role in affecting the health of a population. They represent a credible source with the authority to educate patients about the importance of physical activity and encourage them to integrate it into their daily routine (7-9). However, minimal research has been done in Qatar on exploring the physical activity involvement of health care professionals and their attitudes towards incorporating physical activity in their consultation as part of the management plan for their patients.

The main purpose of this study was to evaluate the level of awareness among healthcare providers of different backgrounds regarding physical activity and assess their situation concerning incorporating physical activity within their therapeutic plans, in an attempt to predict the appropriate educational and strategic needs for the implementation of exercise interventions in the health care setting.

Method

The study recruited 102 health care providers from different health professional backgrounds to meet the study's goal regarding assessing their level of physical activity awareness, physical activity behavior and counseling practice of physical activity.

Qatar's National Physical Activity Guideline was officially launched in February 2015 in order to highlight the importance of physical activity in health promotion, disease prevention, and treatment for certain chronic conditions. A workshop was conducted to target professionals from different healthcare backgrounds and sectors.

Subjects were handed pre- and post-tests prior to and after delivering the guidelines to evaluate the current status of healthcare providers and the effect of such symposium on raising their awareness. The tests included basic questions to specifically assess the knowledge about physical activity among children and adults and the therapeutic effect of physical activity, and precautions in managing common chronic diseases, e.g. diabetes, hypertension, ischemic heart disease, depression, and osteoarthritis. Some demographic data were collected from subjects with information about their physical activity behavior using physical activity as a vital sign (PAVS), and their use of exercise as their therapeutic plan with their patient. These questions were adopted from the "Active Australia Survey" which was initially designed to measure individuals' participation in physical activity and to assess their knowledge regarding public health messages about health benefits of physical activity(10).

Data were entered directly into the Statistical Package for Social Sciences (SPSS) program using specific codes for each of the test items. All statistical analyses were conducted using the IBM SPSS (SPSS version 21.0, IBM Corp., Armonk, NY, USA).

Results

Baseline data

a. Demographic characteristics

The characteristics of the study subjects are represented in Table 1. The mean age was 39.5 ± 8.8 years, and the subjects had an average experience of 13.5 ± 8.4 years. The study subjects were mainly specialized in family medicine (16.9%), followed by public health (14.7), as shown in Figure 1.

b. Physical activity vital sign (PAVS)

When exploring the PAVS with respect to the background and specialty of each subject (Figure 2), the subjects have a mean PAVS 148.8 ± 90.1 mins/ week. it was noticed that health care professionals with a public health background had the highest PAVS with an average of 290 minutes per week, followed by physiotherapy (216 minutes per week) and family medicine (158 minutes/week). While other specialties reported PAVS below 150 minutes.

c. Use of physical activity intervention

On the other hand, the correlation between different factors and the type of advice given to patients was explored and illustrated in Table 2. Most subjects provide verbal advice to their patients. Those who exercise the most during the day (45 minutes/day) tend to prescribe a pedometer to their patients. Interestingly, those who reach a mean physical activity vital sign (PAVS) up to 170 minutes per week, which is above the average recommended amount of 150 minutes per week, are referring their patients to a fitness coach.

d. National physical activity guideline knowledge assessment

When we assessed the national physical activity guideline knowledge of the participants, we found a significant increase in knowledge after the awareness session. In the pre- and post-tests, the total correct answers were initially 69.3% and increased up to 81.1% after launching

Table 1: Characteristics of the study subjects

Characteristics	Overall Population Mean ± SD
Age *(years)*	39.5 ± 8.8
Experience *(years)*	13.5 ± 8.4
Physical activity vital sign (PAVS) *(minutes/week)*	148.8 ± 90.1

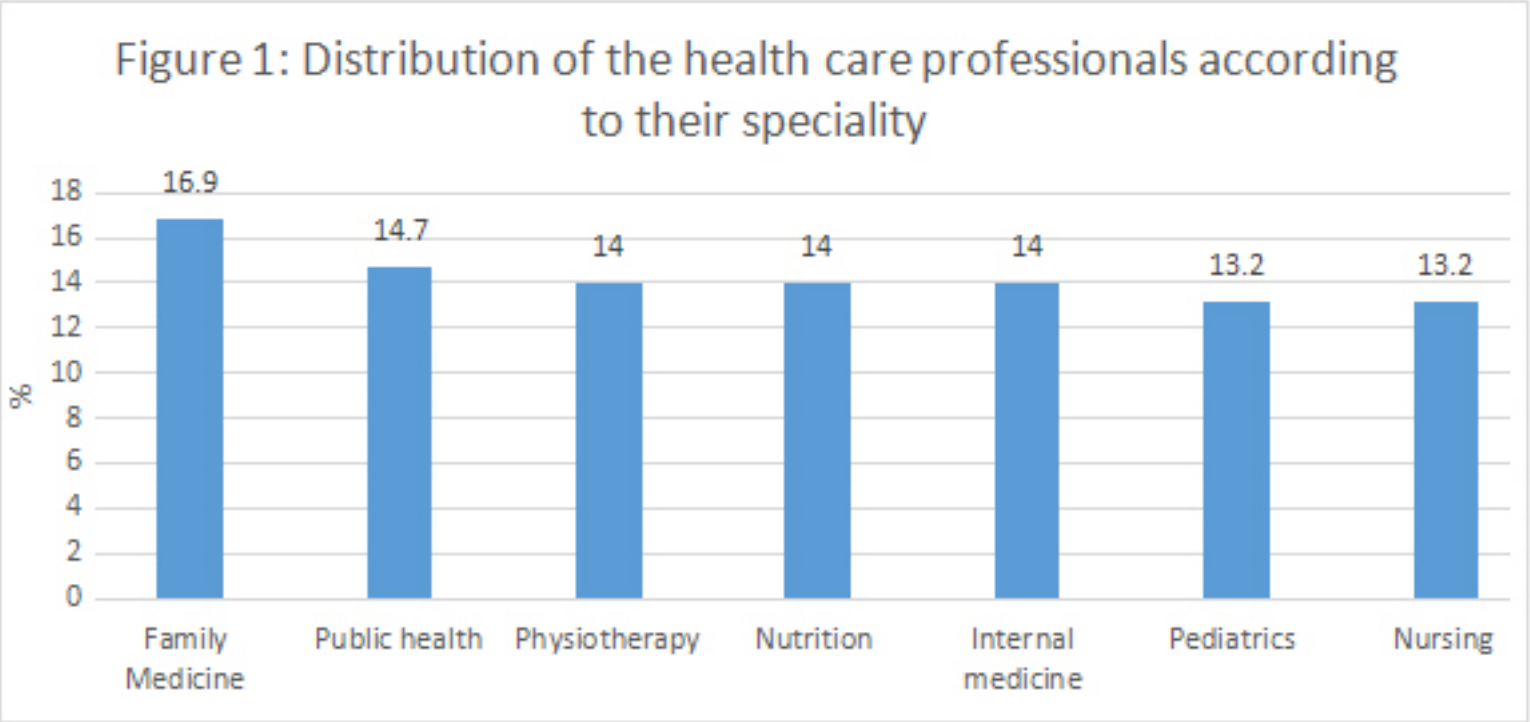


Table 2: Correlation between different factors and the type of advice given to patients

	Verbal advice Mean ± SD	Pedometer Prescription Mean ± SD	Referral to Fitness Coach Mean ± SD
Age *(years)*	39.5 ± 8.7	41.5 ± 13.7	43.3 ± 11.0
Experience *(years)*	13.3 ± 8.0	15.8 ± 9.4	16.1 ± 9.0
PAVS *(Mins/week)*	140.3 ± 89.0	160.0 ± 62.4	170.3 ± 115.0

the physical activity guidelines, t = 19.12, p < 0.0001, as shown in Figure 3. Additionally, when exploring the distribution of correct responses based on the theme of the pre-test questions, as observed in Figure 4, the majority of subjects were found to be more familiar with the therapeutic-related field with a test score of (55.9 %) followed by general guidelines for adults (53.5%), while subjects showed a low level of knowledge in the general guidelines for children with a test score of (19.8%).

Figure 2 : Average PAVS according to the speciality

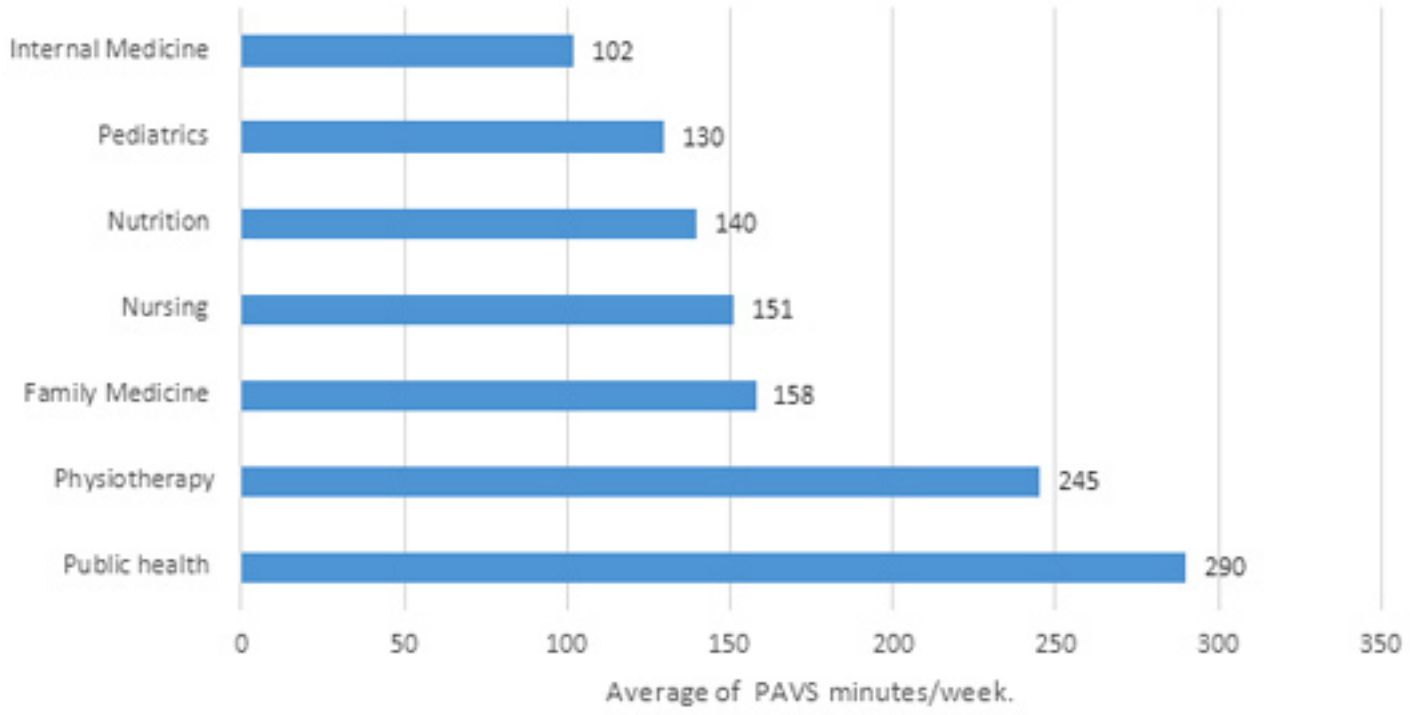
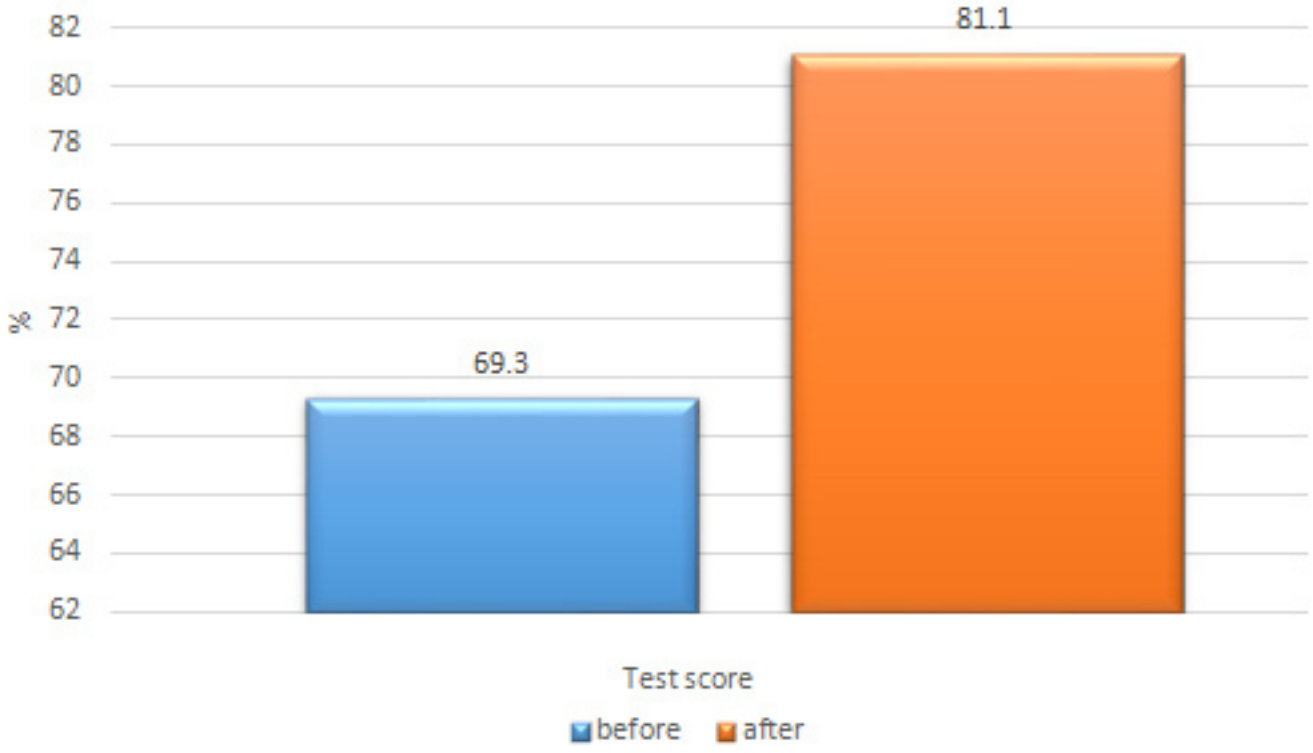
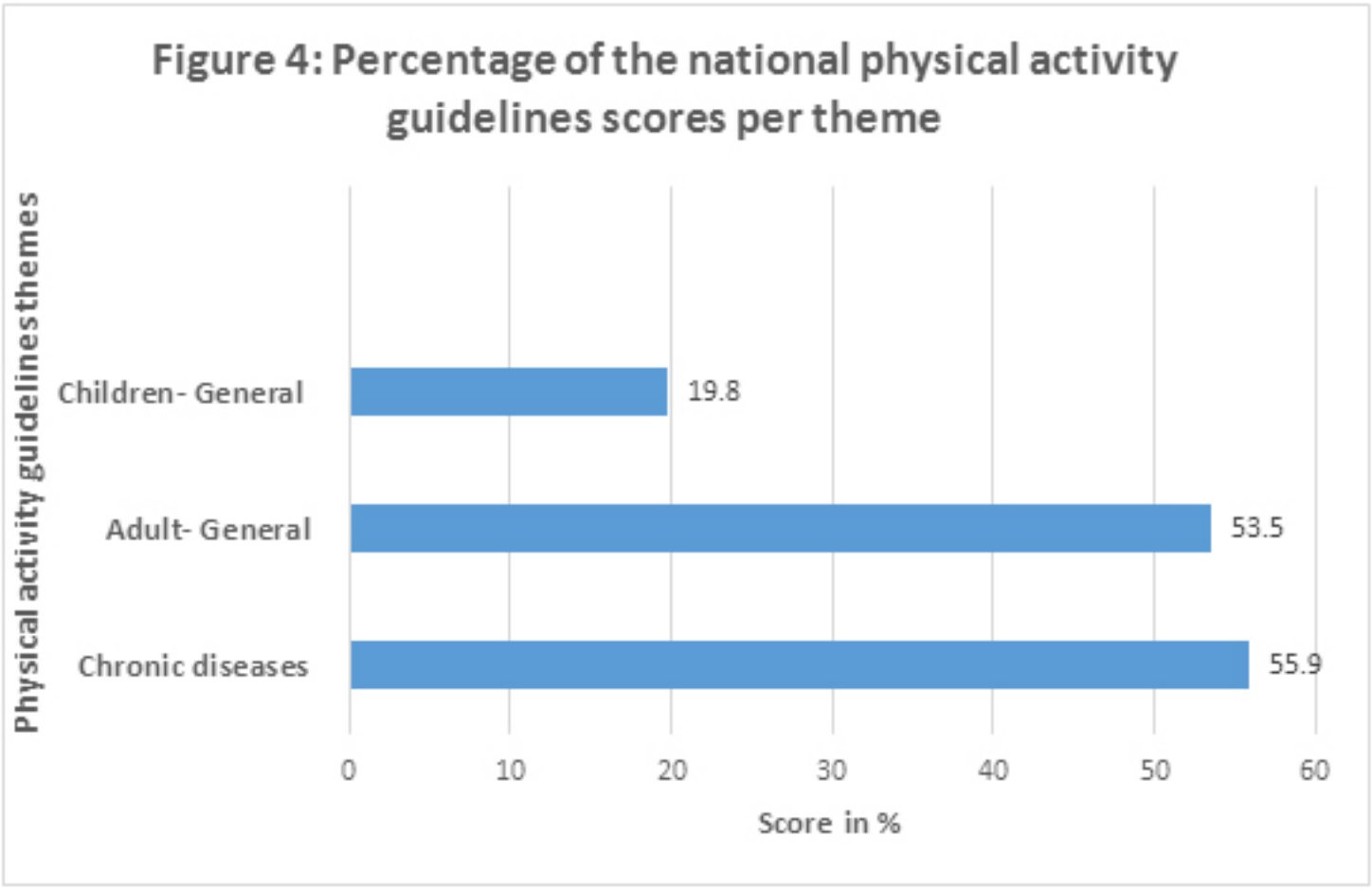


Figure 3: the score of the national physical activity guidelines' test





Discussion

This study attempts to explore the situation of healthcare providers from different backgrounds with respect to incorporating physical activity within the daily clinical practice. The preliminary results of this study demonstrated different findings related to the relationship between the practitioners' behavior, the level of awareness about the national physical activity guidelines, and using the physical activity intervention with their patients.

In terms of the physical activity behavior, the current study showed that primary care providers, i.e. public health professionals, physiotherapists and family medicine practitioners, were exercising more than the recommended weekly amount of physical activity, which is 150 minutes/ week. This is consistent with other studies that found physicians and health care providers participated in physical activity more than the general public (11). Furthermore, being primary care providers gives the advantage that more lifestyle-related medical conditions are seen in primary care(11).

It was noticed that physical activity intervention provided by the health care professionals is correlated to their physical activity behavior and the duration of their clinical experience. In this study, practitioners with experience of more than 15 years and PAVS > 150 mins/week tend to provide more practical physical activity interventions to their patients such as providing a pedometer or referring patients to fitness coaches, which is consistent with other studies in the literature (12). Also, it adds positive influence during the consultation as the patients regard physicians as role models (12). Moreover, a physician's personal health affects their patient care, meaning if health care providers are active, then they promote and counsel about physical activity and other healthy lifestyle behaviors (12-18). However some studies showed no association between health care providers' personal exercise habits and counseling about physical activity (19-20).

The study showed that practitioners have good knowledge about physical activity guidelines. The results show that providing an awareness workshop increases the knowledge of physical activity guidelines. And as expected, physicians were better in the therapeutic-related field, which has also been found in a review article by Ribeiro et al & Kreuter et al (21-22). The results also showed increased knowledge of Adults physical activity guideline more than children, and this is because our sample was mainly primary care physicians and other specialties more than pediatricians. Hence, they were more familiar with adult care; in future workshops we must increase pediatricians and increase the content on children's' exercise knowledge. This study highlighted the effect of training on overcoming one of the major barriers of physical activity counseling which is the lack of updated knowledge and training on physical activity (13,15,18,23,24) . However, the proper knowledge needs to be supported by other interventions such as PAVS system, to make the health care providers counsel more patients about physical activity on each visit.

Conclusion and Recommendations

Based on the aforementioned findings, we can conclude that primary care professionals are influenced by their behavior when prescribing exercise to their patients. It is clearly noted that their level of physical activity affects the way they advise their patients as well. Even though physical activity advice for patients is being practiced among healthcare professionals in Qatar, still, this is not enough.

It is essential to increase awareness among healthcare professionals, especially those working in a clinical setting such as family medicine physicians, pediatricians, and nutritionists, regarding the importance of incorporating physical activity in primary care. Targeting the primary care team and encouraging them to improve their physical activity levels can support this approach and eventually increase the motivation among the patients to exercise more. Primary care professionals can be guided through regular medical education workshops, promoting the use of pedometers within the healthcare settings, and using PAVS in the medical records.

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Satisfaction among patients attending the continuity of care clinic in West Bay health center in Qatar

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Mohamed Salem et al. Satisfaction among patients attending the continuity of care clinic in West Bay health center in Qatar. World Family Medicine. 2020; 18(7): 11-15 DOI: 10.5742MEWFM.2020.93829

Abstract

Background: Patient satisfaction is an important element into assessing quality of health care facilities. Levels of satisfaction affect the shaping of the health system. A satisfied patient is more likely to develop a deeper and longer lasting relationship with their medical provider, leading to improved compliance, continuity of care, and ultimately better health outcomes.

Objective of the Study: To assess the level of patient satisfaction in continuity care clinics at Wwest Bbay health center.

Methods: Descriptive cross-sectional study to assess patient satisfaction regard continuity care clinics in Wwest Bbay health center; two hundred patients were asked to fill out the short form of patient satisfaction questionnaire (PSQ 18).

Results: Patients were satisfied in all domains of patient satisfaction questionnaire however the lowest scores in the domains were for interpersonal manner (3.54 ± 0.74) and time spent (3.80 ± 0.78) . Females have a significant score (4.6 ±0.6) in general satisfaction domain while chronic patients report borderline significant score (4.1 ±0.5) in technical quality domain.

Conclusion: Patient satisfaction scores were appropriate in all domains of care in continuity care clinics but more attention must be focused on training in regard to interpersonal communication and quality projects to improve time spent in health centers.

Key words: Patient Satisfaction, Continuity Care, Qatar

Background

Continuity of care is considered a cornerstone of family medicine (1) . It is described as a longitudinal relationship between patients and caregivers that transcends multiple illness episodes and includes responsibility for prevention and care coordination (2).

Continuity of care is considered as a hallmark and primary objective of family medicine and is consistent with quality patient care provided through a patient-centered medical home. The continuity of care inherent in family medicine helps family physicians gain their patients' confidence and enables family physicians to be more effective patient advocates (3).

It represents an essential aspect of good quality primary care, as is involving patients in assessing, developing, and improving of it (4). Continuity of care can be assessed by the general population, the users (patients), or the providers (professionals or organizations), and is continuity of care is related to other healthcare dimensions and outcomes (5).

Patient satisfaction is an important element of assessing quality of health care facilities. Levels of satisfaction affect the shaping of the health system (6) as well as some predictors (e.g. educational level).

A satisfied patient is more likely to develop a deeper and longer lasting relationship with their medical provider, leading to improved compliance, continuity of care, and ultimately better health outcomes (7).

Patients' own experiences may not directly relate to the quality of the care provided, but rather their expectations of what they believe should be provided or their expectations of their prognosis, treatment, family interaction, and environment. And yet, there is much still unknown (8).

The main aim of this study is to assess the level of patient satisfaction in continuity care clinics at West Bay health center

This research was conducted to answer the question: How are the patients attending the Continuity of Care Clinic satisfied with the available care provided?

Methods

Study Design: Descriptive cross sectional study

Study setting:
This study was conducted in West Bay Training Health Center affiliated to Primary Health Care Corporation in Qatar where the Family Medicine Residency Program runs its activity in the form of academic days and continuity care clinic which is run by residents of family medicine and supervised by faculties from the family medicine department.

Study Subject:
Two hundred patients were asked to fill out the short form of patient satisfaction questionnaire (PSQ 18) (9) in the period from April-May 2018.

Data Collection Methods:
The PSQ 18 is an instrument that contains 18 items tapping each of the seven dimensions of satisfaction with medical care: general satisfaction, technical quality, interpersonal manner, communication, financial aspects, time spent with doctor, and accessibility and convenience.

Data analysis :
Data was collected and analyzed using Mean ±SD for total score in each dimension and relation between patient character and scores for dimensions analyzed by (STATA 9) and P value ≤ 0.05 was considered significant.

Results

Table 1: Shows the sociodemographic character of the sample population. There were 47.5% below 40 years, 56.6% were females ,71% were married, 50% were Qatari, and 61% had a chronic medical condition.

Table 2: Shows the patient satisfaction subscale

Patients showed high scores in all domains of patient satisfaction dimensions however the lowest scores in domains were for interpersonal manner (3.54 ± 0.74) and time spent (3.80 ± 0.78).

Table 3: Shows the relation between patient satisfaction and sociodemographic characters.

Females had a significant score (4.6 ±0.6) P ≤0.02 in general satisfaction domain while chronic patients reported borderline significant score (4.1 ±0.5) P ≤0.05 in technical quality domain.

Table 1. Description of patient Socio-demographic characteristics (N=200)

No.	Character		Frequency	Percentage
1.	Age Group (Years)	< 40	95	47.5
		≥ 40	105	52.5
2.	Gender	Female	113	56.5
		Male	87	43.5
3.	Educational level	Primary	32	16.0
		Secondary	79	39.5
		University	89	44.5
4.	Marital Status	Ever-married	142	71.0
		Never-Married	58	29.0
5.	Nationality	Qatari	101	50.5
		Non-Qatari	99	49.5
6.	Medical Problem	Acute	78	39.0
		Chronic	122	61.0

Table 2. Summary of Patient Satisfaction subscales (N=200)

	Factor	Median	Mean ± Standard Deviation
1.	General Satisfaction	4.50	4.37 ± 0.65
2.	Technical Quality	4.25	4.19 ± 0.65
3.	Interpersonal Manner	3.50	3.54 ± 0.74
4.	Communication	4.50	4.26 ± 0.72
5.	Financial aspects	4.50	4.25 ± 0.69
6.	Time spent	4.00	3.80 ± 0.78
7.	Accessibility & Convenience	4.00	3.89 ± 0.65

Table 3: Relationship between patient sociodemographic characteristics and patient satisfaction sub-scales (N = 200)

		General Satisfaction		Technical Quality		Interpersonal Manner		Communication		Financial Aspects		Time spent		Accessibility & Convenience	
		χ ± σ	P-value	χ ± σ	P-value	χ ± σ	P-value	χ ± σ	P-value	χ ± σ	P-value	χ ± σ	P-value	χ ± σ	P-value
Age Group (Yrs)	< 40	4.4±0.7	0.90	4.2±0.7	0.73	3.5±0.7	0.73	4.3±0.6	0.30	4.3±0.7	0.58	3.8±0.8	0.89	3.9±0.7	0.58
	≥ 40	4.4±0.6		4.2±0.6		3.6±0.8		4.2±0.8		4.2±0.7		3.8±0.7		3.9±0.6	
Gender	Female	4.5±0.6	0.02 *	4.2±0.7	0.61	3.5±0.7	0.85	4.3±0.7	0.81	4.3±0.7	0.32	3.9±0.8	0.15	3.9±0.6	0.72
	Male	4.2±0.7		4.2±0.5		3.5±0.8		4.2±0.7		4.2±0.7		3.7±0.7		3.9±0.7	
Educational level	Primary	4.3±0.6	0.47	4.1±0.6	0.30	3.5±0.8	0.58	4.1±0.7	0.62	4.1±0.8	0.26	3.8±0.7	0.75	3.9±0.6	0.78
	Secondary	4.4±0.6		4.1±0.5		3.5±0.7		4.3±0.7		4.3±0.7		3.8±0.7		3.9±0.6	
	University	4.4±0.6		4.3±0.8		3.6±0.7		4.3±0.8		4.3±0.7		3.8±0.9		3.9±0.7	
Marital Status	Ever-M	4.4±0.6	0.14	4.2±0.5	0.77	3.5±0.8	0.92	4.2±0.8	0.79	4.2±0.7	0.69	3.8±0.8	0.61	3.9±0.6	0.26
	Never-M	4.3±0.8		4.2±0.9		3.5±0.7		4.3±0.6		4.3±0.7		3.8±0.8		3.8±0.6	
Nationality	Qatari	4.3±0.7	0.08	4.1±0.6	0.17	3.4±0.7	0.06	4.2±0.8	0.35	4.3±0.7	0.72	3.8±0.7	0.92	3.9±0.7	1.00
	Non-Qatari	4.4±0.6		4.3±0.7		3.6±0.8		4.3±0.7		4.2±0.7		3.8±0.8		3.9±0.6	
Medical Problem	Acute	4.3±0.7	0.48	4.1±0.5	0.05	3.5±0.7	0.31	4.2±0.7	0.14	4.2±0.7	0.24	3.7±0.8	0.34	3.9±0.7	0.98
	Chronic	4.4±0.6		4.3±0.7		3.6±0.8		4.3±0.7		4.3±0.7		3.8±0.7		3.9±0.6	

χ: Mean, σ: Standard Deviation * P-value <0.05

Discussion

The current study aimed at determining the level of patients' satisfaction with continuity of care clinics. The level of satisfaction with the services provided showed high scores in all domains reaching 4.37 ± 0.65 representing 90% in the general satisfaction domain. These findings match satisfaction of care in Majmaah in Saudi Arabia reaching 81.7% (10). \In another study in Kuwait satisfaction reached 96.5% (11). The high satisfaction rate may be due to that continuity of care has advantages such as being more organized with a good appointment system and patients can see the same physicians each time.

However the lowest scores in domains of satisfaction were for interpersonal manner (3.54 ± 0.74) and time spent (3.80 ± 0.78) which warrant great emphasis upon these domains as cleanliness, competence of the staff, along with respect and good handling are the drivers behind the high level of satisfaction in the Qatar study (12).

With regard to time spent, lower scores of satisfactions could be explained by Generally, during the evaluation of PSQ-18 estimates, we noticed the remarkably low satisfaction estimates of Accessibility and Convenience, and Time Spent with Doctor confirmed in many studies (13). A study found that the shorter consultation time was the strongest prognostic index causing poorer satisfaction (14).

In this study, females have a significant score (4.6 ±0.6) P ≤0.02 in the general satisfaction domain.

This finding matches a study conducted in Kuwait where females were more satisfied with the health services provided than the males (11), while males were more satisfied than females about the provided PHC centers' services in a Saudi Study (10). This could be explained by that the high level of satisfaction among the females may be due to the fact that the work load on female staff is high and moving them into the continuity care side saves time and gives more care.

The present study stated that there is no significant relation in regard to age, gender, marital status and satisfaction domains. This matches with a Saudi study (15) showing no association between patients' satisfaction and gender, marital status and average monthly income.

Conclusion

Patient satisfaction scores were appropriate in all domains of care in continuity care clinics but more attention must be focused on training regarding interpersonal communication and time spent in consultation with physicians.

Competing interests: No conflict of interest
Ethical Considerations: This research project is approved from IRB (Institutional Review Board) in Primary Health Care Corporation

Acknowledgement: Authors would like to acknowledge the respondents who accepted to participate in this study. Our appreciation extends to the staff of the PHC centers that assisted in this work. We extend our acknowledgement to Mr. Mohamed Aslam – Family Medicine Program co-ordinator.

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Knowledge, Attitude and Practice of self-medication Among Undergraduate Medical Students in Jeddah city, Saudi Arabia

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Reham Al-Jamea, Asseil Bossei, Hanan Al Zhrani, Faisal Bossei, Wed Faiz, Maaly Alqurashi, Hydi Ahmed. Knowledge, Attitude and Practice of self-medication Among Undergraduate Medical Students in Jeddah city, Saudi Arabia. World Family Medicine. 2020; 18(7): 16- 24 DOI: 10.5742MEWFM.2020.93830

Abstract

Background: Self-medication (SM) may be a common habit globally and also the unauthorized use of medication could be a reason for concern. Developing authorization, as a result of improved academic levels and larger access to data, combined with an extreme pursuit of personal health, is leading to a growing demand for direct involvement in health-care decisions. Most medications will have important unwanted side effects and this might result in clinical consequences with potential life threatening complications. The aim of this study is to estimate the prevalence of SM practice of undergraduate medical students listed at Saudi Arabian Medical schools.

Method: A Descriptive/Analytic cross-sectional study was performed, using a survey on a sample of 352 male and female students randomly selected from 2 health programs in Medical schools in Jeddah city, Makkah region, Saudi Arabia in a period of 1 year.

Results: The current study was administered among 352 Pharm. D and MBBS students, of whom a hundred and fifteen (32.7%) were males and 237 (67.3%) were females. We found that 231 (65.6%) students practiced SM, female participants outnumbering male participants. The prevalence of SM was wide-ranging amongst different years of scholars, the prevalence increasing from the initial to the final year. The knowledge of usage came from medical textbooks by sixty-one (26.4%) of students. Among the self-medicators, the bulk used Non-prescription over-the-counter medicine, 134 (58%).

Conclusion: SM was quite common among undergraduate medical students, due to straightforward accessibility of medicines and data from text books. A number of the scholars showed inadequate information and inappropriate regard toward some points concerning self-medication. Practice of SM is alarming. Medication distribution should be coordinated by the Saudi health care professionals through instituting precautionary and interventional policies; so that correct use of medicines is accomplished.

Key words: Self-medication, Undergraduate Medical Students, Drugs, Clinical pharmacy

Introduction

Self-medication (SM) is a universal problem. It is existing in all ages, although its degree varies across cultures and countries. Once self medication was never used but it has now become a crucial facet of self care. [1]. Self medication is not recommended due to the possibility of adverse drug reactions or medication-related issues. The price may also be an issue , in consideration of the cost of treatment and hospital admission [2,3,4]. SM could be a common global practice universal and the illegal use of medication could be a concern. . It is highlighted because the use of treatment by a patient is on their own initiative or on the recommendation of a chemist or a lay person rather than though consulting a professional. Research shows there is incontestable augmented SM use from a range of totally dissimilar countries . The practice of SM is globally widespread currently, particularly in developing countries where numerous medications are distributed over-the-counter while not prescribed [5]. However, prevalence values being reported to be approximately 4-75% in Asia, which is a huge value. [6] The occurrence of SM among undergraduate medical students is very high in Pakistan [7]. The high availability of pharmaceutical products recently, improved access to drugs; quality of health-care, the augmented potential to manage diseases through self-care; and economic, political and cultural factors have contributed to the expansion of SM globally. Compared to the general public, there are several aspects that increase practice of SM amongst undergraduate medical students like simple availableness of medicine, advertising of drug makers, earlier experience with symptoms or illness [5]. Accuracy regarding correct drug information, home-kept pharmaceuticals [8] and simple access to information increases the problem . There is a developing situation , ensuing from improved academic levels and larger access to information, combined with increased focus on individual health, which is leading to growing demand for direct participation in health-care choices. SM is related to several adverse issues such as incorrect self-diagnosis, inadequate treatment of an illness, all of which might lead to advancement of illness and complications. Most medication has important unwanted effects. This could lead to serious clinical problems with potentially serious complications. Consequently, the diagnosis by the medical practitioner is vital for the right treatment. Clinical Pharmacy and medicine students square are expected to be more knowledgeable relating to rational use of medicines as compared to the overall public and are expected to be more knowledgeable relating to rational use of medicines as compared to the overall public. In keeping with the WHO recommendations, participation of consumers in health regulation is very important for drug regulation and this is supported in most developed countries like the USA and Canada . [9] Despite the prevalence of SM practice among people in the Kingdom of Saudi Arabia, few comprehensive studies have been conducted to assess this practice. As very little information is available regarding SM practice between undergraduate medical students, the goal of our study was to evaluate the prevalence, attitudes, determinants, and sources of SM among Jeddah medical and nonmedical students. The aim of this study is to estimate the prevalence of SM practices of healthy undergraduate students registered at Medical schools in Jeddah city to inform and update future academic efforts on drug misapprehensions so as to inspire harmless medication practices amongst incoming undergraduate medical students as well as to assess the frequency of SM for many unremarkably occurring medical conditions and take into account the possible role of the clinical chemist or physicians in SM use.

Methods

Design: A Descriptive/Analytic cross-sectional study was performed, using the questionnaire on a sample of 352 male and female students randomly selected from two health programs at Ibn Sina National college for medical studies (ISNC), Jeddah, Saudi Arabia.

Analysis: Data Analysis was performed by the statistical team using SPSS program (version 16). The means and standard deviations of normally distributed variables were compared using paired t tests and for categorical variables, the X2 test was used. The p-value of less than 0.05 was considered to be a statistically significant difference.

Participants: Undergraduate medical students enrolled at Medical colleges in Jeddah city who voluntarily agreed to participate in the online survey.

Survey Instrument: Randomly chosen consenting participants were requested to answer a 16 items self-structured online form. It was initially directed to 12 undergraduate medical students of our college and pilot tested. Appropriate adjustments were then prepared before confirming it for the research. The survey included items to collect information on demography, frequently used self-medications, prevalence and forms of self-medications. Undergraduate medical Students were assured about the privacy of their answers. Meanwhile knowledge of medications improves as we develop. The survey contained questions about sociodemographic, education, clinical information, history and pattern of doctor visits, students' beliefs and knowledge about the OTC intake and prescribed drugs, reasons for the self-prescribed habit, knowledge source, and recurrent indications boosting self-medication. Some questions had more than 1 answer. The survey was settled after an inclusive evaluation of the related articles and discussion between the research group. It was face-validated via discussion with specialists in the field and was furthermore objectively validated for clarity.

Implications of results:
Results will be used in educational awareness provision and interventions for incoming undergraduate medical students to encourage harmless medication practices.

Results

Table 1: Prevalence of SM based on Specialty

	Self-medication	
	Yes	No
Medicine	163	75
	30%	14%
Pharm. D.	162	82
	30%	15%
Dentistry	29	13
	5%	2%
Nursing	8	6
	0,4871 %	0,1151 %

Table 2: Frequency of self-medication

	Total Number	%	male		female	
No self-medication	11	3%	5	45%	6	55%
Rarely (Once a month)	211	58%,3	54	26%	157	74%
Often (Once every two weeks)	92	25%,4	27	29%	65	71%
Frequently (Once a week)	27	7%,5	10	37%	17	63%
Very frequently (more than once a week)	21	5%,8	5	24%	16	76%

Table 3: Illnesses for which SM was used

	Total Number	%	male		female	
Headache, fever and pain, Dysmenorrhea	107	30%	31	29%	76	71%
Cold and Flu	82	23%	31	38%	51	62%
Insomnia/ Anxiety	7	2%	2	29%	5	71%
Allergy (eye, skin, nose)	37	10%	10	27%	27	73%
Gastric symptoms (Diarrhea/ constipation/ Vomiting /indigestion)	29	8%	5	17%	24	83%
Respiratory symptoms (Sore throat, cough, epistaxis)	12	3%	3	25%	9	75%
Skin infection	7	2%	1	14%	6	86%
None	81	22%	18	22%	63	78%

Table 4: Types of SM used for illnesses

	Total Number	%	male		female	
Analgesics/Antipyretics (Paracetamol/NSAIDs)	199	55%	55	28%	144	72%
Antibiotics (Amoxicillin, Cefixime)	26	7%,2	6	23%	20	77%
Cough and Flu (Pseudoephdrine)	60	16%,6	17	28%	43	72%
(Lactulose)	10	2%,8	3	30%	7	70%
Anti-histamines (Loratadine, Citirizine)	43	11%,90	4	9%	39	91%
Multivitamins	20	0%,55	3	15%	17	85%
CNC	4	1%,10	1	25%	3	75%

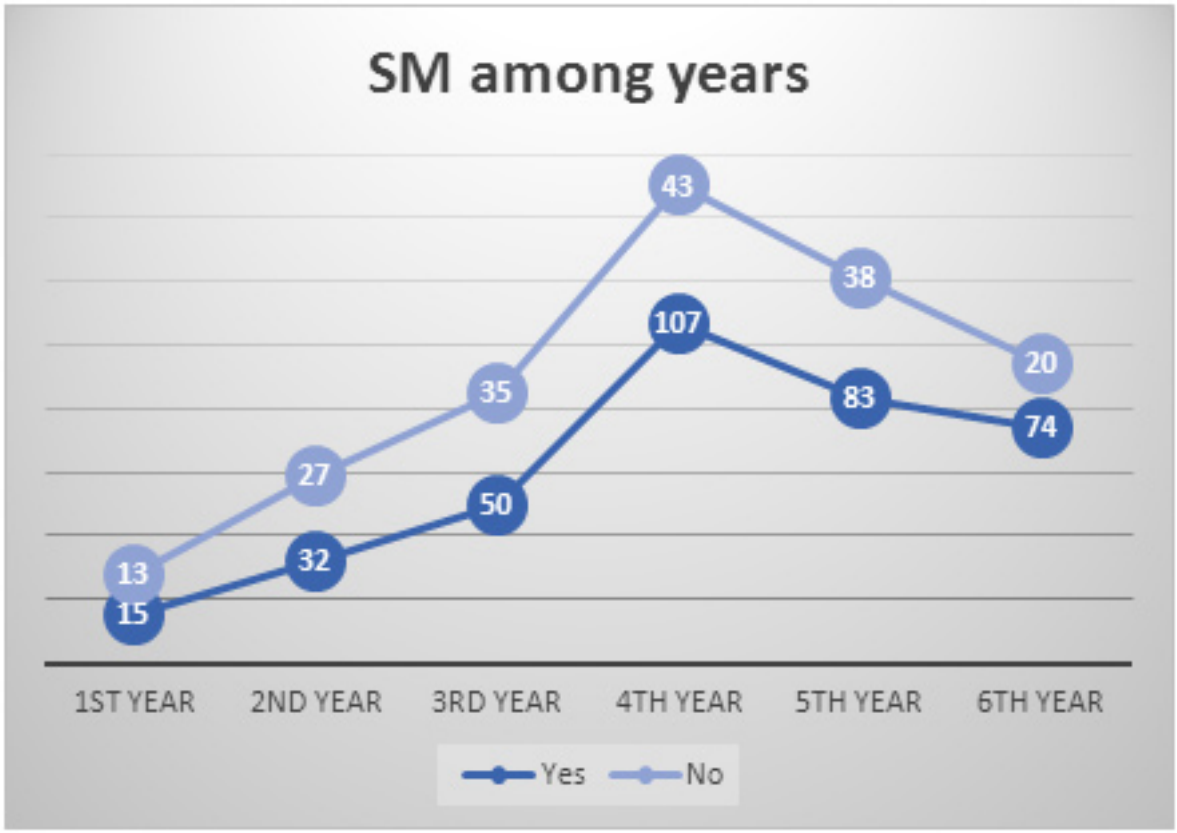
Table 5: View of students regarding Self Medications

	Total Number	%	male		female	
I am always in favor of SM practice	110	20%,4	31	28%	79	72%
I am against SM but it can be used in rare situations	382	71%,0	99	26%	283	74%
I am always against self-medication practice	46	8%,6	15	33%	31	67%

Table 6: Reason in favor of SM practice

	Total Number	%	male		female	
Emergency use	157	29%,20	40	25%	117	75%
Previous experience	168	31%,20	45	27%	123	73%
Saving doctor consultation time	52	9%,70	14	27%	38	73%
Lack of trust in prescribers	8	1%,50	4	50%	4	50%
Self-knowledge is enough to self-medicate rationally	125	23%,20	33	26%	92	74%
Informed by elders/family members and friends	28	5%,20	9	32%	19	68%

Figure 1: Prevalence of SM based on Academic years



Ac. Year	%
1ST	5%
2ND	11%
3RD	16%
4TH	28%
5TH	22%
6TH	18%

Figure 2: Frequency of self-medication

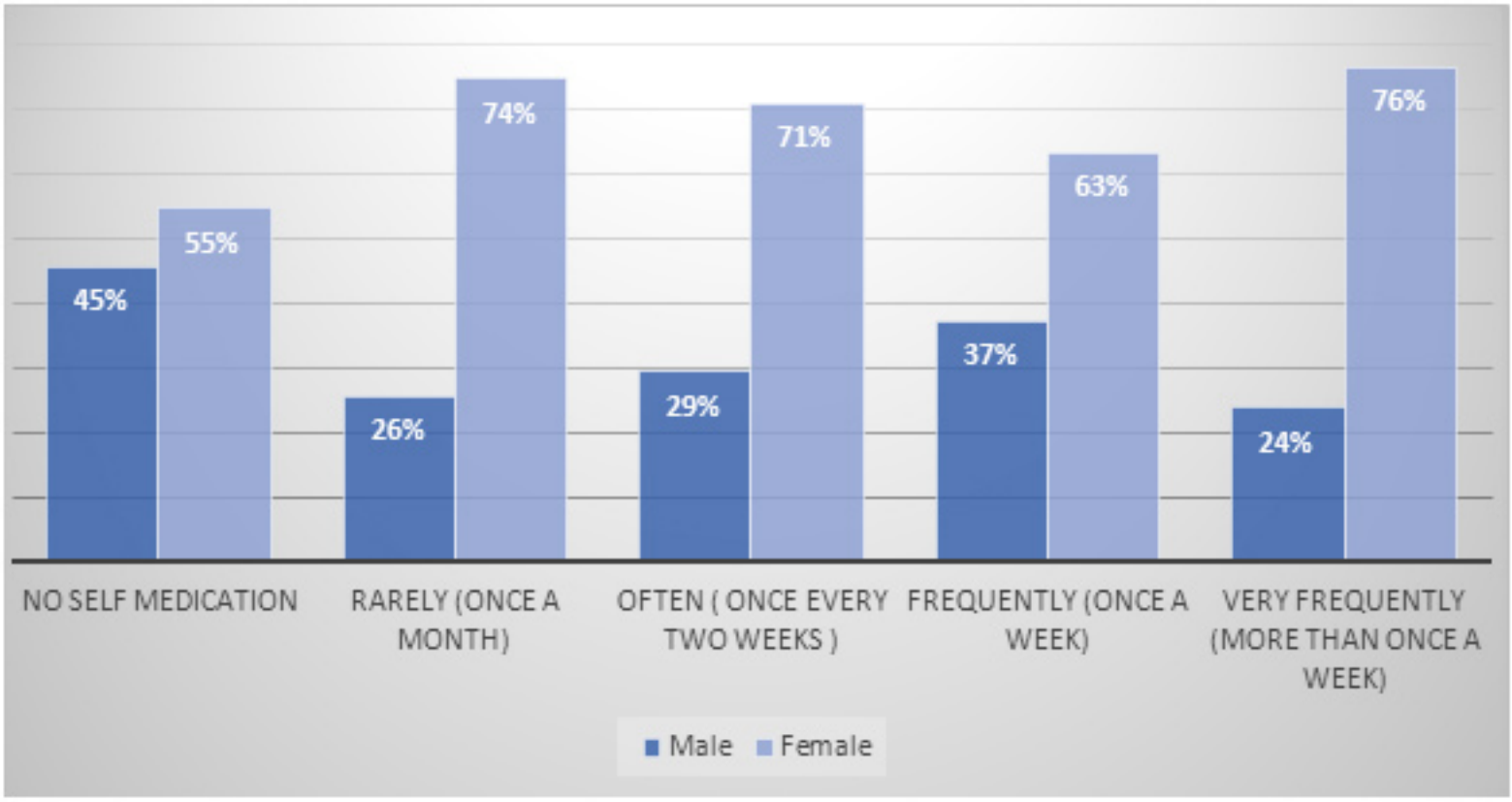


Figure 3: Illnesses for which SM were used

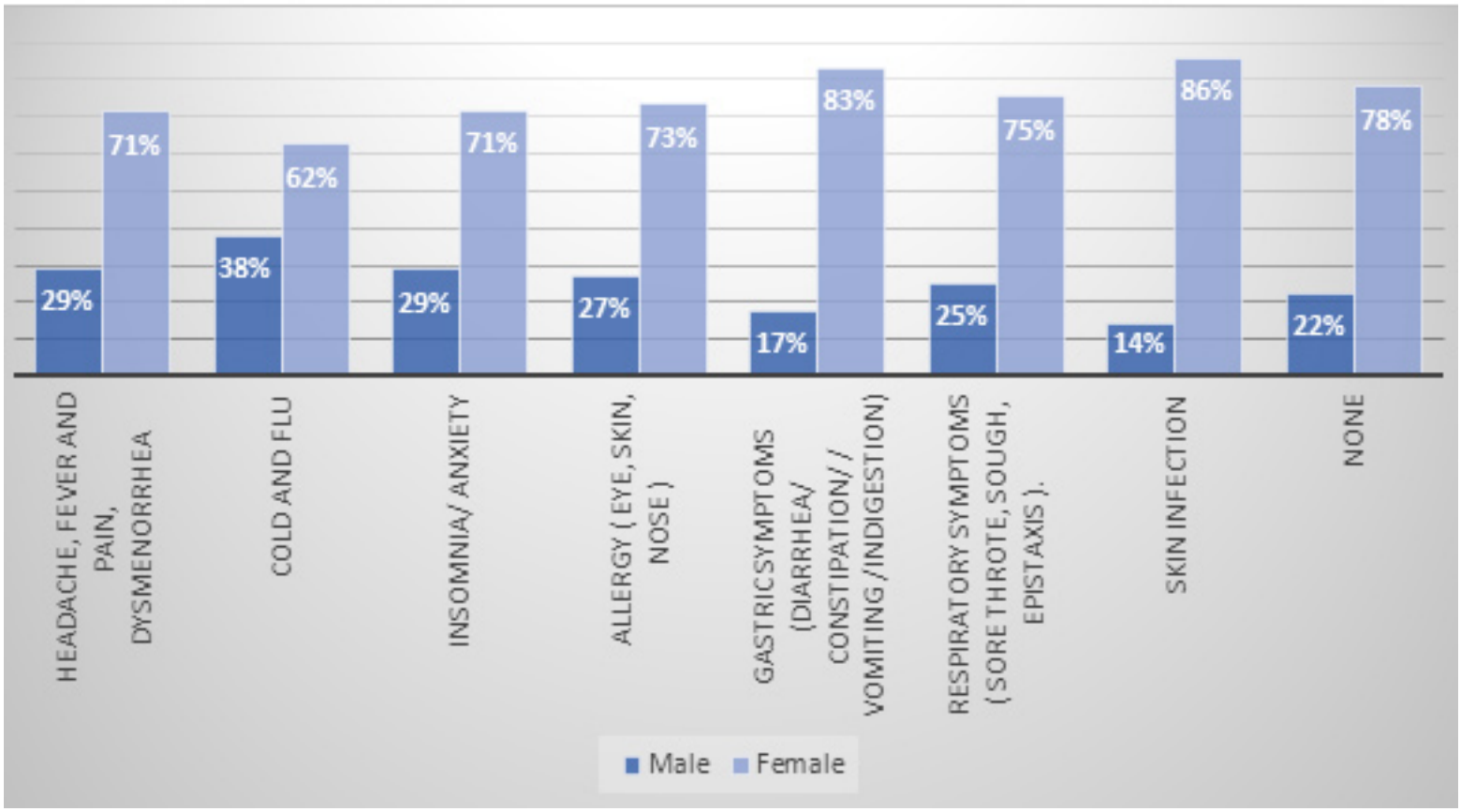


Figure 4: Reason in favor of Self-medication practice

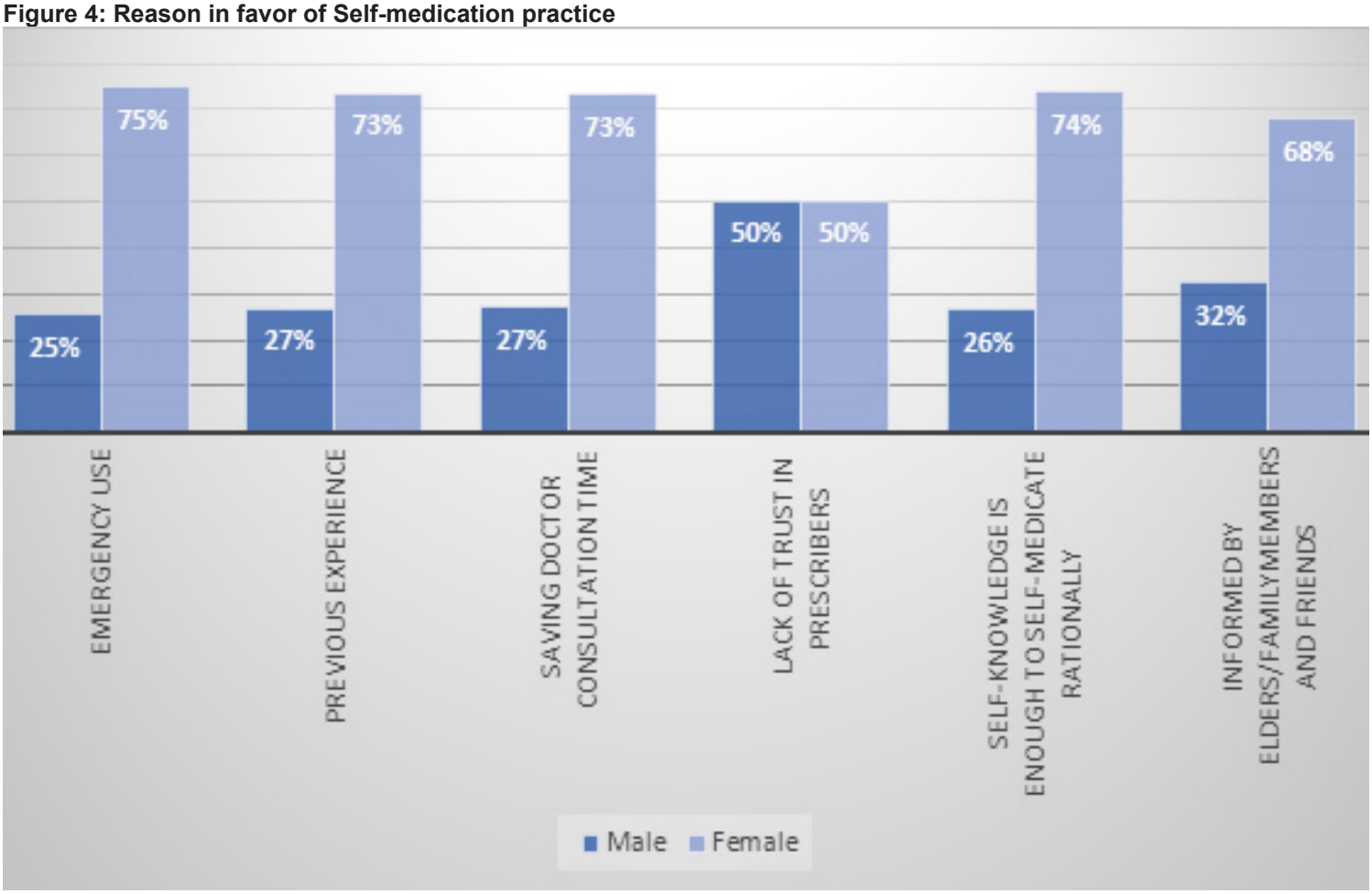


Figure 5: Illnesses for which Self-medication was used

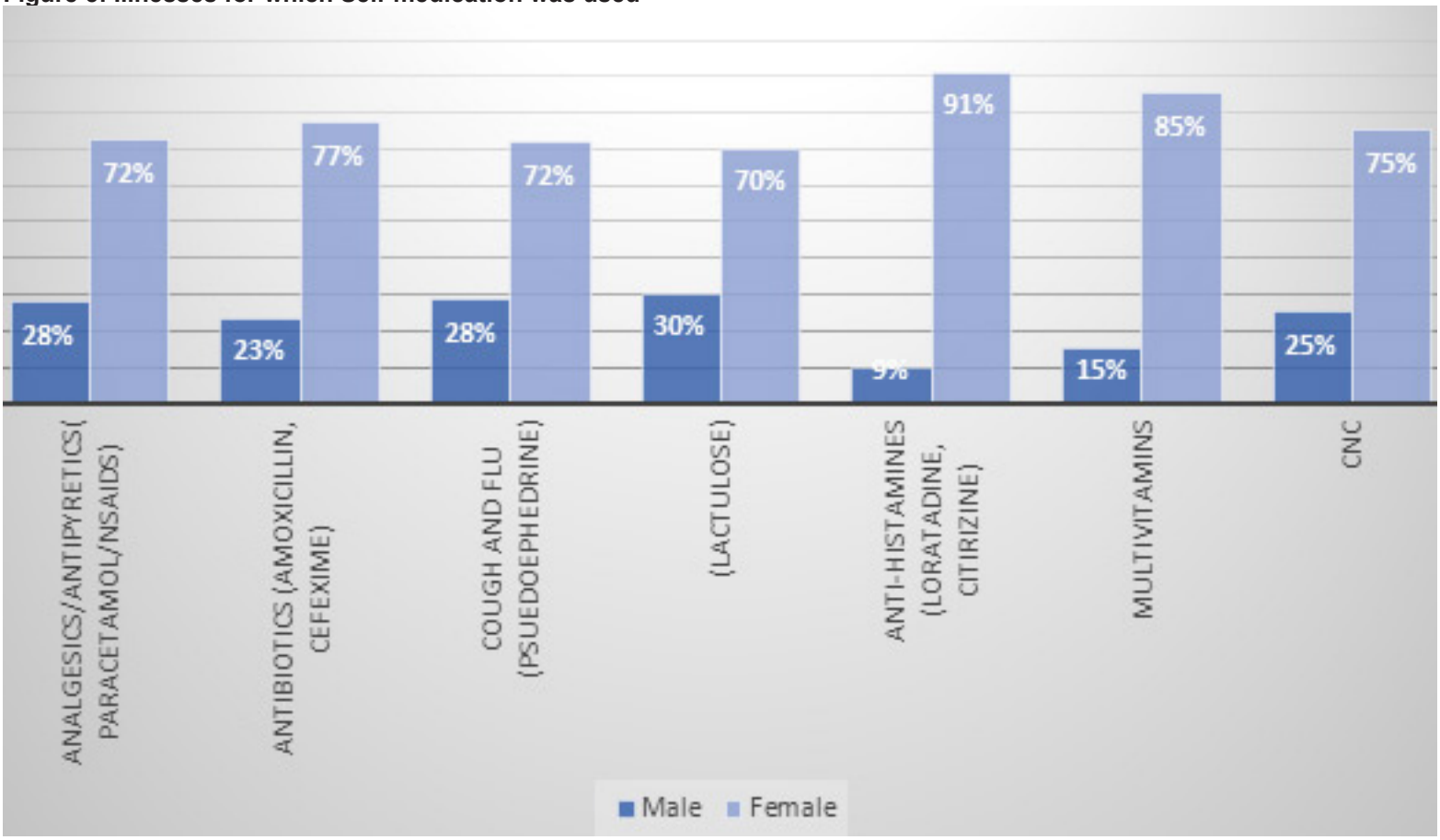
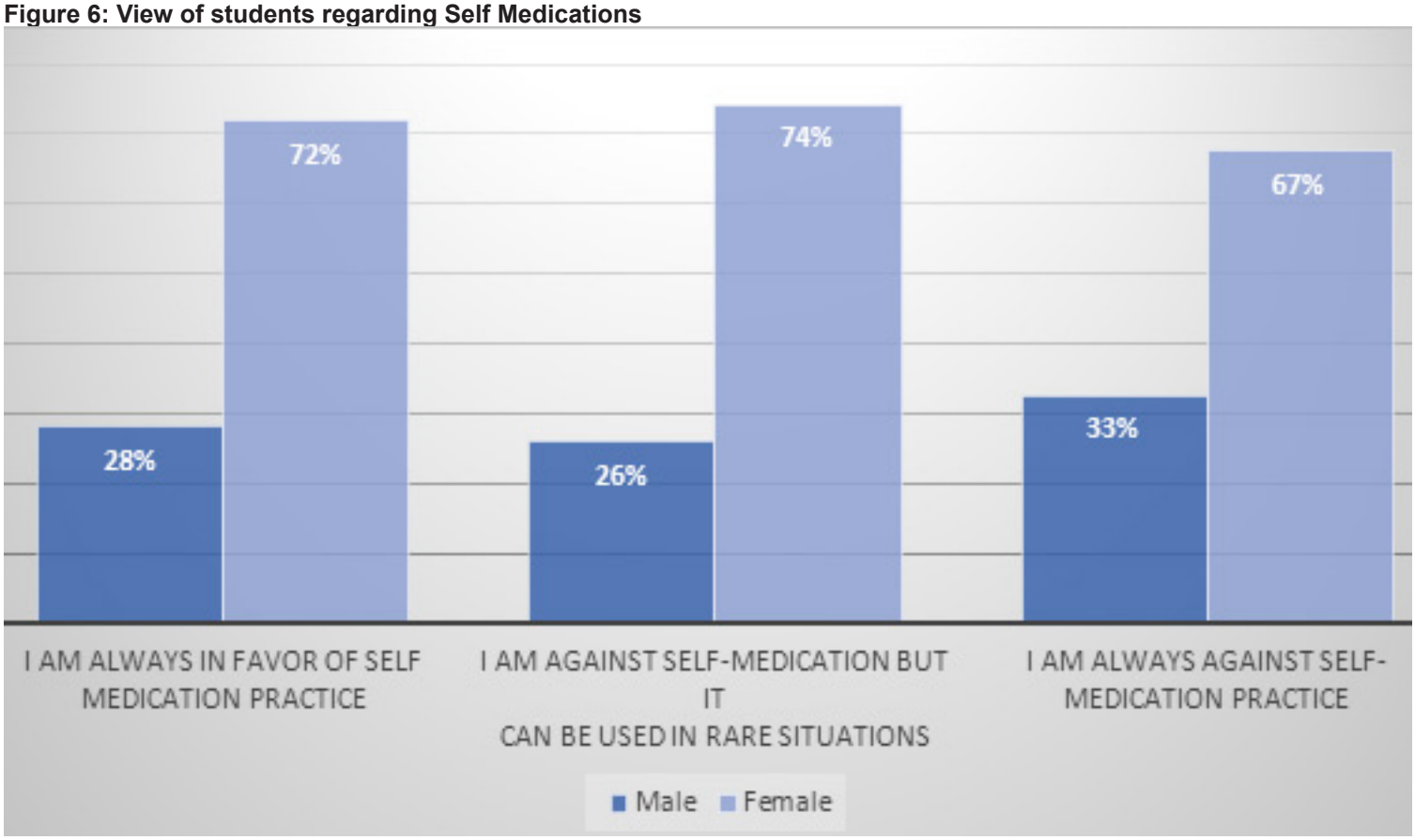


Figure 6: View of students regarding Self Medications



Discussion

This study evaluated knowledge, practice and attitude of SM between undergraduate medical students and revealed that SM practice is very common amongst undergraduate medical students. In our study, a total of 352 medical students participated, of whom 115 (32.7%) were males and 237 (67.3%) were females. We have noted that the majority of students with overall prevalence of SM is 67.3% which was similar to the prevalence (63.7%) stated among medical students (plus interns) in Kahramanmaraş, Turkey and greater than the prevalence (55.2%) reported from Egypt. The prevalence of SM amongst college students fluctuated from 38.5% in Ethiopia[10] to 98% in Palestine [11]. A meta-analysis of 27 articles of SM amongst doctors and medical students stated SM prevalence of >50% in 76% of the articles [12]. In Jordan, previous research conducted on medication use was focused on medical students[13] or community,[14],[15] with special consideration to the use of antimicrobial medications [16-18]. The students' general knowledge and attitude of SM in the current research was reassuring. The results were significantly higher amongst fourth year students compared to other academic years. SM, when implemented properly, can be more appropriate, may alleviate acute pain, and lower treatment cost and doctor communication periods [19]. Nevertheless, it can threaten individual health and result in severe complications when applied improperly, such as practicing SM by using prescription-only medications [20]. For example, developing medication resistance is of huge concern with the recurrent and incorrect use of antibiotics that could be accessible without a prescription. A study conducted among Jordanian families stated that 39.5% of the applicants had used antibiotics without prescription [21]. Other grave consequences that might be triggered with repeated use of OTC drugs include incorrect dosing, treatment duplication, medications interaction, treatment failure, covering of health problems and symptoms, and delay in prescribing the proper medication [22]. Undergraduate Medical students who were trained by doctors may think themselves in a comfortable situation consuming prescription-only medication as likened to undergraduate pharmacy students since they are inbuilt with a prescribing ability. The teaching in clinical pharmacy and medicine at colleges begins when the students have improved from the preparatory year into the second year. As the students' progress in their instructive profession, they become more well-read and knowledgeable about the phenomenon. Specialized education may encourage their perception of SM practice and consume prescription-only medication. The prevalence of SM is wide-ranging among different academic years, the prevalence growing from preliminary to final academic years as shown in Figure 1. Therefore, our study found that the number of students self-medicating with prescription-only medication decreased as they progressed in their instructive profession [23]. The most used source of information was medical texts by (26.4%) students. In another preceding study in Nepal among paramedical and medical students, 60.3% used the pharmacist as a basis of evidence which is greater than that stated in our study . In our study, 26.4% of respondents stated that they use medical books as a source of information. In Egypt, a study revealed that neighbors and households, own choice, and Internet were common resources for SM information among students [24]

Another study stated that colleagues and household, chemist, and Internet were the primary 3 resources of SM among undergraduate medical students in Nepal [25]. Other reasons for the elevated prevalence of SM in this study might include ease, and lack of time to seek GP appointment. Among the self-medicators, the bulk used Non-prescription OTC medications, 134 (58%). The US Food And Drug Administration describes over-the-counter (OTC) drugs as "medications that are safe and effective for use by the general public without seeking treatment by a health professional"[26]. A previous article revealed that the reasons behind the prevalent consuming of OTC drugs may include the following: the wish to save money, occurrence of insignificant health illnesses that do not need a call on the doctor, previous practice with medication efficacy, and the lengthy waiting time at hospitals. [27] A significant number of undergraduate medical students advised that they were against the SM habit, in belief, but asserted that SM might be used under certain conditions. This was a novel outcome as earlier studies conducted amongst the equivalent population stated that most of the students of Taibah University (87%) and Jazan University (52.6%) were absolutely against the habit [28,29].

Limitations

The study was built on self-reported information about self-medication in the past 1 year hence bias can't be ruled out. The study didn't include how many students have doctors in their household so their impact as a source of prescription can't be ruled out.

Conclusion

From our study, we conclude that SM was quite common among undergraduate medical students, which may be due to easy accessibility of medications and information from texts. Certain students revealed insufficient knowledge and wrong attitude concerning some points about SM. Practice of SM is disturbing. Developing understanding about the responsibility of the pharmacist as a medication advisor for cautious use of drugs obtainable for SM would be strongly suggested. The distributing of drug has to be meticulous by Saudi health care authorities to provide effective precautionary and interventional policies; thereby, proper usage of drugs is accomplished.

Conflict of Interest

Authors have no conflict of interest.

Acknowledgement

Authors thank all the participants who participated in this study.

Financial support and sponsorship

There is no funding was obtained for this research project by all of the authors.

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What a low prevalence of diabetes mellitus between the most desired values of high density lipoproteins in the plasma

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Mehmet Rami Helvaci, Abdulrazak Abyad, Lesley Pocock. What a low prevalence of diabetes mellitus between the most desired values of high density lipoproteins in the plasma. . World Family Medicine. 2020; 18(7): 25-31
DOI: 10.5742MEWFM.2020.93831

Abstract

Background: We tried to understand the most desired values of high density lipoproteins (HDL) in the metabolic syndrome.

Methods: Patients with plasma HDL values lower than 40 mg/dL were collected into the first, lower than 46 mg/dL into the second, lower than 50 mg/dL into the third, and 50 mg/dL and higher into the fourth groups.

Results: The study included 256 cases (153 females). Parallel to the highest HDL values, mean age, female ratio, body mass index (BMI), fasting plasma glucose (FPG), low density lipoproteins (LDL), white coat hypertension (WCH), hypertension (HT), and diabetes mellitus (DM) were the highest in the fourth group. Whereas coronary heart disease (CHD) was the highest in the first group in contrast to the lowest HDL and LDL values. Interestingly, BMI, FPG, WCH, DM, and CHD were the lowest in the second group, and prevalence of DM was only 3.1% in this group against 22.2% of the others ($p<0.001$).

Conclusions: The highest mean age, female ratio, BMI, FPG, WCH, HT, and DM parallel to the highest HDL and LDL, and the highest CHD in contrast to the lowest HDL and LDL values may show initially positive but eventually negative acute phase proteins features of HDL and LDL. BMI, FPG, DM, and CHD were the lowest between HDL values of 40 and 46 mg/dL, and DM was only 3.1% between these values against 22.2% of the remaining. The moderate HDL values may also be a result, instead of a cause of the lower prevalence of DM.

Key words: High density lipoproteins, diabetes mellitus, low density lipoproteins, triglycerides, acute phase proteins, body mass index, metabolic syndrome

Introduction

Chronic endothelial damage may be the most common type of vasculitis, and the leading cause of end-organ insufficiencies, aging, and death in the human being (1-4). Much higher blood pressure (BP) of the afferent vasculature may be the major underlying mechanism by inducing recurrent injuries on vascular endothelium. Probably, whole afferent vasculature including capillaries are mainly involved in the process. Thus the term venosclerosis is not famous in the medical literature. Due to the chronic endothelial damage, inflammation, edema, and fibrosis, vascular walls thicken, their lumens narrow, and they lose their elastic nature, and eventually reduce blood flow to terminal organs and increase systolic BP further. Some of the well-known underlying causes and indicators of the inflammatory process are physical inactivity, sedentary lifestyle, animal-rich diet, smoking, alcohol, overweight, hypertriglyceridemia, dyslipidemia, impaired fasting glucose, impaired glucose tolerance, white coat hypertension (WCH), chronic inflammations and infections, and prolonged cancers for the development of terminal consequences including obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), chronic renal disease (CRD), mesenteric ischemia, osteoporosis, stroke, other end-organ insufficiencies, early aging, and premature death (5-10). Although early withdrawal of the underlying causes can delay terminal consequences, after development of HT, DM, cirrhosis, COPD, CRD, CHD, PAD, mesenteric ischemia, osteoporosis, stroke, other end-organ insufficiencies, and aging, endothelial changes cannot be reversed completely due to their fibrotic nature. The underlying causes and terminal consequences are researched under the titles of metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome in the literature, extensively (11-13). Although their normal limits have not been determined clearly yet, increased plasma triglycerides values may be one of the most sensitive indicators of the metabolic syndrome (14-17). Due to the growing evidence about the strong association between higher plasma triglycerides and prevalence of CHD, Adult Treatment Panel (ATP) III determined lower cutpoints for triglycerides abnormalities than did ATP II (18, 19). Although ATP II determined the normal plasma triglycerides values as lower than 200 mg/dL in 1994 (19), World Health Organisation in 1999 (20) and ATP III in 2001 reduced the normal limits as lower than 150 mg/dL (18). Although these cutpoints, there are still suspicions about the safest values of plasma triglycerides in the plasma (15-17). Beside that although the higher sensitivity of plasma triglycerides in the metabolic syndrome, basic functions and desired values of high density lipoproteins (HDL) and low density lipoproteins (LDL) are still suspicious (21). We tried to understand the most desired values of HDL in the metabolic syndrome.

Material and Methods

The study was done in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Consecutive patients at the age of 15 years and greater were included into the study. Medical pasts of the cases including HT, DM, COPD, and already used medications were learned, and a routine check up including fasting plasma glucose (FPG), HDL, LDL, and triglycerides was performed. Current daily smokers with six pack-months and cases with a past of three pack-years were accepted as smokers. Due to the very low prevalence of alcoholism in Turkey (22), we did not include regular alcohol intake into the study. Patients with devastating illnesses including type 1 DM, malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on body weight. Additionally, anti-hyperlipidemic drugs, metformin, and acarbose users were excluded to avoid their possible effects on blood lipid profiles and body weight (23, 24). Body mass index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared (18). Patients with an overnight FPG value of 126 mg/dL and higher on two occasions or already using antidiabetic medications were defined as diabetics (18). An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG value between 110 and 126 mg/dL, and diagnosis of cases with a 2-hour plasma glucose value of 200 mg/dL and greater is DM (18). Additionally, office blood pressure (OBP) was checked after a 5-minute rest in seated position with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in the normotensives in the office due to the risk of masked HT after a 10-minutes of education about proper BP measurement techniques (25). An additional 24-hour ambulatory blood pressure monitoring was not taken due to the similar effectivity with the HBP measurements (3). Eventually, HT is defined as a mean BP of 140/90 mmHg and higher on HBP measurements, and WCH as an OBP of 140/90 mmHg and higher but a mean HBP measurement of lower than 140/90 mmHg (25). 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 is diagnosed either angiographically or with the Doppler echocardiographic findings as the already developed movement disorders in the cardiac walls. The spirometric pulmonary function tests were performed in required cases after the physical examination, and the criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in one second/forced vital capacity of less than 70% (26). Finally, patients with plasma HDL values lower than 40 mg/dL were collected into the first, lower than 46 mg/dL into the second, lower than 50 mg/dL into the third, and 50 mg/dL and higher into the fourth groups, respectively. The mean age, female ratio, smoking, BMI,

FPG, triglycerides, LDL, HDL, WCH, HT, DM, COPD, and CHD were detected in each group, 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 256 cases (153 females and 103 males), totally. Parallel to the highest HDL values, the mean age, female ratio, BMI, FPG, LDL, WCH, HT, and DM were the highest in the fourth group. Whereas CHD was the highest in the first group in contrast to the lowest HDL and LDL values. Interestingly, the mean age, female ratio, BMI, FPG, WCH, DM, and CHD were the lowest in the second group. But the difference was the greatest for DM, and its prevalence was only 3.1% in the second group against 21.3% (p<0.001) of the first, 22.2% (p<0.001) of the third, and 23.2% (p<0.001) of the fourth groups. Triglycerides were also the highest parallel to the highest prevalence of smoking in the second group, and they were the lowest parallel to the lowest prevalence of smoking in the fourth group. So prevalence of smoking was parallel with the male ratio in the study (Table 1).

Table 1: Characteristics features of the cases according to high density lipoproteins values in the plasma

Variable	Lower than 40 mg/dL	*p*-value	Lower than 46 mg/dL	*p*-value	Lower than 50 mg/dL	*p*-value	50 mg/dL and higher
Number	75		63		45		73
Age (year)	45.4 ± 15.2 (16-79)	Ns*	45.3 ± 15.1 (19-78)	Ns	*46.5 ± 13.5 (19-73)*	*0.026*	*51.8 ± 11.6 (21-77)*
Female ratio	46.6%	Ns	*42.8%*	*0.001>*	*66.6%*	*0.01>*	*83.5%*
Smoking	34.6%	Ns	36.5%		24.4%	Ns	17.8%
BMI† (kg/m^2)	27.2 ± 4.5 (18.4-39.9)	Ns	*25.7 ± 4.2 (18.6-34.3)*	*0.024*	*27.7 ± 4.6 (19.6-36.0)*	Ns	29.3 ± 6.1 (17.8-48.6)
FPG‡ (mg/dL)	*119.4 ± 48.4 (76-287)*	*0.006*	*97.6 ± 13.5 (67-154)*	Ns	114.9 ± 59.0 (63-386)	Ns	134.1 ± 77.0 (74-400)
Triglycerides (mg/dL)	162.7 ± 92.8 (43-470)	Ns	175.3 ± 103.0 (27-617)	Ns	144.9 ± 72.2 (47-411)	Ns	134.5 ± 81.5 (37-418)
LDL§ (mg/dL)	*105.3 ± 33.1 (10-211)*	*0.000*	*126.0 ± 32.7 (39-197)*	Ns	134.7 ± 36.6 (77-223)	Ns	135.3 ± 32.3 (54-239)
HDL‖ (mg/dL)	*34.1 ± 3.8 (22-39)*	*0.000*	*42.8 ± 1.6 (40-45)*	*0.000*	*47.5 ± 1.1 (46-49)*	*0.000*	*58.2 ± 8.0 (50-91)*
WCH**	25.3%	Ns	23.8%	Ns	31.1%	Ns	36.9%
HT***	10.6%	Ns	11.1%	Ns	*17.7%*	*0.05>*	*28.7%*
DM****	*21.3%*	*0.001>*	*3.1%*	*0.001>*	*22.2%*	Ns	23.2%
COPD*****	14.6%	Ns	17.4%	Ns	20.0%	Ns	10.9%
CHD******	*20.0%*	*0.05>*	*11.1%*	Ns	13.3%	Ns	16.4%

***Nonsignificant (p>0.05) †Body mass index ‡Fasting plasma glucose §Low density lipoproteins ‖High density lipoproteins **White coat hypertension ***Hypertension ****Diabetes mellitus *****Chronic obstructive pulmonary disease ******Coronary heart disease**

Discussion

Adipose tissue produces leptin, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, and adiponectin-like cytokines acting as acute phase reactants in the plasma (27, 28). Excess weight-induced chronic low-grade vascular endothelial inflammation plays a significant role in the pathogenesis of accelerated atherosclerosis in the whole body (1, 2). Additionally, excess weight leads to myocardial hypertrophy terminating with a decreased cardiac compliance. Combination of these cardiovascular risk factors eventually terminate with increased risks of arrhythmias, cardiac failure, and sudden cardiac death. Similarly, the prevalence of CHD and stroke increased parallel to the increased BMI in the other studies (29, 30), and risk of death from all causes including cancers increased throughout the range of moderate to severe weight excess in all age groups (31). The relationship between excess weight, elevated BP, and hypertriglyceridemia is described in the metabolic syndrome (14), and clinical manifestations of the syndrome include obesity, dyslipidemia, HT, insulin resistance, and proinflammatory and prothrombotic states (12). For example, prevalence of excess weight, DM, HT, and smoking were all higher in the hypertriglyceridemia group (200 mg/dL and higher) in a previous study (32). On the other hand, the prevalence of hyperbetalipoproteinemia was similar both in the hypertriglyceridemia and control groups in the same study (32). Additionally, although the higher plasma trigycerides values, LDL values were also lower in the group with the plasma HDL levels lower than 40 mg/dL in the other study ($p<0.001$ for all) (33). Similarly, plasma triglycerides were higher in the first group with the lowest LDL and HDL values in the present study. On the other hand, the lowest triglycerides value of the fourth group can be explained by the lowest prevalencesof smoking and male ratio since there is a significant relationship between hypertriglyceridemia, smoking, and male ratio (34, 35).

Probably, alcohol and smoking are also found among the most common causes of vasculitis. Both of them cause a chronic inflammatory process on the vascular endothelium depending on the concentrations of products of alcohol and smoke in the blood. So both of them can cause an accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. Thus both of them should be added into the major components of the metabolic syndrome. Atherosclerotic effects of smoking are the most obvious in Buerger's disease. It is an obliterative vasculitis characterized by inflammatory changes in the small and medium-sized arteries and veins, and it has never been reported in the absence of smoking in the literature. On the other hand, smoking in the human being and nicotine administration in animals may be associated with decreased BMI values (36). Nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (37). According to an animal study, nicotine lengthens intermeal time and decreases amount of meal eaten (38). Additionally, the mean BMI seems to be the highest in the former, the lowest in the current, and medium in never smokers (39). Smoking may be associated with a postcessation weight gain (40). Similarly, although CHD was detected with similar prevalence in both genders, prevalence of smoking and COPD were higher in males against the higher BMI, LDL, triglycerides, WCH, HT, and DM in females (41). Similarly, the incidence of a myocardial infarction is increased six-fold in women and three-fold in men who smoke 20 cigarettes per day (42). In another definition, smoking may be more dangerous for women due to the associated weight excess and its consequences. So smoking is probably a powerful atherosclerotic risk factor with some suppressor effects on appetite (43). Smoking-induced weight loss may be related with the smoking-induced chronic vascular endothelial inflammation all over the body since loss of appetite is one of the major symptoms of the disseminated inflammation in the body. Physicians can even understand healing of the patients by means of normalizing appetite of them. Several toxic substances found in cigarette smoke get into the circulation by means of the respiratory tract, and cause a vascular endothelial inflammation until clearance from the circulation. But due to the repeated smoking habit, the clearance never terminates. So the patients become ill with loss of appetite, permanently. In another explanation, smoking-induced weight loss is an indicator of being ill instead of being healthy (37-39). After smoking cessation, normal appetite comes back with a prominent weight gain but the returned weight is the patients' physiological weight, actually.

Although ATP III reduced the normal limits of plasma triglycerides as lower than 150 mg/dL in 2001 (18), much lower values may indicate better health conditions (15-17). For example, the greatest number of clinical and laboratory deteriorations was observed just above the plasma triglycerides value of 60 mg/dL in the above study (17). Similar to the present study, prevalence of smoking was the highest with the highest triglycerides values in the other study (16) that may also indicate the inflammatory role of smoking in the metabolic syndrome, since triglycerides may actually be sensitive acute phase reactants in the plasma. In the above study (16), the mean age, male ratio, smoking, BMI, FPG, WCH, HT, DM, and COPD increased parallel to the increased plasma triglycerides values from the first up to the fifth groups, gradually. On the other hand, increased plasma triglycerides values by aging may be secondary to the aging-induced decreased physical and mental stresses, those eventually terminate with onset of excess weight and its consequences. Although the borderline high triglycerides values (150-199 mg/dL) is seen together with physical inactivity and overweight, the high (200-499 mg/dL) and very high triglycerides values (500 mg/dL and greater) may be secondary to smoking, genetic factors, and terminal consequences of the metabolic syndrome such as obesity, DM, HT, COPD, cirrhosis, CRD, PAD, CHD, and stroke (18). But although the underlying causes of the borderline high, high, and very high plasma triglycerides values may be a little bit different, probably risks of the terminal consequences do not change in them. For example, prevalence of HT, DM, and COPD were the highest in the group with the highest triglycerides values in the above study (16). Eventually, although some authors reported that lipid assessment can be simplified

as the measurements of total cholesterol and HDL values alone (44), the present study and most others indicated significant relationships between plasma triglycerides, HDL, and LDL values and terminal consequences of the metabolic syndrome (33, 45).

Cholesterol, triglycerides, and phospholipids are the major lipids of the body. Cholesterol is an essential structural component of the animal cell membrane, bile acids, adrenal and gonadal steroid hormones, and vitamin D. Triglycerides are the major lipids of the fat tissue. Phospholipids are triglycerides that are covalently bound to a phosphate group, and regulate membrane permeability, remove cholesterol from the body, provide signal transmission across the membranes, act as detergents, and help in solubilization of cholesterol. Cholesterol, triglycerides, and phospholipids do not circulate freely in the plasma, instead they are bound to proteins, and transported as lipoproteins. There are five major classes of lipoproteins in the plasma. Chylomicrons carry exogenous triglycerides to the liver via the thoracic duct. Very low density lipoproteins (VLDL) are produced in liver, and carry endogenous triglycerides to the peripheral organs. In the capillaries of adipocytes and muscle tissue, VLDL are converted into intermediate density lipoproteins (IDL) by removal of 90% of triglycerides by lipases. Then IDL are degraded into LDL by removal of more triglycerides. So VLDL are the main source of LDL in the plasma, and LDL deliver cholesterol from the liver to the peripheral organs. Although the liver removes the majority of LDL from the circulation, a small amount is uptaken by scavenger receptors of the macrophages that migrate into the arterial walls, and become the foam cells of atherosclerotic plaques. HDL remove fats and cholesterol from cells including the arterial wall atheroma, and carry the cholesterol back to the liver and steroidogenic organs such as adrenals, ovaries, and testes for excretion, re-utilization, and disposal. All of the carrier lipoproteins are under dynamic control, and are readily affected by diet, illness, drug, and weight excess. Thus lipid analysis should be performed during a steady state. But the metabolic syndrome alone is a low grade inflammatory process on vascular endothelium. Thus the metabolic syndrome alone may be a cause of abnormal lipoproteins levels in the plasma. On the other hand, although HDL are commonly called 'the good cholesterol' due to their role in removing excess cholesterol from the blood and protecting the arterial wall against atherosclerosis (46), recent studies did not show similar results, and low plasma HDL values may alert us to searching for some inflammatory pathologies in the body (47-49). Normally, HDL show various anti-atherogenic properties including reverse cholesterol transport and anti-oxidative and anti-inflammatory properties (47). However, HDL may become 'dysfunctional' in pathological conditions which means that relative composition of lipids and proteins, as well as the enzymatic activities of HDL are altered (47). For example, properties of HDL are compromised in patients with DM due to the oxidative modification and glycation of HDL, as well as the transformation of HDL proteomes into the proinflammatory proteins. Additionally, three highly effective agents for increasing HDL levels including niacin, fibrates, and cholesteryl ester transfer protein inhibitors did not reduce all cause mortality, CHD mortality, myocardial infarction, and stroke (50). In other words, while higher HDL values may correlate with better cardiovascular health, specifically increasing one's HDL may not increase cardiovascular health (50). So they may just be some indicators instead of the main actors in the metabolic syndrome. Beside that, HDL particles that bear apolipoprotein C3 are associated with increased risk of CHD (51). For example, although the similar mean age, gender distribution, smoking, and BMI in both groups, DM and CHD were higher in the group with the plasma HDL values lower than 40 mg/dL in the above study (33). Similarly, although the lower mean age, BMI, FPG, LDL, and HDL, the highest CHD of the first group may also indicate eventual features of HDL as the negative acute phase proteins (APP) in the present study.

APP are a group of proteins whose plasma concentrations increase (positive APP) or decrease (negative APP) as a response to inflammation, infection, and tissue damage (52-54). In case of inflammation, infection, and tissue damage, neutrophils and macrophages release cytokines into the blood. The liver responds by producing many positive APP to them. At the same time, production of some proteins are reduced. Thus these proteins are called negative APP. Some of the well-known negative APP are albumin, transferrin, retinol-binding protein, antithrombin, and transcortin. The decrease of such proteins is also used as an indicator of inflammation. The physiological role of decreased synthesis of such proteins may be protection of amino acids for production of positive APP, effectively. Due to the same reason, production of HDL and LDL may also be suppressed in the liver. By this way, although the similar mean age, gender distribution, smoking, and BMI in both groups, the higher triglycerides, DM, and CHD against the significantly lower HDL and LDL values can be explained in the above study (33). Beside that although the lower mean age, BMI, FPG, LDL, and HDL, the highest CHD of the first group can also be explained by the same theory in the present study. Similarly, although the mean triglycerides, fibrinogen, C-reactive protein, and glucose values were higher in cases with ischemic stroke, the oxidized LDL values did not correlate with age, stroke severity, and outcome in another study (55). Additionally, significant alterations occurred in the lipid metabolism and lipoproteins composition during infections, and triglycerides increased whereas HDL and LDL decreased in another study (56). Furthermore, a 10 mg/dL increase of LDL was associated with a 3% lower risk of hemorrhagic stroke in another study (57). Similarly, the highest HT and DM parallel to the increased LDL and HDL values, and the highest COPD, CHD, and CRD in contrast to the lowest LDL and HDL values may show initially positive but eventually negative acute phase proteins functions of LDL and HDL in the metabolic syndrome in another study (58), and the safest values of LDL were between 80 and 100 mg/dL in the plasma in the same study (58).

There may be several mechanisms of the significantly lower prevalence of DM between the HDL values of 40 and 46 mg/dL in the present study. According to the results of our previous studies, the moderate HDL values may not

be a cause, instead just be a result of the lower prevalence of DM between these HDL values in the plasma. Since chronic hyperglycemia may cause a chronic low grade inflammation on vascular endothelium all over the body, and the inflammation may initially increase but eventually decrease HDL production by the liver. Secondly, DM may cause a relative immunosuppression increasing risks of various infections all over the body. In this way, HDL production of the liver can be altered again. Thirdly, chronic hyperglycemia alone may cause a relative hepatic dysfunction and decrease production of HDL by the liver. Even diabetic nephropathy induced proteinuria may decrease HDL production of the liver. In another definition, there may be hundreds of mechanisms with variable priorities for the significantly lower prevalence of DM between the HDL values of 40 and 46 mg/dL in the plasma, and the result of the study should not be surprising for us.

As a conclusion, the highest mean age, female ratio, BMI, FPG, WCH, HT, and DM parallel to the highest HDL and LDL, and the highest CHD in contrast to the lowest HDL and LDL values may show initially positive but eventually negative acute phase proteins features of HDL and LDL. BMI, FPG, DM, and CHD were the lowest between HDL values of 40 and 46 mg/dL, and the prevalence DM was only 3.1% between these values against 22.2% of the others. The moderate HDL values may also be a result instead of a cause of the lower prevalence of DM.

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Evaluation of Postpartum Stress in Breastfeeding and Non-breastfeeding Mothers of Kathmandu, Nepal

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Kharel Sushil, Raut Binod, Mainalee Mandira. Evaluation of Postpartum Stress in Breastfeeding and Non-breastfeeding Mothers of Kathmandu, Nepal. World Family Medicine. 2020; 18(7): 32-37 DOI: 10.5742MEWFM.2020.93832

Abstract

Background: Breastfeeding physiologically plays a vital role in establishing the attachment relationship between child and mother. Breastfeeding is considered a protective factor for postpartum stress. This study was carried out in an urban Nepalese population to compare the prevalence of stress between breastfeeding and non-breastfeeding mothers.

Methods: A cross-sectional study was conducted at Kathmandu Medical College, Nepal, from August 2019 to January 2020. After obtaining informed written consent, 81 breastfeeding and 81 non-breastfeeding mothers between two to four months postpartum were enrolled in the study through random sampling. Perceived stress was evaluated by using universally accepted COHEN PERCEIVED STRESS SCALE (CPSS-10). The mothers were given a questionnaire which was completed by them individually. Results were analyzed by calculating Mean ± SD, using Student's t test and ANOVA test.

Results: A total of 162 mothers (81 breastfeeding and 81 non-breastfeeding) were studied. The mean COHEN PSS score was 15.74(SD 2.36) for breastfeeding and 26.24(SD 3.78) for non-breastfeeding mothers. There was a significant difference in prevalence of stress between breast feeding and non-breast feeding mothers ($P < 0.05$).

Conclusion: Levels of perceived stress were high in non-breastfeeding mothers as compared to breastfeeding mothers.

Key words: Postpartum, Perceived stress, Breastfeeding

Introduction

Breast feeding (BF) has significant benefits for mothers and infants. To achieve optimal health and well being of newborns, World Health Organization (WHO) has prescribed exclusive BF for the first six months of an infants' life (1). Breastfeeding tendency is considered as important for the infant for their better development and growth. Therefore, the ability of women to produce breast milk was also important. Based on the existing report, the production of milk is related with stress and depression (2). The postpartum period exposes the mother to various challenges and demands. This period is regarded as a vulnerable time for maternal psychological health (3). Mothers experience the physical demands of recovering from childbirth, feeling exhausted and uncomfortable. Most of the time, mothers are able to take care of their infant and adapt to a new role and affection within the family members (4). Breastfeeding provides many health benefits for the mother and her child. Breast milk is the best food for a newborn baby, which contains almost all the nutrients infants need for normal growth and development. Breastfeeding promotes facial development as a result of the suckling reflex, prevents different types of food allergies, and enhances the child's neurophysiologic development. Breastfed children are at lower risk for diabetes mellitus types I and II, obesity, hypertension, and cardiovascular diseases later in life (5). In addition to the nutritional benefits of breast milk, breastfeeding is a unique stimulant for mother and baby. During breastfeeding, the mother gives the baby a feeling of warmth, safety, and protection. Establishing intimate emotional attachments in childhood is seen as the prevention of various later undesirable behaviors in a child, various addictions and unsocial activities (6). Stress level is related to a person's physiological features. Elevated heart rate, reduced skin resistance and hypertension are the remarkable changes that can be found under stressful conditions (7). Postpartum anxiety disorders (PPAD) are found in 4%–39% of pregnant women and 16% of women in the postpartum period (8). PPAD increase the risk of postpartum depression and have been associated with maternal low self-confidence, low self-efficacy in the parenting role, stress and difficulty in caring for the infant. Also, it has been discovered that women with PPAD breastfeed for shorter periods of time and are less likely to breastfeed exclusively. In the offspring, PPAD have been linked to early complications (insecure attachment behavior, delayed cognitive development, negative attitude), and later adverse child development (low social engagement) (9). The hormones (Lactogenic hormones, oxytocin and prolactin) produced during breastfeeding are associated with anti-stress, anti-depressant and anxiolytic effects (10). Some studies have suggested that breastfeeding has a protective effect on maternal psychological health because it attenuates stress responses (11, 12).

Methods

A community based cross sectional study was conducted in August 2019-January 2020 after getting ethical clearance and approval from the Institutional Review Committee (IRC) of Kathmandu Medical College. The study populations were the postpartum mothers (two to four months postpartum) of Kathmandu and Bhaktapur. A total number of 162 mothers (81 breastfeeding and 81 non-breastfeeding) (22 to 37 years) were enrolled in the study. Three different wards of Bhaktapur and Kathmandu were selected by random sampling. Participants were asked to complete demographic, obstetric data questionnaires and Cohen Perceived Stress Scale (CPSS-10) which was translated into Nepali language. Demographic and obstetric data questionnaires contained maternal age, employment history, educational level, economic status, previous history of stress, type of delivery, number of previous pregnancies and infant gender satisfaction. After 10 minutes of resting, Blood Pressure (BP) was recorded twice in left arm of each mother in sitting position; with 10 minutes interval between two recordings and mean value was taken. Blood pressure was recorded using a mercury Sphygmomanometer. The appearance (phase I) and disappearance (phase V) of Korotkoff sounds were considered for systolic and diastolic BP, respectively (13). The participants were asked to sign a consent form before taking any form of data for the research. They were told to complete the questionnaire sincerely. COHEN PERCEIVED STRESS SCALE (CPSS-10) was used to learn the perceived stress (14).

Individual scores on the PSS range from 0 to 40 with higher scores indicating higher perceived stress.

► Scores ranging from 0-13 were considered as low stress.
► Scores ranging from 14-26 were considered as moderate stress.
► Scores ranging from 27-40 were considered as high perceived stress

The collected data was analyzed statistically by SPSS Version 21. Statistical significance was assessed at a type I error rate of 0.05.

Results

The total sample size of the study was 162 (81 Breastfeeding and 81 Non-breastfeeding) mothers. The age of the studied population ranged from 22 to 37 years. The mean postpartum CPSS Score was 15.74(SD 2.36) for breastfeeding and 26.24(SD 3.78) for non-breastfeeding mothers. Table 3 shows the distribution of postpartum stress in the study population. The overall prevalence of postpartum stress among breastfeeding mothers was 28.39% (moderate and high). Among non-breastfeeding mothers the prevalence of postpartum stress was 65.53%. Difference between stress in breastfeeding and non-breastfeeding mothers was found significant ($p < 0.05$). Most of them had vaginal delivery (breastfeeding -72% and non-breastfeeding-74%) and negative previous history of stress (Table 1). In our study, the mean Blood Pressure (both SBP and DBP) in non-breastfeeding mothers was high as compared to breastfeeding mothers and statistically significant with a 'p' value of 0.02 (Table 4 and Figure 2). Most of our study populations were aged between 20 and 30.

Table 1: Demographic profile of Breastfeeding (BF) and Non-breastfeeding (Non-BF) mothers

VARIABLES	BF No	Percentage (%)	Non-BF No	Percentage (%)	P Value
Age (Years)					
20-30	66	81.48	68	75.3	0.40
30-40	15	18.52	13	24.7	
Educational Status					
Middle school	02	02.46	03	03.70	
High School	19	23.46	20	24.70	
College	48	59.26	45	55.55	
University	11	13.58	09	11.11	0.017
Illiterate	01	01.24	04	04.94	
Employment					
Employed	61	75.30	58	71.60	
Non-employed	20	24.70	23	28.40	
Economic Status					
High	13	16.05	15	18.51	
Medium	50	61.72	47	58.02	
Low	18	22.23	19	23.47	

Table 2: Obstetric data of the study population (Breastfeeding and Non breastfeeding mothers)

VARIABLES	BF No (N=81)	Percentage (%)	Non-BF No (N=81)	Percentage (%)
Delivery Type				
Vaginal	58	71.60	60	74.07
Cesarean Section	23	28.40	21	25.93
Previous Delivery				
One	32	39.50	20	24.69
Two	07	08.64	08	09.87
Three or more	02	02.48	05	06.18
None	40	49.38	48	59.26
Infant Gender satisfaction				
Yes	66	81.48	59	72.83
No	15	18.52	22	27.17
Previous History of Stress				
Yes	02	02.48	03	03.71
No	79	97.52	78	96.29

Table 3: Prevalence of perceived stress in the study population (Breastfeeding and Non breastfeeding mothers)

Score and grade of Stress (out of 40)	Breastfeeding (N=81)	Non-breastfeeding (N=81)
Low Stress CPSS score 0-13	58 (71.60%)	28 (34.56%)
Moderate Stress CPSS score 14-26	15 (18.51%)	37 (45.67%)
High Stress CPSS score 27-40	08 (09.89%)	16 (19.77%)

Table 4: Distribution of mean blood pressure in the study population.

Mean Blood Pressure	Breastfeeding (N=81)	Non-breastfeeding (N=81)	P Value
Mean Systolic BP in mmHg	119.1 ±11.52	132.3 ±14.73	0.02
Mean Diastolic BP in mmHg	75.3 ± 8.14	87.4 ± 9.78	

Figure 1: Comparison of Perceived Stress (COHEN Perceived Stress Scale-CPSS) in Breastfeeding and Non-breastfeeding mothers

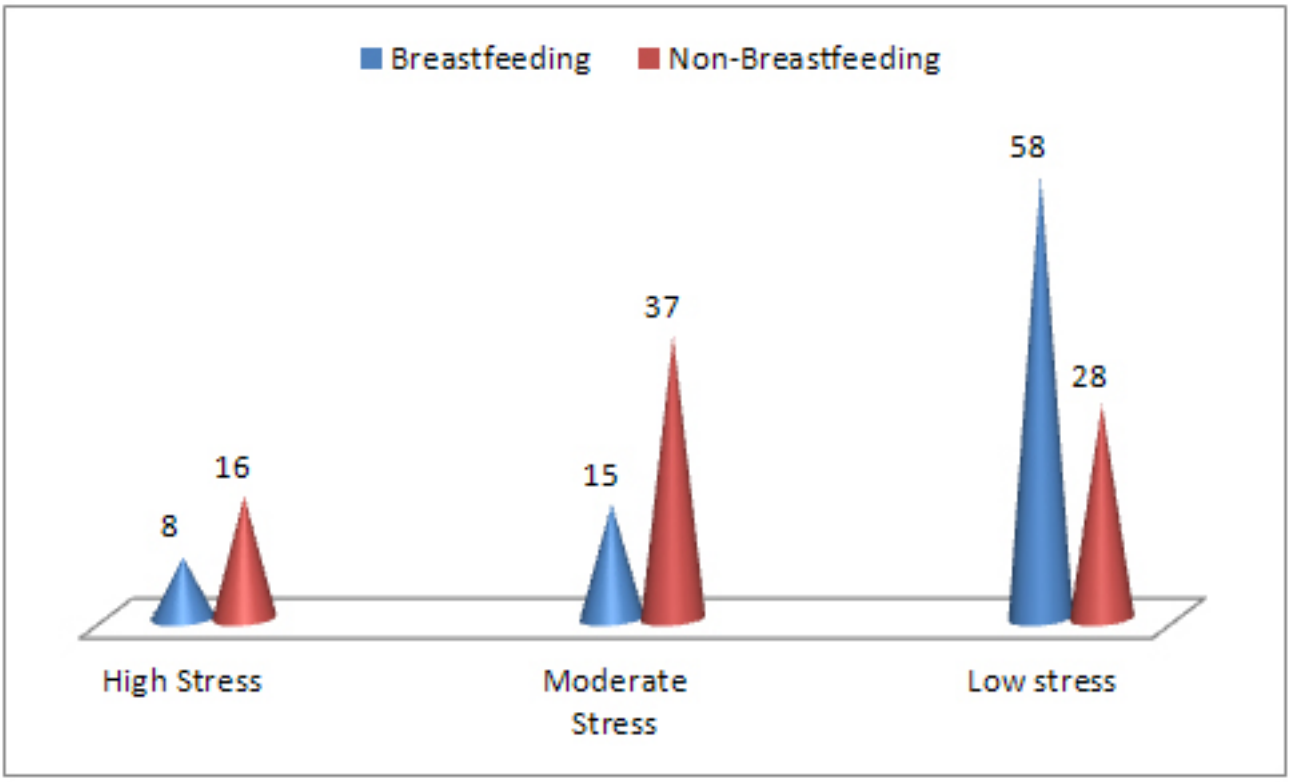
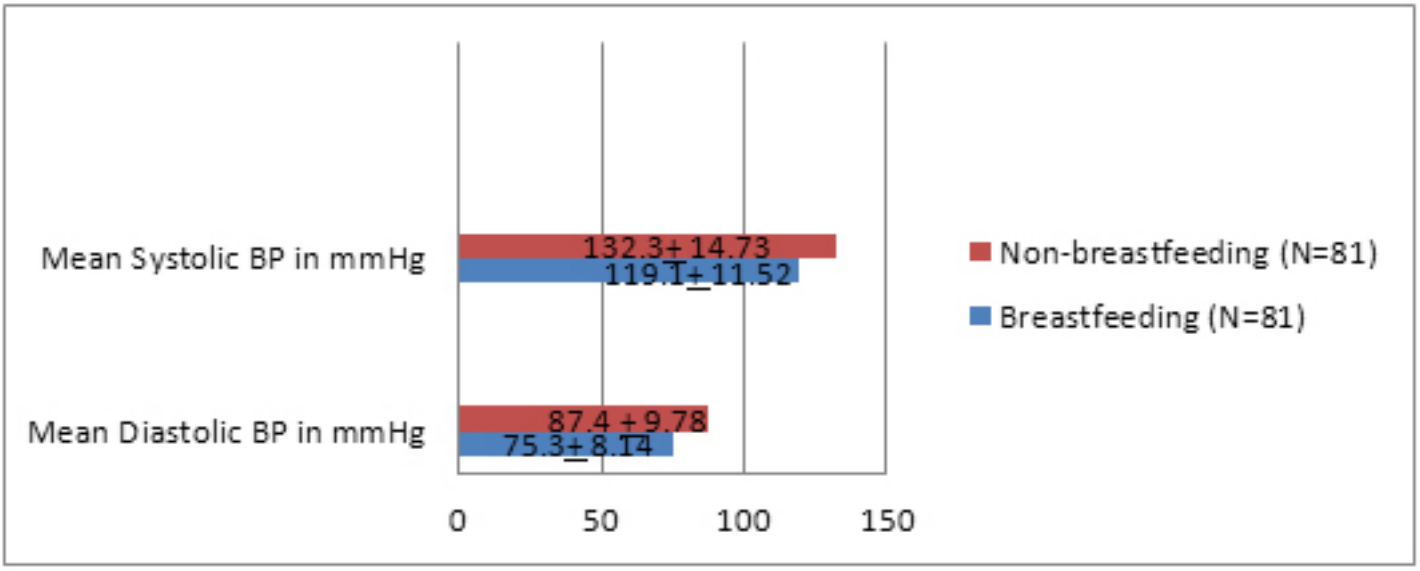


Figure 2: Comparison of Mean Blood Pressure in Breastfeeding and Non-breastfeeding mothers



Discussion

In our study, prevalence of postpartum stress in non-breastfeeding mothers was significantly higher than in breastfeeding mothers. The present study proposed a wider classification for postpartum stress, to include measures of not only stress, but also hypertension as well. Our study revealed that non-breastfeeding mothers have high postpartum stress (26.24+SD 3.78)) as compared to breastfeeding mothers (15.74 + SD 2.3). In the similar study done by Thome et.al they investigated that postpartum depressive symptoms and parenting stress were related to exclusive breastfeeding in mothers at 2-3 months postpartum. They found that depressive symptoms were related to lower levels of exclusive breastfeeding and that exclusive breastfeeding was more likely with higher level of maternal education (15). In another study done by Abou-Saleh MT et al. they also found that BF mothers have significantly lower levels of stress and depression symptoms. Sixty two postpartum women were screened for depression by the Edinburgh Postnatal Depression Scale (EPDS) after delivery and 34 of them were assessed by the Present State Examination (PSE) at 8 +/- 2 weeks after delivery and found that postpartum women had a significantly greater level of cortisol, prolactin, thyroxine and oestrogen than non-puerperal women (16). Galler JR et al. assessed 226 mothers worrying about infant or lactation related to depression and found that women who believed that BF was better than bottle feeding at seven weeks postpartum were more likely to continue BF up to six months postpartum, having less depression at seven weeks and six months postpartum (17).

Conclusion

Our results suggest that stress may be higher in non-BF mothers as compared to exclusive BF mothers. The postpartum is associated with significant stressors, and excessive stress poses a threat to maternal, child, and family well-being. It is important to determine if postpartum physiology plays a role in the mother's stress response. This study focuses on a need for early recognition, diagnosis and intervention in postpartum non-breastfeeding women so that future complications can be avoided.

Acknowledgements
I express my deep sense of gratitude to my participants; without their cooperation this study might not have been successful.

Conflict of the interests
None

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Osteoporosis in Psoriasis and Psoriatic Arthritis Patients

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Jinan Q. Mohammed,.Abdulsatar J. Mathkhor, Alaa H. Abed. Osteoporosis in Psoriasis and Psoriatic Arthritis Patients. World Family Medicine. 2020; 18(7): 38-42 DOI: 10.5742MEWFM.2020.93833

Abstract

Background: There is evidence of occurrence of osteoporosis in patients with psoriasis and psoriatic arthritis. This study aimed to assess the occurrence of osteoporosis in patients with psoriasis and psoriatic arthritis.

Patients and methods: A cross-sectional study involved 154 (88 males and 66 females) patients with psoriasis; of them 42 (23males and 19 females) fulfilled the classification criteria of psoriatic arthritis, from Oct. 2018 –Jan.2020. Extensive data collection involving full investigations, disease activity, PASI and DAS28 were measured for both psoriasis group and psoriatic arthritis group, respectively. Dual energy X ray absorptiometry (DXA) was performed for both groups.

Results: From the total sample of 154 patients, 112 patients with psoriasis 65 (58.9%) were males and 47 (41.1%) were females, 42 patients with psoriatic arthritis 23 (54.7%) were males and 19 (45.3%) were females. Whereas 33 patients of the psoriasis group have osteoporosis in a percentage of 29.5%, that is associated with high psoriasis area and severity index (PASI), in particular in males; there were only two patients who have osteoporosis in the psoriatic arthritis group in a percentage of 4.7%, which also was associated with high disease activity. Patients with psoriatic arthritis have less frequency than those patients with Psoriasis of developing osteoporosis particularly those on biologic treatment.

Conclusion: Osteoporosis frequently occurs in patients with psoriasis than Psoriatic arthritis patient, in particular male patients. It is less frequently occurring in patients with psoriatic arthritis, in particular those on anti TNF treatment.

Key words: psoriasis, psoriatic arthritis, osteoporosis.

Introduction

Psoriasis is defined as an inflammatory skin disorder which presents with an erythematous scaly rash on the extensor surfaces and trunk. It also affects the scalp, palms, and soles and may affect the nails resulting in either pits or onycholysis. Inflammatory arthritis may develop in 30% of patients with psoriasis and present with pain and stiffness in the affected joints (1). Psoriatic arthritis (PsA) is an inflammatory arthritis that is usually preceded by psoriasis. Psoriasis and PsA affect women and men in a ratio of 1:1(2). PsA has heterogeneous presentations and may involve both the axial skeleton (spondylitis and/or sacroiliitis) and the peripheral joints. It also affects skin, nails and entheses.

In contrast to rheumatoid arthritis, PsA is associated with the activation of osteoclasts as well as osteoblasts, and as a consequence, there are features of both bone destruction and new bone formation(3). Whereas rheumatoid arthritis is a disease of osteoclast activation, resulting in increased risk of generalized bone loss and the development of osteoporosis (4–7). Studies reported an association between psoriasis and PsA and the appearance of osteoporosis (8,9). Whereas others found no difference in bone mineral density (BMD) between patients with PsA and the background population (10–14). With the introduction of the new biological therapies in the treatment of psoriasis and psoriatic arthritis there was an obvious improvement in controlling the inflammatory process hence disease activity [15]. Therefore, there is a need for updating the information regarding osteoporosis in PsA.

Osteoporosis is defined as the generalised reduction in bone mass that results in disruption of the microarchitecture of bone, and decreased bone strength leading to an increased risk of bone fractures. The World Health Organization defines osteoporosis as a bone mineral density (BMD) below 2.5 standard deviations of the mean for young healthy adults of the same sex, whereas T scores between -2.5 and -1 standard deviations are defined as osteopenia (16).

Patients and methods

A cross-sectional study was carried out at the Dermatology Outpatient Unit, Department of Rheumatology and Rheumatology Outpatient Unit in Basra Teaching Hospital from Oct. 2018 – Jan.2020. A sample of 154 (88 males and 66 females) patients with psoriasis, was randomly selected. The diagnosis of psoriasis was confirmed by dermatologist. Out of the total psoriatic patients 42 patient (23 male and 19 female), had Psoriatic arthritis and fulfilled the classification criteria of psoriatic arthritis (17). Data collection was done through interview with the patients using a special questionnaire developed by the researchers. The questionnaire included information regarding: age, sex, disease duration and drug history. All patients were examined and investigated for complete blood cell count, erythrocyte sedimentation rate (ESR), dual-energy X-ray absorptiometry (DXA) was done and BMD was measured for all patients. Psoriasis area and severity index (PASI) was calculated by the dermatologist for all patients with psoriasis and disease activity score using 28 joints (DAS28) and ESR was measured for all patients with psoriatic arthritis by a rheumatologist. Elderly patients, postmenopausal women, patients with endocrine, metabolic, renal, and malabsorption diseases, and patients using systemic steroids were excluded from the study. Informed consent was taken from all participants.

Bone density measurements:
BMD (as g/cm2) was measured at the lumbar spine (L1–L4), and hip (femoral neck and total hip) by DXA machine in the Rheumatology unit in Basra Teaching Hospital. The T score (comparison with normal, young subjects of same sex) and Z score (comparison with age, sex and weight matched normal controls) were based on the reference values in the DXA machine provided by the manufacturer. We also calculated the percentage of patients with T score ≤−2.5 SDs and Z score ≤−1.0 SD. The definition of osteoporosis according to WHO guidelines was (T score ≤−2.5 SD) and (T score ≥ −1.0 SD) defined as normal BMD) (18).

Statistical analyses:
Statistical analysis was performed with Chi squared and Mann-Whitney tests to explore the significance of any differences or associations between the relevant variables. To conclude significance, a p-value less than 0.05, was considered significant.

Results

The demographic distributions of patients are shown in Table 1. From the total sample of 154 patients, 112 patients with psoriasis 65 (58.9%) of whom were males and 47 (41.1%) were females with median age and disease duration of 52 and 12 years respectively. Out of the forty two patients with psoriatic arthritis, 23 (54.7%) were males and 19 (45.3%) were females with median age and disease duration of 51.5 and 11 years respectively. Whereas, 33 patients of the psoriasis group have osteoporosis in a percentage of 29.5%, which is associated with high PASI, in particular in males with p-value of 0.0001, which is statistically highly significant as shown in Table 2 and Figure 1. There were only two patients with osteoporosis in the psoriatic arthritis group in a percentage of 4.7% also associated with high disease activity as shown in Table 3 and Figure 1. Osteoporosis less frequently complicates psoriatic arthritis especially those patients treated with biologic treatment compared to those on other treatments with statistically significant difference of p-value of 0.002 as shown in Table 4.

Table 1: The demographic distribution of patient groups

Characteristic	Psoriasis	Psoriatic arthritis	P-value
Total No. (154)	112	42	
Men (88)	65 (58.9%)	23 (54.7%)	0.715
Women (66)	47 (41.1%)	19 (45.3%)	
Age (Median)/ Years	52	51.5	0.367
Disease duration (Median)/ Years	12	11	0.476

Table 2: PASI in psoriasis patients with osteoporosis compared with psoriasis patients without osteoporosis

	Psoriasis group	With osteoporosis	Without osteoporosis	P-value
Men	65(58%)	29(25.9%)	36(32.1%)	0.0001
Women	47(42%)	4(3.6%)	43(38.4%)	
Total	112(100%)	33(29.5%)	79(70.5%)	
PASI (Median)	15	61.5	13	0.0001

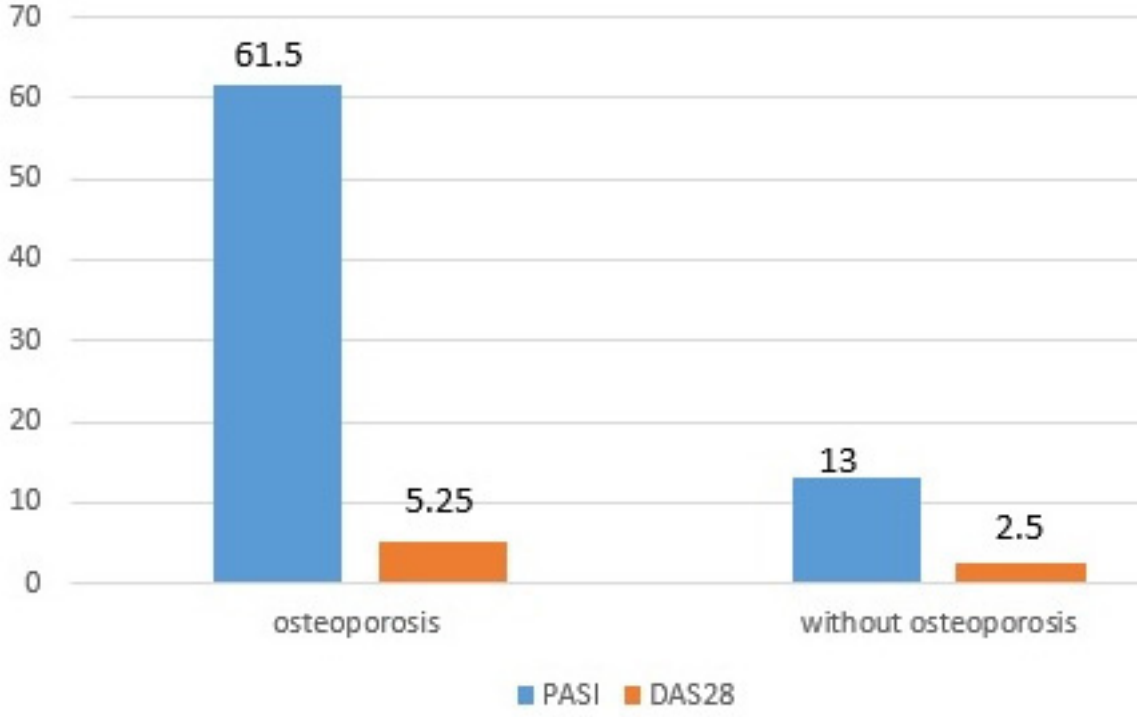
Table 3: DAS28 in psoriatic arthritis patient with osteoporosis compared with psoriatic arthritis patients without osteoporosis

	Psoriatic arthritis group	With osteoporosis	Without osteoporosis	P-value
Men	23(54.8%)	1 (2.4%)	22 (52.4%)	1.000
Women	19(45.2%)	1 (2.4%)	18 (42.8%)	
Total	42(100%)	2 (4.8%)	40 (95.2%)	
DAS28(Median)	2.55	5.25	2.5	0.018

Table 4: Percentage of osteoporosis in patients treated with anti TNF and patients without anti TNF

Patient characteristics	No. (%)	Anti TNF user	Anti TNF non- user	P-value
Total	154 (100%)	33 (100%)	121(100%)	
Patients with osteoporosis	35 (22.7%)	1 (3%)	34(28.1%)	0.002
Patients without osteoporosis	119 (77.3%)	32 (97%)	87(71.9%)	

Figure 1: Relationship between PASI and DAS28 in psoriasis and psoriatic arthritis patient with osteoporosis compared with those in patients without osteoporosis



Discussion

In this cross-sectional study, we found osteoporosis more prevalent among patients with psoriasis but it was less prevalent among those with PsA in a percentage of 29.5% and 4.6% respectively. The results indicate that generalized bone loss is an important comorbidity in patients complaining of psoriasis, which is comparable to a study conducted by Frediani B.et al (8), and was also shown by Martinez-Lopez Antonio et al that psoriatic patients has less BMD (19).

This may be explained by the previous global studies that related Psoriasis with low Vit D levels (20,21) and lower levels of its metabolizing enzymes, CYP27A1 and CYP27B1, within psoriatic lesions (22,23).

On the other hand, vitamin-D supplementation and treatment with oral calcitriol have been associated with clinical improvement in psoriasis lesions (24).

Several mechanisms may be implicated in the association between psoriasis and osteoporosis, such as the elevated systemic levels of inflammatory cytokines (interferon [IFN]-c, interleukin [IL]-6, tumor necrosis factor [TNF]-a), the use of antipsoriatic drugs (corticosteroids, methotrexate, cyclosporin), and prolonged immobilization due to joint dysfunction and severe pain for patients suffering from PsA.(25,26). The results, reflected by the high PASI in psoriasis patients with osteoporosis which is related to poor disease control, may correlate to the shortage of biologic treatment for dermatologic disease in our locality. We found male patients are obviously more affected by osteoporosis than female patients; a result consistent with Jacob Dreiher et al finding who conclude, an association between psoriasis and osteoporosis was observed among males, but not among females. (16). Further studies are needed to confirm our observation. The low percentage of osteoporosis in patients with psoriatic arthritis in this study is consistent with the findings of another study done by Reddy SM. et al (9) who reported a modest association between PsA and osteoporosis. Further, we found that osteoporosis less frequently occurs in patients with psoriatic arthritis; a result that is comparable to other studies (9,12-14,27,28). These results, in part, may be related to the disease nature; the activation of both osteoclasts and osteoblasts, and as a consequence, patients may show signs of both bone destruction and new bone formation (3), or it may be related to the use of TNF inhibitors in this group of patients (drugs authorized only for rheumatologic disorders in our locality). TNF inhibitors have been shown to increase BMD in lumbar spine and hip in spondyloarthropathies (29–31). In this study there is an inverse relationship between the PASI and BMD in psoriasis patients with osteoporosis, this was in contradiction with Sara D'Epiro et al 2014 who found no association between bone resorption and severity of skin involvement (PASI score) (32).

Patients with high PASI that reflects poor disease control is associated with low bone mineral density, and again an inverse relationship between DAS28 and BMD in psoriatic arthritis patients with osteoporosis; patients with high disease activity that is associated with poor disease control and low bone mineral density.

Conclusion

Osteoporosis frequently occurs in patients with psoriasis, in particular male patients. It is less frequently found in patients with psoriatic arthritis, in particular those on anti TNF treatment.

Recommendations:
We recommend the introduction of biological therapies for dermatological disorders in our locality, and further studies are needed to confirm our observation about involvement of mainly males with psoriasis in osteoporosis.

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COVID-19 in Pakistan: A Grim-looking Trajectory

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Salman Tariq, Naveen Tariq, Waris Qidwai. COVID-19 in Pakistan: A Grim-looking Trajectory. World Family Medicine. 2020; 18(7): 43-49 DOI: 10.5742MEWFM.2020.93834

Abstract

The beginning of the year saw the rapid spread of the COVID-19 pandemic across the globe, and country after country succumbed to the damage it had begun to inflict. The first cases in Pakistan emerged towards the end of February, and the government took some vital early steps to isolate itself and contain the spread of the virus in the country. I

In this article, we aim to cast light on some of those measures. We also desire to draw attention to the recent downward trajectory and analyze the causes responsible for it. The chief among them being the indecision and misjudgment on the part of the government as it fumbled from one situation to the next. We finally conclude by providing some recommendations, foremost among them being the urgent need to reimpose a lockdown as instructed by the WHO and paying more considerable attention to the voices of the medical experts in the country. A failure to do so could lead to the development of a catastrophic situation in a country which has already been reeling off late due to a faltering economy.

Key words: Coronavirus. COVID-19. Pakistan. Trajectory. Government

Introduction

In December 2019, cases began to emerge from Wuhan, China, of pneumonia of unknown origin [1]. CDC China later declared the cause to be a novel coronavirus [2]. The virus spread swiftly to more than 30 provinces within a month of the first reported case, and the Chinese government notified the WHO of an epidemic like situation in early January. It subsequently labeled the outbreak as the 6th PHEIC (Public health emergency of international concern) on January 30th, 2020. As the situation deteriorated further due to the unchecked travel of asymptomatic carriers across the globe, it was ultimately declared a Pandemic on March 11th, 2020 [3]. Globalization soon screeched to a rapid halt as countries began to shut down their borders and implement social distancing rules among their populations to isolate themselves from the psychological, social, and economic damage that the virus had swiftly begun to inflict.

The Ministry of Health, Government of Pakistan, reported its first two cases of the COVID-19 from Karachi and the capital Islamabad, on February 26th, 2020 [4]. Both had a history of recent travel from Iran. All four provinces and other territories compromising the state of Pakistan had reported their first cases by March 18th, 2020. The government of Pakistan quickly sprang into action and took many beneficial steps and implemented guidelines, which ensured that Pakistan was coping well with the pandemic, while its neighbors like Iran and China struggled amidst a rapidly developing crisis[5]. However, effective policy making was in short supply as a couple of months later, the country's situation is quite dire, and deteriorating rapidly, due to a lack of caution and indecision on many crucial matters.

As of June 14th, 2020, the number of confirmed COVID-19 cases globally had surpassed 7•4 million, with 418,000 deaths. In Pakistan, the total cases reported so far have been139,000, with 2,632 deaths[6].

In this article, we aim to review measures implemented by the government, assess the trajectory of the disease in the country, while identifying some of the factors responsible for a recent downward trend.

Initial measures

As cases in neighboring countries of China and Iran rose sharply early on, Pakistan took quick steps and shut down all borders, including the Pakistan-China border, as well as the Iran and Afghanistan borders, on March 16th, 2020[7].

The government of Pakistan also imposed a nationwide lockdown on April 1st, 2020. The total number of cases reported at this time were 2,039, with 26 deaths. It was extended twice and lasted until May 9th, 2020, after which the government decided to ease it out slowly.

At the same time, the federal and respective provincial governments were encouraging social distancing across all channels of communication. The government was also promoting quarantine and isolation, and had set up 35 hospitals, equipped with more than 118,000 beds, across the country to deal with the outbreak.

A National Command and Operation Centre (NCOC) was set up to advise and implement solutions and to monitor the developing situation, while a high-level National Coordination Committee was formed to take vital decisions that curb the spread of the virus throughout the country. In addition, a website was launched to track data regarding the virus and to provide accurate medical information regarding its signs and symptoms.

Financial measures were also taken as the Government of Punjab announced a Rs10 billion relief package to support 2.5 million families of daily-wage earners [8]. These were especially critical as Pakistan is a third world country where two-thirds of the population depends on a daily wage. Moreover, since the Pakistani economy has been amongst the worst performing globally for the past two years, its society was already under tremendous stress.

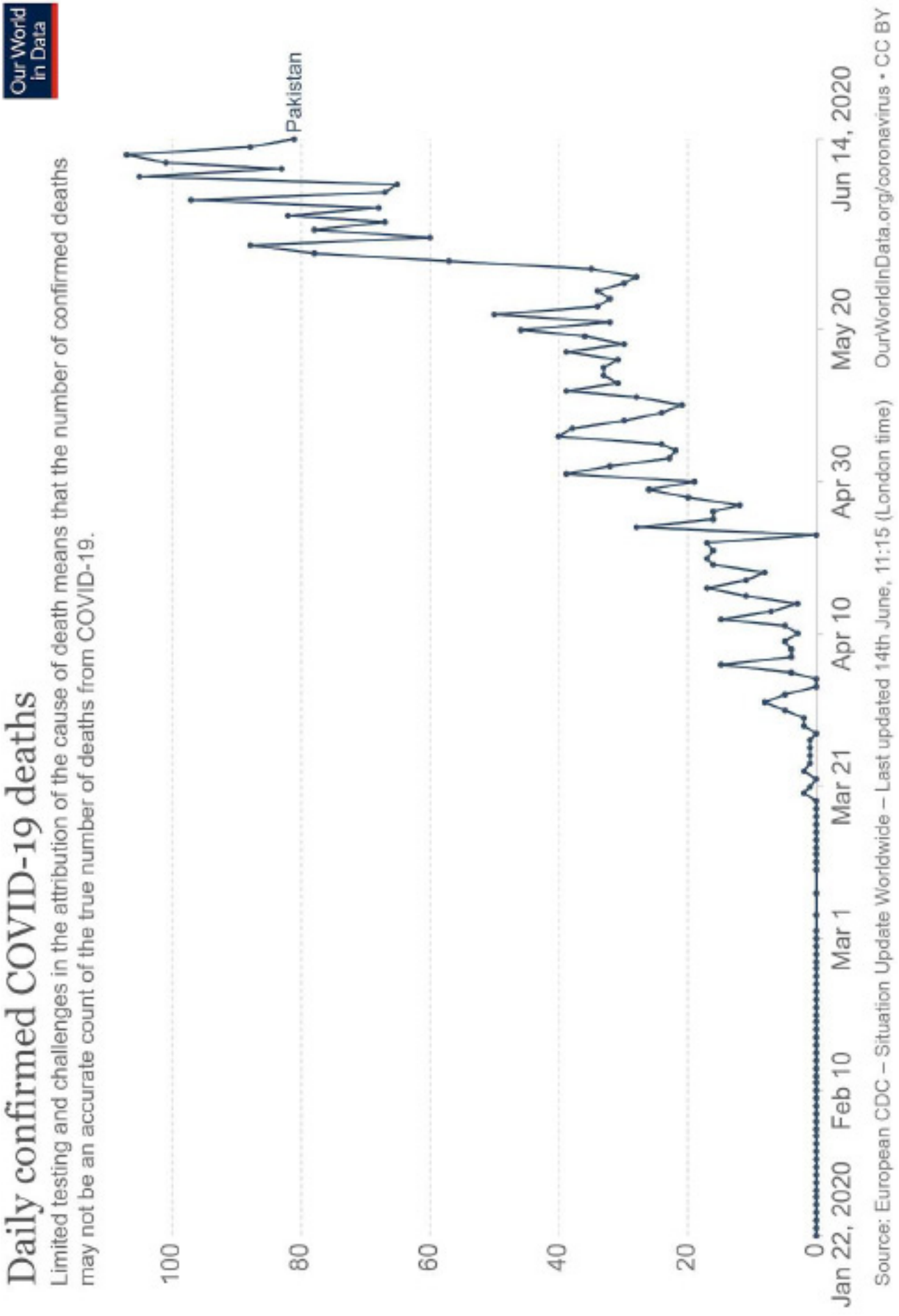
Others have shed much light on these and additional early measures carried out by the government [9][10][11].

Around the end of May, however, things began to take a downturn and the daily death rate started to spike, as can be seen above. There were various causes for this, and here we shall try to identify a few of them.

Social distancing measures had not been as successful as initially hoped for because the public was not enthusiastic about participating in them [12]. Pakistan being a developing country, has a low literacy rate. Theories abound among a superstitious populace as to how the pandemic is a western conspiracy hatched to control sections of the world. The government's sometimes contradictory public statements and a lack of orderly policy to educate and inform the masses, continue to ensure that inadequate attention is paid to the cautionary opinions of most medical experts. To make matters worse, the Center was often at odds with the provincial government in Sindh, and there is often no semblance of a coherent policy to combat the spread of the virus.

Compounding this lack of coordination was the considerable pressure exerted on the government by the religious clergy, which demanded that it be allowed to participate in congregational prayers during the nights of the holy month of Ramadan. These were aided in their quest by business owners who wanted a reopening of the economy due to the holy festival of Eid being around the comer. It is traditionally a time where commercial activity flourishes. The federal government had earlier decided to extend the lockdown until the middle of Ramadan after being advised

Trajectory headed in the wrong direction



to do so by the Pakistan Medical Association and other senior doctors. However it caved in to pressure exerted by a restless population, religious leaders, and business owners, and permission was granted by a committee headed by President, Arif Alvi, for congregational prayers to be held in mosques across the country, after consultations with religious scholars[13]. It was also decided that the lockdown would be eased so that people may get their necessary shopping for Eid done.

The government has never made its stance clear on the lockdown. Mixed messages were the norm as the Prime Minister, and many senior ministers were often at complete odds with each other regarding strategy. Once the PM stated on national television that the country could not afford a lockdown because of having vast numbers of daily wage eamers [14] and the Supreme court stepped in and supported the government on this issue. The lockdown did not stand much chance and had to be lifted. He has instead been advocating for a 'smart lockdown' whereby a lockdown is imposed in certain virus hotspots while measures are relaxed in other places. It has also been theorized that the easing of the lockdown allowed many thousands of workers to travel back to their villages, taking the virus with them. Once the virus has spread from the urban centers to rural areas, a lockdown will hardly be effective in containing the spread of the disease. Another problem is that the country lacks the training and resources required to test and treat people in remote and rural areas. This may also be a cause of the low death and case rate in the country. Statistics from rural areas are simply not being reported accurately.

One also got the sense that the government, like many governments aroud the worrld had a tremendously skewed sense of priorities, as in late June, it was focused on reopening the tourism industry, while the disease rate in the country was spiking [15]. It has also been recently reprimanded by the WHO regarding the easing of the lockdown, even though it was still far removed from the peak of the pandemic. The PM's advisor dismissed the WHO's concerns, declaring that it was only focused on health while they had to balance health concerns with those of the economy [16].

As can be seen from the chart opposite, the death rate in the country is rapidly escalating. This situation is equally terrible in the neighboring countries of India and Afghanistan. Moreover, since all three countries have dismissed suggestions of reimposing a lockdown, one would only expect conditions to get much worse.

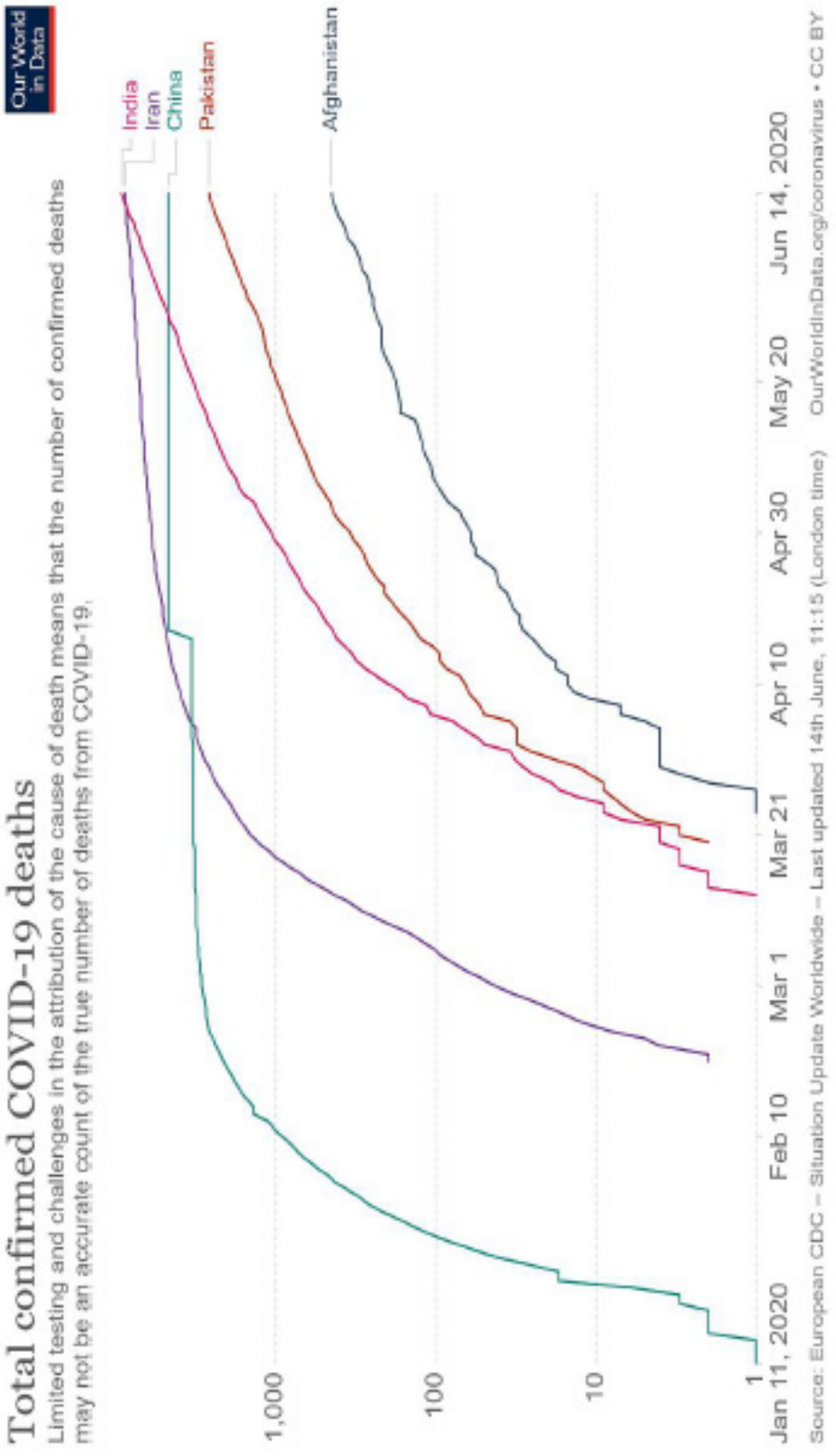
Indeed such predictions have already been made by various infectious disease models [17]. If such scenarios were remotely to come true, it is easy to imagine a situation where the healthcare facilities are completely overwhelmed. Reports have already begun to emerge of hospitals in major cities turning away critically ill and potentially sick patients from their doorsteps on account of not having adequate facilities to deal with the large number of cases [18]. An already resentful population is deeply dissatisfied by the situation due to economic hardship compounded by a rising death count. This disillusionment and resentment can easily spill over onto the streets as a bitter youth and largely unemployed masses decide to take their frustrations out against the state. There is also a possibility this anger gets directed to the medical community and healthcare services that are already stretched thin on the frontlines, as they bravely try to cope with the grave situation.

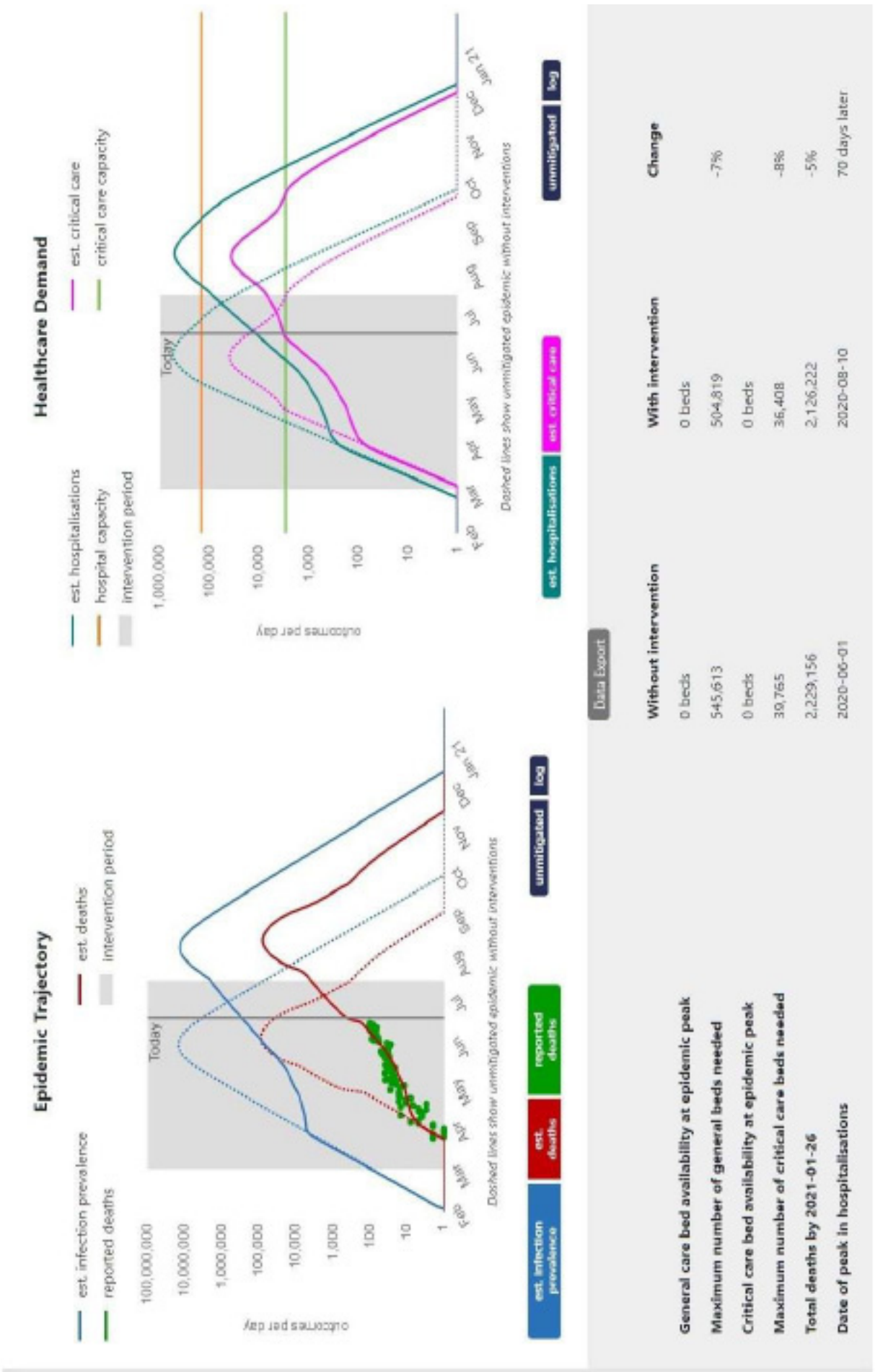
Impact on the healthcare community

The medical community in Pakistan has borne the brunt of the damage caused by the virus. According to government numbers, as of June 14th, 2020, at least 3,635 healthcare workers, including doctors, nurses, and paramedics, have tested positive for the virus. Out of these, forty have succumbed to the disease. In Pakistan, doctors have repeatedly complained about the lack of personal protection equipment (PPE) required to remain safe while dealing with infected patients. A lack of equipment has not only endangered the lives of healthcare workers but also ensured that they infect their coworkers, thereby making the entire situation even more precarious. There were also incidents where, in response to health workers getting infected, maternity wards of various hospitals were closed down since they did not want to risk the already challenged reproductive health of Pakistani women. Psychological issues faced by healthcare workers is also something that needs to be kept an eye on and continues to be highlighted in various papers all over the globe[19][20]21]. Additionally, there have been humiliating episodes that have broken the spirit of many medical professionals.

One such incident took place on April 6th, 2020, when police broke up protests in Quetta by more than 100 doctors who had very valid demands for proper PPEs.[22]. Fifty-three of these doctors were arrested, and countless others were roughed up and humiliated. Lastly, there have been countless reports of doctors and other medical experts expressing horror at how the entire episode is being handled in the country, at the abysmal conditions they are being forced to work under, and at the prospects of an already overburdened healthcare system being inundated with exponentially increasing patient load as the peak of the disease keeps drawing nearer.

While the government flounders, many institutes do realize the gravity of the situation and are putting up a brave fight against the virus[23]. Among them is the National Institute of Blood Diseases (NIBD), a private institution, where a clinical trial is being carried out under the supervision of Dr. Tahir Shamsi, aiming to assess the efficacy of convalescent plasma therapy as a cure for severely ill or critical patients with COVID-19[24]. While it has been used with some efficacy in several countries, plasma therapy is still not a proven approach and more trials are needed. Plasma therapy has historically been used in pandemics, where there has been no proven cure for the disease. Reports of its efficacy against Ebola and SARS have been published. Moreover, since no cure or vaccine has yet been discovered against the virus, plasma therapy may be of great importance in critical patients, particularly as disease rates go up and a shortfall of ventilators


Our World in Data
Total confirmed COVID-19 deaths
Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.
India
Iran
China
Pakistan
Afghanistan
1,000
100
10
1
Jan 11, 2020
Feb 10
Mar 1
Mar 21
Apr 10
Apr 30
May 20
Jun 14, 2020
Source: European CDC – Situation Update Worldwide – Last updated 14th June, 11:15 (London time)
OurWorldInData.org/coronavirus • CC BY


Epidemic Trajectory
est. infection prevalence
reported deaths
est. deaths
intervention period
Today
outcomes per day
100,000,000
10,000,000
1,000,000
100,000
10,000
1,000
100
10
1
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Jan '21
Dashed lines show unmitigated epidemic without interventions
est. infection prevalence
est. deaths
reported deaths
unmitigated
log
Healthcare Demand
est. hospitalisations
hospital capacity
intervention period
est. critical care
critical care capacity
Today
outcomes per day
1,000,000
100,000
10,000
1,000
100
10
1
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Jan '21
Dashed lines show unmitigated epidemic without interventions
est. hospitalisations
est. critical care
unmitigated
log
Data Export
Without intervention
With intervention
Change
General care bed availability at epidemic peak
0 beds
0 beds
Maximum number of general beds needed
545,613
504,819
-7%
Critical care bed availability at epidemic peak
0 beds
0 beds
Maximum number of critical care beds needed
39,765
36,408
-8%
Total deaths by 2021-01-26
2,229,156
2,126,222
-5%
Date of peak in hospitalisations
2020-06-01
2020-08-10
70 days later

develops. Drives to collect plasma have now been initiated all over the country, and this is something that the government should keep an eye on as the expected peak strikes Pakistan in late July/August.

Conclusion

This study provides an overview of the developments taking place in response to the pandemic and the trajectory of the disease in the country. More effort needs to be made, particularly when it comes to educating the masses in developing nations like Pakistan. Emphasis also needs to be placed by health organizers and medical experts on governments, forcing them to adhere more strictly to medical opinion, and less to those that aim to appease the populace.

Also, it is critical that the government heed the advice of WHO and other medical experts and immediately reimpose a strict lockdown. Plans need to be drawn to cope with the influx of patients and prevent healthcare services from becoming overwhelmed when the virus peak strikes. Plasma donation drives must also be stepped up all over the country as it can provide benefit to critically ill patients. In under-resourced areas, measures like scorecards can also be implemented, as these can be quite advantageous for rapid triage since COVID-19 cases are likely to be under detected due to limited testing facilities[25]. It may also provide much-needed relief to a resource-poor healthcare system, which is already stressed out as it deals with the rising tide of cases. Finally, an eye also needs to be kept on the eventual political fallout as a restless population deals with the psychological and health-related impact of the pandemic, coupled with the loss of livelihood. It needs to be ensured that healthcare facilities continue to function throughout any such scenario that may very well develop.

The government must pay heed to Brazil, Italy, the USA, the UK, and other countries where indecision and a lack of caution caused damage to the economy, psychological trauma, and mass panic, as well as a tremendous loss of precious lives.

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Diabetes Management in Ramadan – A Clinical Review

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Jazeb Razaq, Shayaan Ahmed Saqib. Diabetes Management in Ramadan – A Clinical Review. World Family Medicine. 2020; 18(7): 50-58 DOI: 10.5742MEWFM.2020.93835

Abstract

Ramadan is the month of fasting and is considered an integral part of the Islamic faith. Throughout the holy month it is compulsory for all healthy adult Muslims to fast. Individuals can be exempt from fasting if they are unwell or suffer from chronic medical conditions such as diabetes. Despite this, a considerable proportion of diabetic patients disregard medical advice and continue to fast. As a result, patients face potential complications leading to significant management challenges for healthcare professionals. With the increasing global prevalence of diabetes, the rates in the Muslim population are also expected to see a dramatic rise, it is therefore imperative to have clear up-to-date guidance for the management of diabetes during Ramadan.

In this article we aim to summarise the latest guidance and practical recommendations available for best managing diabetic patients who choose to fast during Ramadan.

Key words: Diabetes, Ramadan, Fasting, blood glucose monitoring, hypoglycaemia, hyperglycaemia

Introduction

Ramadan is the ninth month of the Islamic calendar. Fasting during Ramadan forms one of the five pillars of Islam. The fast involves abstinence from, food, drink, oral medications, smoking and sexual activity from dawn to dusk (1). It is obligatory for all healthy adults to fast. However, fasting is not intended to create excessive hardship and therefore exemptions exist. One such group of individuals who are exempt include those with chronic illnesses such as diabetes for whom fasting may be detrimental to their health. Despite this, many Muslims who could seek exemption choose to fast for cultural, social and religious reasons (2).

It is estimated that there are over a 150 million Muslims with diabetes worldwide, and studies have shown that many of these patients choose to observe fasting during Ramadan (3,4,5).

For countries in the northern hemisphere fasting hours in the summer months can be in excess of 16 hours; this can pose challenges for both patients and healthcare professionals.

The potential risks for diabetic patients who choose to fast in Ramadan include, hypoglycaemia (blood glucose of <70 mg/dL [3.9 mmol/L]), hyperglycaemia (blood glucose of >300 mg/dL [16.7mmol/L]), diabetic ketoacidosis, dehydration and thrombosis (6). In addition to the risk of adverse events patients can also make unsafe choices regarding their diabetes management during this month. They will often not consult with clinicians for advice prior to fasting, arbitrarily change medication doses, timings, frequency and or omit them altogether.

It is therefore important that healthcare professionals are proactive in identifying and engaging with diabetic patients who wish to fast during Ramadan at an early stage. An individualised Ramadan management plan should be discussed and agreed upon, with the aim of providing the best possible care and support to minimise the risk of any complications.

What does fasting involve?
'Sawm' is the Arabic word for fasting and involves abstinence from all forms of oral intake including food, water and medications during daylight hours. The month of Ramadan is when Muslims around the world observe fasting for a total of 29-30 days. During this month, patients will have only two main meals a day, the first which is the predawn meal called suhoor (sehri) and the second which is called iftar (fatoor) taken at sunset.

Who is exempt from fasting?
The elderly and frail, acutely unwell adults, individuals with chronic health conditions such as diabetes who are at risk of harm or complications, those with mental health issues and learning disabilities, prepubertal children, pregnant or breast-feeding women are all exempt from fasting.

What if you cannot fast?
Patients who are exempt from fasting have the option of offering charity or providing food for the poor. If appropriate, the fast may be postponed and made-up at a later date (1). For more detailed advice on these matters, the opinion of a religious scholar can be sought.

Management of diabetes during Ramadan

Pre-Ramadan assessment and counselling
The National Institute for Health and Clinical Excellence advocate an individualised approach to diabetes care tailored to the patient`s personal, social and cultural preferences (7).

It is advised diabetic patients wishing to fast should have an assessment with their GP or diabetic specialist at least 6- 8 weeks before Ramadan begins. This should be an opportunity to assess and discuss glycaemic control, lipids and blood pressure alongside the risks involved with choosing to fast. Patients should be advised according to their personal circumstances, allowing healthcare professionals to formulate a safe and personalised care plan for each individual.

It is recommended that prior to the commencement of Ramadan, diabetes education should focus on the following key components (8):

- Risk Assessment
- Dietary and fluid advice
- Exercise and smoking advice
- Blood glucose monitoring
- Awareness of complications such as hypo or hyperglycaemia and when to break the fast
- Medication review and adjustment

Risk assessment
For patients who intend to fast, it is important to quantify the associated risk from fasting. In doing so, particular focus should be given to the following key areas: the type of diabetes, medications being taken, the individual's risk of hypoglycaemia, the presence of complications or comorbidities, social and work circumstances and their previous experience of fasting during Ramadan (9). Based on this information, patients can be categorised as either very high, high, moderate or low risk of adverse events, see Table 1 (8).

Table 1: Risk stratification for patients with diabetes who fast during Ramadan
Adapted from Hassanein M et al, 2017 (8)

Category	Patient Background	Recommendations
Very High Risk	• Severe hypoglycaemia in the 3 months preceding Ramadan • Diabetic ketoacidosis in the 3 months preceding Ramadan • History of recurrent hypoglycaemia • History of hypoglycaemia with unawareness • Hyperosmolar hyperglycaemic coma in the 3 months preceding Ramadan • Type 1 diabetic - poorly controlled • Acute illness • Chronic kidney disease stage 4 & 5 and those on dialysis • Advanced macrovascular complications • Old age with ill health • Gestational diabetes mellitus treated with insulin or sulphonylureas or pregnancy in pre-existing diabetics	Patients advised NOT to fast due to high risk of harm. If patients insist on fasting, they should: o Be given detailed structured education o Arrange regular follow up with clinician o Observe close self-monitoring of blood glucose o Adjust medication regimen as advised o Have awareness of hypo & hyperglycaemia and be prepared to break the fast
High Risk	• Type 2 diabetic – poor glycaemic control • Type 1 diabetic well controlled • Type 2 diabetic on multiple daily injections or mixed insulin • Diabetic performing intense physical labour • Chronic kidney disease stage 3 • Stable macrovascular complications • Treatment with medication that may affect cognitive function • Patients with comorbidities that present additional risk factors • Pregnant type 2 diabetic or gestational diabetes mellitus controlled by diet or metformin alone	
Moderate/Low Risk	• Well controlled Type 2 diabetic treated with one or more of the following: o Diet & Lifestyle o Metformin, acarbose, second generation sulphonylureas dipeptidyl peptidase-4 inhibitors, thiazolidinediones, SGLT2 inhibitors or basal insulin	• Patients advised they can fast • Patients should: o Be given detailed structured education o Observe self-monitoring of blood glucose o Adjust medication regimen as advised

Patients who are deemed to be very high or high risk are advised not to fast. Those that fall into the moderate and low risk categories may fast taking into account the recommendations that are made after discussion with a healthcare professional. This advice has also been reviewed and endorsed by leading religious scholars specialising in Islamic jurisprudence (10,11).

Despite the advice for patients in the two highest risk categories to not fast, most will choose to do so against medical advice and it is important to respect their decision. Healthcare professionals should continue to provide the best possible care, and support patients to fast as safely as possible.

Dietary and fluid advice

The month of Ramadan is a time for self-control and discipline and this is something that should be reflected in an individual's dietary habits. Patients should aim to eat a healthy balanced diet with adequate hydration. They should refrain from eating foods rich in fat and sugar as this can lead to weight gain and postprandial hyperglycaemia. The daily caloric intake should be divided between the evening meal of iftar and early morning meal of suhoor. Portion sizes should be moderate and aim to include 45–50% carbohydrate, 20–30% protein and <35% fat (12).

Suhoor should be taken as late as possible, ideally just before sunrise rather than midnight in order to minimise the risk of hypoglycaemia. It is suggested that complex carbohydrates with a low glycaemic index which release energy slowly are ideal before and after fasting. One or two small snacks such as fruit, nuts, or vegetables may be consumed between the meals.

As there is a risk of dehydration with prolonged fasting, it is recommended that fluid intake is increased during non-fasting hours. Beverages should include sugar free fluids, decaffeinated drinks and water. A practical summary of dietary and cooking advice is provided in Table 2 (page 54).

Exercise and smoking advice

Regular levels of light and moderate exercise and activity should be maintained. However, excessive or rigorous exercise should be avoided, especially in the few hours before the iftar meal due to the increased risk of hypoglycaemia and or dehydration. If a patient participates in the extra prayers of Taraweeh (which take place after breaking the fast), this should be considered as part of their daily exercise as it involves a series of movements such as standing, bowing and kneeling.

As smoking is prohibited whilst fasting, Ramadan provides an ideal opportunity to focus on smoking reduction and cessation. Patients who smoke should be directed to specialist smoking cessation services at the earliest opportunity (13,14).

Blood glucose monitoring

Patients should be educated that blood glucose monitoring through finger prick testing does not break the fast (15). It is vital patients who are fasting are provided with the means to check their capillary blood sugars on a regular basis. Patients are encouraged to check their blood sugars immediately after opening their fast, if they feel unwell and or have symptoms of hypo or hyperglycaemia.

The frequency of self-monitoring blood glucose levels will depend on a number of factors such as type of diabetes, the medications the patient is taking and their level of risk (Table 1). For those in the low to moderate risk group this can mean monitoring their blood glucose two or three times a day. High and very high-risk groups should check their blood glucose five to six times a day (16,17). Table 3 (page 54) shows the recommended frequency with which to check blood glucose levels whilst fasting in Ramadan.

Patients who are taking medications that can cause hypoglycaemia such as insulin and sulphonylureas are advised to check their blood sugars more frequently. Self-monitoring of blood glucose is also useful in those patients who are willing and able to adjust their diabetes treatment, such as insulin dose titration (17,18).

Awareness of complications and when to break the fast

Patients need to be educated on the signs and symptoms of dehydration, hypoglycaemia and hyperglycaemia. They should break their fast if any such complication or acute illness occurs and seek the advice of a healthcare professional. A summary is provided in Table 4 (page 55).

Medication review and adjustment

During Ramadan, diabetic patients who are observing the fast are expected to take their medication between iftar and suhoor. The type of medication being taken can increase the risk of adverse events and complications. It is therefore important healthcare professionals are proactive in engaging with patients early on to conduct a detailed individualised medication review. The review will aim to highlight the need to adjust the dose, frequency and or timings of the medication.

Table 5 and 6 (pages 56 and 57) provide a summary of recommendations for oral diabetic medication and insulin respectively.

Table 2. Dietary and cooking advice for patients with diabetes who fast during Ramadan (12)

Foods to Avoid	Alternative
Ghee (clarified butter), samosas, pakoras, paratha, fried dumplings, fried kebabs, pastries, puri, chevera, katlamas, oily meat curries.	Rapeseed oil, olive oil, chickpeas, hummus, baked samosa, boiled dumplings, grilled kebabs, wholegrain cereals, granary bread, brown rice, chapatti, beans, pulses, vegetables, salads, grilled red meat and chicken.
Sugary desserts, traditional sweets eg: Jalebis, Gulab Jamun, Rasgulla, Baklawa, Kanafeh, Umm Ali	Fresh fruit e.g: dates, apples, bananas etc, dried fruit and nuts e.g: apricots, figs, raisins, prunes, almonds, cashews, pistachio, walnuts etc.
Cooking Methods to Avoid	**Alternative**
Deep frying, using excessive oil	Shallow fry, bake, boil, grill or air fry food.

Table 3. Recommended frequency of blood glucose monitoring for patients during Ramadan depending on their risk stratification
Adapted from Hassanein M et al, 2014(16) and 2016 (17)

High risk group: NB These patients should be advised against fasting during Ramadan, however if they insist on fasting blood glucose monitoring should be done at the following times.

1. Before suhoor
2. 2 hours after suhoor
3. Midday
4. Before iftar
5. 2 hours after iftar
6. If symptoms of feeling unwell, hypoglycaemia or hyperglycaemia

Low risk group: Recommended times for blood glucose monitoring

1. Before suhoor
2. Midday
3. Before/After iftar
4. If symptoms of feeling unwell, hypoglycaemia or hyperglycaemia

Table 4. Recognising possible complications and when to end the fast
Adapted from: Hassanein M et al, 2016 (17)

Patient should end their fast immediately if any of the following occur:
Hypoglycaemia - (blood glucose of <70 mg/dL [3.9 mmol/L])
Symptoms include: • Shaking • Sweating • Palpitations • Hunger • Headache • Lack of concentration, confusion, irrational behaviour, loss of consciousness
Hyperglycaemia - (blood glucose of >300 mg/dL [16.7mmol/L])
Symptoms include: • Extreme thirst • Increased urinary frequency • Hunger • Fatigue • Confusion • Nausea/vomiting • Abdominal pain
Dehydration
Symptoms include: • Extreme dry mouth and thirst • Fatigue • Drowsiness • Difficulty urinating • Increased breathing and pulse rate • Ketones in the urine • Lack of concentration
Acute illness
Symptoms include (not an extensive list): • Fever • Diarrhoea or vomiting • Disorientated, limb weakness • Dizziness or collapse • Chest pain • Shortness of breath

Table 5. Recommended changes to oral diabetic medications
Adapted from Hassanein M et al, 2017 (19). Al-Arouj M et al, 2010 (20)

	Medication	Direction	Recommendation
Oral diabetic medication	Biguanides e.g. Metformin – Immediate Release	OD: Daily dose remains unchanged	Take at iftar.
		BD: Daily dose remains unchanged	Take at iftar and suhoor.
		TDS: Daily dose remains unchanged	Morning dose after suhoor, combine afternoon & evening dose at Iftar.
	Metformin – Modified release	Daily dose remains unchanged	Take at Iftar.
	Acarbose		No dose modification
	Thiazolidinediones / Glitazones e.g. Pioglitazone, Rosiglitazone		No dose modification. Dose can be taken with iftar or suhoor.
	Meglitinides e.g. Repaglinide		Reduce TDS dose to BD, to be taken with iftar and suhoor.
	Glucagon-like peptide-1 receptor agonists e.g. Exenatide & Liraglutide	Continue with maintenance dose	No dose modification is needed
	Dipeptidyl peptidase-4 inhibitors e.g Sitagliptin, Vildagliptin, and Saxagliptin		No dose modification is needed
	Sulfonylureas (SU) e.g. Glibenclamide*, Gliclazide, and Glimepiride *Glibendamide should be avoided Switch to newer SU (Gliclazide, Glimepiride) where possible	OD	Take at iftar. Dose may be reduced in patients with good glycemic control.
		BD	Take at iftar and suhoor. Iftar dose remains unchanged Suhoor dose may be reduced in patients with good glycemic control.
	Sodium-glucose cotransporter 2 inhibitors e.g. Dapagliflozin, and Canagliflozin		Take at iftar. No dose modification is needed Increase hydration. Avoid in the elderly, patients with renal impairment, hypotension or in those taking diuretics.

Table 6. Recommended changes to Insulin dosing during Ramadan
Adapted from Hassanein M et al, 2017 (19)

	Type of Insulin	Direction	Recommendation
Insulin	Long or intermediate acting basal insulin e.g. NPH/Detemir/Glargine	OD	Take at iftar. Reduce dose by 15–30%.
		BD	Take usual morning dose at iftar. Reduce evening dose by 50% and take at suhoor.
	Rapid or short-acting prandial/bolus insulin		Take normal dose at iftar. Omit lunch time dose. Reduce suhoor dose by 25–50%.
	Premixed insulin	OD	Take normal dose at iftar.
		BD	Take usual morning dose at Iftar. Reduce evening dose by 25–50% and take at suhoor.
		TDS	Omit afternoon dose. Adjust iftar and suhoor doses.

Summary

In summary, low and moderate risk diabetic patients can participate in fasting during Ramadan but should do so with appropriate precautions. Those who are categorised as high or very high-risk are usually advised not to fast, however if they wish to do so, their decision must be respected. All diabetic patients should seek medical advice prior to commencing fasting, in order to optimise their diabetic control, adjust diabetic medication as well as discuss dietary and monitoring requirements during Ramadan. The role of the healthcare professional is to ensure that the diabetic patient is able to fast as safely as possible by means of education and guidance. The patient should be made aware of the symptoms of potential complications during fasting with diabetes, including advice on when they should break the fast on medical grounds.

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Parkinson's Disease: An update on Pathophysiology, Epidemiology, Diagnosis and Management Part 3 : Diagnosis , Symptoms, and Prognosis of Parkinson's Disease

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Abdulrazak Abyad. Parkinson's Disease: An update on Pathophysiology, Epidemiology, Diagnosis and Management. Part 3 : Diagnosis , Symptoms, and Prognosis of Parkinson's Disease. World Family Medicine. 2020; 18(7): 59-69 DOI: 10.5742MEWFM.2020.93836

Abstract

Parkinson disease is a clinical diagnosis. For the condition, there are no laboratory biomarkers, and findings on routine magnetic resonance imaging and computed tomography scans are unremarkable. Medical diagnosis involves 2 of 3 cardinal signs: Resting tremor Bradykinesia and Rigidity. Parkinson's disease often has a multitude of non-motor symptoms; some may precede the diagnosis, while others may occur early or late after the diagnosis is made, depending on motor features. Careful attention to the history is needed in patients with Parkinsonism to exclude secondary causes such as medication, toxins, or trauma. Medicines that block receptors of striatal dopamine, such as metoclopramide and neuroleptics, can cause drug-induced parkinsonism. Parkinsonism can also be caused by other chemicals, such as MPTP (1-methyl-4-phenyl-1,2,3,6- tetrahydropyridine) and manganese (at high exposure). Practical laboratory testing for PD is not available; the diagnosis is based on the clinical characteristics or excluding other causes of parkinsonism. However there are some promising developments in radiology.

Key words: Parkinson's disease, pathophysiology, epidemiology, management, diagnosis, symptoms, prognosis

Introduction

Parkinson's disease diagnosis tends to be focused on having signs and symptoms present. Tremor is the most apparent clinical symptom and mostly begins at one end and gets worse with precipitating factors like stress, exhaustion and cold weather. It may be confused with the more common essential tremor, but it can be distinguished by noting whether the tremor occurs mainly in rest (Parkinson's disease) or with motion (essential tremor). Essential tremor normally occurs in both limbs, while Parkinson's disease patients generally have a one-sided tremor that can affect one arm or leg. Bradykinesia is usually the symptom with the most trouble.

Patients report slowness in carrying out their daily living activities, including dressing, walking and doing household chores. Writing may become micrographic, with the size of a character increasingly smaller as the author continues to write. It is beneficial to watch a patient get up from a chair and walk. Parkinson's disease patients can need to force themselves up, take longer to get up or fall backwards. Very early features of the disease may be reduced arm swing, flexed posture and a shuffling gait. Muscle rigidity on passive movement is typical of Parkinson's disease but must be differentiated from the rigidity arising from, for example, upper motor neuron lesions in patients with a stroke.

In Parkinson's disease, passive joint movement reveals continuous resistance throughout the whole range of motion, the rigidity of the so-called "lead pipe." With upper motor neuron lesions the muscles, after an initial period of rigidity and resistance to movement, suddenly relax or give way, the so-called "clasp-knife" rigidity. Additionally, patients with Parkinson's disease may show a cogwheel type of rigidity. Here the muscles, on passive movement, have a ratchet-like feel. If rigidity and cogwheeling are not present when the patient is relaxed, the signs may be brought on by having the patient open and close their contralateral hand during the examination (Table 1).

Diagnostic Considerations

Parkinson's disease, and essential tremor, are the most common tremor disorders. If a patient is shaking, the clinician should pay careful attention to the areas of the body involved, the positions / conditions in which the tremor occurs (i.e., rest, postural, kinetic, intention), and the magnitude of the tremor. Looking for possible related signals, too, is important. For symptoms of parkinsonism (bradykinesia, weakness, postural instability), dystonia, and other neurological signs, the patient should be checked.

An upper extremity tremor of 8-12 Hz (postural/kinetic) which is temporarily relieved by drinking alcohol is typical of essential tremor, while the occurrence of pill-rolling rest tremor, bradykinesia, and rigidity is consistent with Parkinson's disease and argues against essential tremor. Careful attention to the history is needed in patients with parkinsonism to exclude secondary causes such as medication, toxins, or trauma. Medicines that block receptors of striatal dopamine, such as metoclopramide and neuroleptics, can cause parkinsonism caused by the medication. Parkinsonism can also be caused by other chemicals, such as MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) and manganese (at high exposure).

Consider assessing osteoporosis and osteopenia in patients with parkinsonism. In a meta-analysis of 23 studies, Tornsey and colleagues found evidence that individuals with Parkinson's disease have an increased risk of osteoporosis and osteopenia (2014). For example, a pooled analysis of 2 of the studies indicated that the odds ratio for developing osteoporosis in patients with Parkinson's disease was 2.61 compared to healthy controls, although the increase was lower in men than in women. Review of 14 studies showed that bone mineral densities were significantly lower in patients with Parkinson's disease in the hip, lumbar spine, and femoral back, although researchers concluded that bone fracture risk was doubled in Parkinson's patients after an analysis of 9 studies (Tornsey et al, 2014).

Early clinical findings indicating an atypical parkinsonism instead of Parkinson's disease include the following (Suchowersky et al., 2006):

- Falls at presentation or early in the disease.
- Poor response to levodopa
- Symmetry at disease onset
- Rapid disease progression
- No tremor
- Dysautonomia (e.g. urinary incontinence, fecal incontinence, catheterization for urinary retention, persistent erectile failure, prominent symptomatic orthostatic hypotension)

The atypical parkinsonisms are usually associated with little or no tremor, difficulty in speaking and balance relatively early, and little or no response to dopaminergic drugs. Multiple system atrophy (MSA) is relatively symmetric and characterized by parkinsonism, often with some combination of autonomic, corticospinal, and cerebellar dysfunction. Progressive supranuclear paralysis (PSP) is relatively symmetrical and characterized by early-fallen parkinsonism (often in the first year) and a supranuclear gaze palsy in which the patient has difficulty with voluntary down-gaze. Corticobasal ganglionic degeneration (CBD) is generally very asymmetric and has both cortical (difficulty recognizing items, apraxia) and basal ganglionic (usually marked stiffness in an arm) characteristics.

Lewy body disorder is characterized by severe cognitive impairment within 1 year of the parkinsonism onset. Hallucinations are common. Patients with an onset of parkinsonism before age 40 should be tested for Wilson disease, starting with serum ceruloplasm measurement and Kayser-Fleischer rings ophthalmological assessment.

The differential Diagnoses include the following

Alzheimer Disease
Cardioembolic Stroke
Chorea in Adults
Cortical Basal Ganglionic Degeneration Dementia with Lewy Bodies Dopamine-Responsive Dystonia Essential Tremor
Pantothenate Kinase-Associated Neurodegeneration (PKAN) Huntington Disease
Lacunar Syndrome
Multiple System Atrophy
Neuroacanthocytosis
Neurological Manifestations of Vascular Dementia Normal Pressure Hydrocephalus Olivopontocerebellar Atrophy
Parkinson-Plus Syndromes Progressive Supranuclear Palsy Striatonigral Degeneration

Available Investigations that Help with Diagnosis
Practical laboratory testing for PD are not available; the diagnosis is based on the clinical characteristics or excluding other causes of parkinsonism. However there are some promising developments in radiology.

Examination
A focused examination to assess whether a patient has symptoms and signs that may suggest other forms of parkinsonism than Parkinson's disease (Table 1) should be performed. To rule out progressive supranuclear paralysis, it is important to evaluate changes in vertical eye movement. To rule out multiple system atrophy, postural blood pressure changes, other autonomic abnormalities including a history of bladder instability, and cerebellar features such as early gait instability should be evaluated. Although falls and swallowing problems are consistent with late Parkinson's disease, they may be suggestive of progressive supranuclear palsy or multiple system atrophy if they occur early and are accompanied by a lack of treatment response. Early dementia and other characteristics may suggest dementia to the Lewy body, corticobasal degeneration or parkinsonism to the vascular. Patients with early onset parkinsonism (aged < 40 years) should always be assessed for Wilson 's disease with serum copper and ceruloplasm level measurement, 24-hour copper excretion urine collection, and Kayser –Fleischer ring slit-lamp examination,

Imaging
While PD is a clinical condition, imaging can help in diagnosing differentials. Magnetic Resonance Imaging (MRI) is not useful for diagnosing PD; its usefulness depends on excluding ischemic, inflammatory, neoplastic and infectious causes or other forms of parkinsonism.

Typical findings of MRI in atypical parkinsonism include 'hot cross bun sign' in MSA, 'hummingbird sign' and 'morning glory sign' in PSP, front-temporal atrophy in FTD and asymmetric cortical atrophy in CBD; fluorodeoxyglucose positron emission tomography (FDG-PET) may reveal hypo-metabolism in the same areas of CBD and FTD atrophy (Deutschländer et al., 2017).

Recommendations for Imaging in the Diagnosis of Parkinson Disease

Imaging modality	*American Academy of Neurology*	*National Institute for Health and Clinical Excellence*	*Scottish Intercollegiate Guidelines Network*
Fludeoxyglucose positron emission tomography	Evidence insufficient to make recommendation	Use only in research settings	Not recommended
Magnetic resonance imaging	Possibly useful to distinguish Parkinson disease from multisystem atrophy	Not recommended for diagnosis of Parkinson disease Consider for diagnosis of parkinsonian syndromes	Not recommended for routine diagnosis of idiopathic Parkinson disease
Single-photon emission computed tomography	Possibly useful to distinguish Parkinson disease from essential tremor	Distinguish Parkinson disease from essential tremor	Distinguish Parkinson disease from nondegenerative parkinsonism or other tremor disorders
Ultrasonography	Evidence insufficient to make recommendation	No recommendation	Not recommended

Advances in neuroimaging research including transcranial Doppler ultrasonography (Alonso-Cánovas et al., 2014), positron emission tomography (PET), single-photon computed tomography (SPECT), morphometric MRI tests, tractography, functional MRI and perfusion imaging are used to distinguish Parkinson's idiopathic disease from other parkinsonian disorders (Stoessl et al., 2011).

Radionuclide imaging modalities such as PET and SPECT have become the best approach for assessing the metabolism and deficiency of dopamine, using a dopamine transporter ligand. Tracer absorption in the posterior or dorsal striatum is limited, which is asymmetric in Parkinson's disease (Stoessl et al . 2011. Stoessl et al. 2014).

No evidence of dopaminergic deficit on dopamine transporter SPECT and fluorine-18 fluoro-L- dopa PET imaging scans will be available to a subgroup of patients suspected of having new-onset Parkinson's disease (Marek et al., 2014). Disease development, through imaging or clinical tests, is low in this group of patients, as is their risk of developing idiopathic Parkinson's disease (Marek et al., 2014). However, a few may eventually be diagnosed with Parkinson's disease, based on clinical progression, imagery and genetic evidence and a positive response to levodopa (Erro et al., 2016).

Ultrasounds may detect abnormal SN hyperechogenicity in patients with PD; however, this technique's sensitivity and specificity for the diagnosis of PD is suboptimal (75% and 70% with atypical parkinsonism and 78% and 85% with ET) (Shafieesabet et al., 2017).

These imaging techniques are still considered experimental, and at the time of initial presentation of patients with early Parkinson's disease, studies to assess their positive predictive value were not conducted to identify their clinical value. Because current management strategies would not change due to a quick diagnosis of Parkinson's disease, most experienced clinicians choose to follow the patient's clinical course and make treatment decisions based on the needs of the individual patient, rather than relying on any information obtained from neurological imaging.

Lumbar Puncture

Where signs of normal-pressure hydrocephalus (NPH) are observed (e.g., incontinence, ataxia, dementia), lumbar puncture should be considered. Clinical signs in NPH improve characteristically after removal of around 20 mL of cerebrospinal fluid.

Dopa-responsive dystonia ought to be contemplated in patients with juvenile-onset dystonia and parkinsonism, especially those with diurnal symptom fluctuations. A trial of levodopa in such patients is critical. Measurement of CSF concentrations of biopterin, neopterin and neurotransmitter metabolites of homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA), and 3-methoxy-4-hydroxyphenylglycol (MHPG) are additional measures for this disorder. A modified pattern of decreases in these compounds is observed in both forms of dopa-responsive dystonia.

In the cross-sectional analysis of 63 drug-naive patients with early-stage PD and 39 healthy controls, the CSF levels of Alzheimer's biomarkers β-amyloid 1-42 (Aβ1-42), total tau (T-tau), tau phosphorylated threonin 181 (P-tau181), and α-synuclein in the PD patients were lower than in the controls. Aβ1-42 and P-tau181 were important predictors of Parkinson's disease and the extent of the motor dysfunction was correlated with T-tau and α-synuclein. In particular, lower concentrations of Aβ1-42 and P-tau181 were associated with the postural instability – gait disturbance – dominant PD phenotype, but were not linked to the tremor-dominant or intermediate phenotypes (Kang et al., 2013).

Autopsy

Autopsy confirmation is the sole conclusive method of diagnosis. The UK Brain Bank Criteria were developed to improve the accuracy of the Parkinson's disease clinical diagnosis (Hughes et al., 1992). This study evaluated the presenting clinical features in 100 cases which predicted confirmation of the disease by autopsy. They found that the best predictors of pathological diagnosis were the unilateral onset of symptoms with features including tremor, and at least one of bradykinesia and rigidity with a good initial response to L-dopa. A specific neurological disease was diagnosed at autopsy in 24 percent of the cases relative to those diagnosed during childhood.

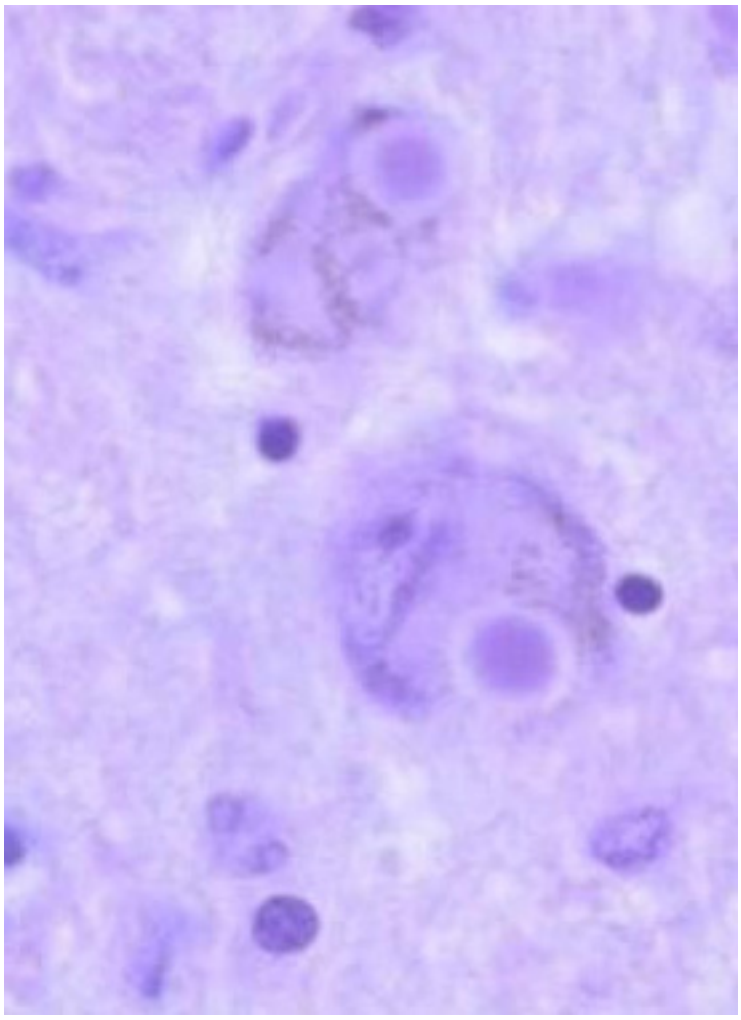
Lewy bodies are eosinophilic intracytoplasmic inclusions, often with halos, which are easily seen in pigmented neurons, as shown in this histologic slide (Figure 1). They contain polymerised alpha-synuclein; thus, alpha synucleinopathy is Parkinson's disease.

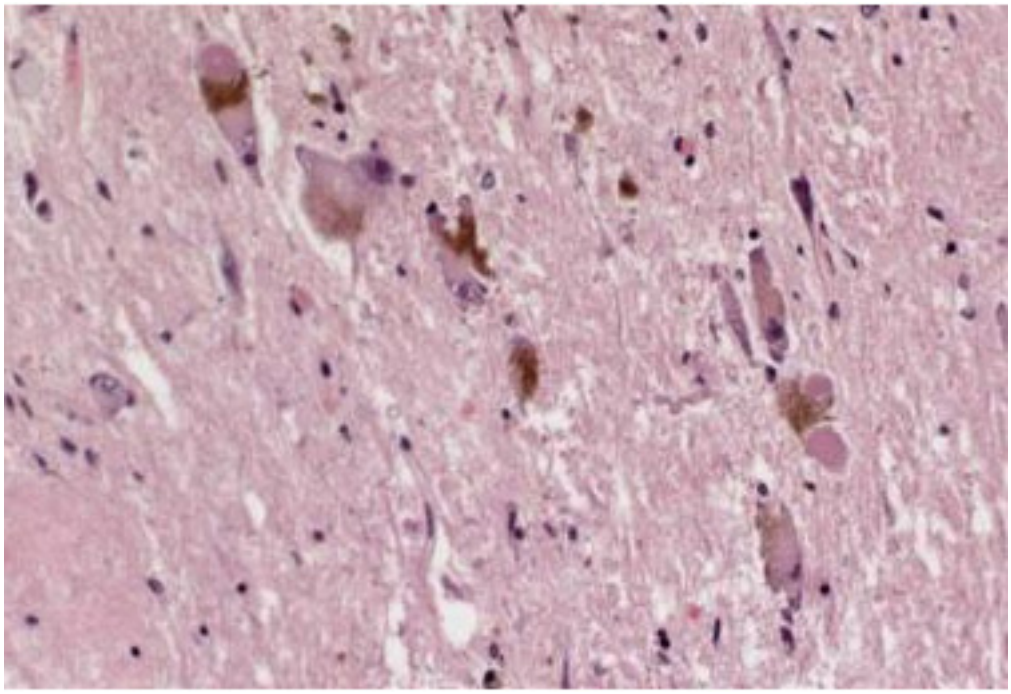
Characteristic pathological findings in Parkinson's disease include neuronal degeneration containing neuromelanin, especially in the substantia nigra and the locus ceruleus. Surviving neurons often have eosinophilic cytoplasmic inclusions, called Lewy bodies (see image below). The primary biochemical defects are the loss of striatal dopamine resulting from the degeneration of dopamine-producing cells in the substantia nigra, as well as cholinergic neuron hyperactivity in the caudate nucleus.

Alpha-synuclein is one of Lewy bodies' main structural components; all Lewy bodies stain for alpha-synuclein, and most stain for ubiquitin. Lewy bodies with peripheral halos and thick cores are compact, eosinophilic, cytoplasmic inclusions. The presence of Lewy bodies within the substantia nigra pigmented neurons is indicative of Parkinson's disease, but not the pathognomonic one. Also found are Lewy bodies in the cortex, nucleus basalis, locus ceruleus, spinal cord intermediolateral column and other areas.

According to the Braak hypothesis, Lewy body pathology in the brain starts in the olfactory bulb and lower brainstem and slowly ascends to affect dopamine neurons in the substantia nigra and ultimately the cerebral cortex (Brakk et al., 2004). Lewy body pathology is also observed in the gut and heart autonomous nerves.

Figure 1. Lewy bodies in the locus coeruleus from a patient with Parkinson disease





Biomarkers

There are currently no proven clinically relevant biomarkers. The α-synuclein cerebrospinal fluid levels may predict cognitive decline, but do not correlate with motor progression (Stewart et al., 2014).

How is the diagnosis made?

Diagnosis of Parkinson's disease is currently based on historical clinical features and examination, and over time, based on dopamine agent reaction and motor fluctuation (Suchowersky et al., 2006). Mild, early illness can be hard to recognize as it usually starts subtly. It is particularly difficult to detect PD in older people because aging can cause similar problems, such as loss of balance, slow movement, muscle stiffness, and stuffy posture.

Motor manifestations of the condition (Table 1) begin asymmetrically, and typically involve a resting tremor, a soft voice (hypophonia), masked facies (initially described as a reduced blink rate), small handwriting (micrography), stiffness (rigidity), slow motion (bradykinesia), shuffling steps and balance difficulties. A classic symptom is a resting tremor, usually affecting one upper limb, although 20 percent of patients do not have it; (Jankovic, 2008) 30 percent may first be trembling at a lower limb, and there may also be a resting lip, jaw, or even tongue shaking. (2012 by Baumann). Tremors of the head and voice are rare, and in such cases one should consider essential tremor in the differential diagnosis (Jankovic, 2008). Of all the main characteristics, bradykinesia has the strongest correlation with dopamine deficiency (Vingerhoets et al 1997).

The diagnosis was formalized using the criteria of the UK Parkinson 's Brain Bank Disease Society (Jankovic, 2008), with diagnostic accuracy of up to 90 percent (Table 2) (Hughes et al., 1999). Patients with PD would live for 20 years or longer, depending on the age at the beginning; the mortality rate is around 1.5 times that of ordinary people of the same age. Death from PD is usually caused by a concurrent unrelated disease, or by the effects of decreased mobility, aspiration, or increased fall with subsequent physical injury.

How do early and late-onset disease differ in presentation?

Patients with early Parkinson's disease are less likely to experience gait disturbance as the symptom presenting, but have more pronounced stiffness and bradykinesia than those with late onset disease (Gomez et al., 1997). In one study, resting tremor presentation occurred in 41 percent of patients with early-onset disease and 63 percent of patients with late-onset disease (Gibb & Lees, 1988), but further studies did not show a consistent difference between early and late-onset Parkinson's disease for tremor onset (Ferguson et al., 2016).

Motor and Non Motor Symptoms

PD is a disease of the motor system. The four main symptoms are tremor (trembling) in the hands, arms, legs, mouth, and face; weakness or rigidity of the limbs and trunk; bradykinesia (slow motion); and postural instability (impaired balance and coordination) (Jankovic, 2008; Ahlskog, 2001).

Parkinson's disease often has a variety of non-motor symptoms; some may precede diagnosis, while others may appear early or late (Table 2) after diagnosis which is made on the basis of motor functions. Table 2 lists the frequencies of early non-motor symptoms that may precede the diagnosis of Parkinson's disease including constipation, rapid eye movement, sleep behavior disorders, depression, and olfactory impairment. Red flags indicating an alternative diagnosis to Parkinson's disease idiopathic, such as another parkinsonian conditions.

The disorder is chronic and progressive but, in the same way, it does not affect everyone. For some patients PD can appear to be progressing faster than in others. Some patients become severely disabled; others experience only minor motor functional disruptions. The motor and non-motor symptoms are listed in detail in Table 2.

Motor (Physical) Symptoms

Tremor. For some patients, tremor is the primary symptom, but it may only be a minor complaint for others, for whom other symptoms may be more troubling. Typically the tremor associated with PD takes the form of a back-and-forth rhythmic motion of the thumb and forefinger at three beats per second. This is sometimes referred to as "pill rolling." Tremor usually begins in a hand, though a foot or jaw may be affected first. When the hand is in repose or the patient is under stress, it is most obvious. In 75 percent of patients, tremor may affect only one part or side of the body, particularly early in the disease; tremor can become more generalized in later stages. Tremor is rarely impaired, and typically disappears during sleep, or improves with deliberate motion.

Although tremor is the most common initial symptom in Parkinson's disease, occurring in about 70 percent of patients, to make the diagnosis it does not need to be present. Tremor is most commonly described as shakiness or nervousness by patients, and usually starts at one upper extremity and may be intermittent at first. Tremor at the upper extremity generally starts in the fingers or thumb but it can also begin in the forearm or wrist. The tremor may spread to the lower ipsilateral extremity or the upper contralateral extremity after several months or years until it is more generalized; but asymmetry is generally retained. Tremor can vary significantly, arising only with stress, anxiety or fatigue. Classically, the Parkinson's disease tremor is a resting tremor (occurring in a resting position with the limb) and disappears with the action or use of the limb, but this is not seen in all patients. The tremor can initially be observed during such activities as eating or reading a newspaper. Though Parkinson's disease is a rare cause of tremor that affects the head or neck, chin, lip or tongue tremors are not uncommon. The amplitude, as with other tremors, increases with stress and resolves during sleep.

Rigidity. Most patients with PD suffer from resistance to motion. A major principle of body movement is that it has an opposing muscle in all muscles. Movements are not only possible because one muscle becomes more active but also because the opposing muscle relaxes. Rigidity comes about when the delicate equilibrium of competing muscles is disrupted in response to signals from the brain. The muscles remain continuously tensed and contracting in such a way as to make the person feel stiff or weak. Rigidity is the increased muscle resistance to passive motion, and it often has a quality of "cogwheeling" (Jankovic, 2008). As the examiner moves a limb, it resists, then in slow, step-like motions it gives way as if it were being driven by a cogwheel (Michigan Parkinson Foundation, 2008).

Bradykinesia. The loss of spontaneous and automatic movement is especially disturbing as it is unpredictable; the patient can move effortlessly at one stage but will require support at the next. This could well be the disease's most impaired and distressing symptom, as the patient is unable to make quick daily movements. Activities that could easily be done before — such as washing or dressing-may take several hours to complete.

Bradykinesia means slow motion. Bradykinesia symptoms are varied, and can be described in different ways by patients. These may include a subjective sense of weakness, with no true weakness on physical examination; loss of dexterity, sometimes described by patients as the "message not reaching the limb;" fatigue; or ache when repeated actions are carried out.

Facial bradykinesia is characterized by decreased blink rate and expression of the face. Speech can become quieter, less pronounced or more monotonous. In more advanced instances, voice is slurred, poorly articulated, and hard to comprehend. Drooling is a rare initial symptom in isolation, but is commonly reported later in the course of the disease (especially at nighttime drooling).

Truncal bradykinesia leads to slowness or difficulty rising from a chair, getting into bed, or walking. If it affects walking, patients can take smaller steps and the cadence of the gait is decreased. Some patients experience a transitory inability to walk, as if their feet were frozen to the ground. This "freezing" is commonly seen in more advanced disease patients; it is more prominent as patients attempt to navigate doorways or narrow areas and may result in patients being trapped behind furniture or unable to easily cross a door threshold.

Bradykinesia may cause weak, effortful handwriting (i.e., micrography) in the upper extremities, and trouble using the hand for fine dexterous tasks such as using a key or kitchen utensils. Unilateral bradykinesia in the lower extremities usually causes the foot to scuff on the ground, as it is not picked up during swinging of the leg. That can also be described as one leg dragging.

Postural instability. Balance and coordination impairment causes patients to lean forward or backward, and fall easily. Patients who lean backward tend to step backward (retropulsion) when pushed from the front or when beginning to walk. There may establish a stooped posture in which the patient's head is bent and the shoulders drooped. Walking may be impacted as the disease progresses. Patients may stop in mid-stride and "freeze" in place, possibly even overturn, or they may walk with a series of fast, tiny steps as if they were hurrying to maintain balance (festination).

Dystonia

Dystonia is a common initial symptom of young-onset Parkinson's disease, described as the onset of symptoms before age 40. In Parkinson's disease, dystonia usually consists of a foot involuntary turning in (inversion) or down (plantar flexion), often associated with cramping or leg pain. The big toe may also get dorsiflexion. Another common dystonia in Parkinson's disease is arm and elbow adduction which causes the hand to rest in front of the abdomen or chest. Dystonic postures can wax and wane, with tiredness or exertion.

It is debatable whether stooped posture is due to truncal dystonia. One study suggests that the stooped posture may be due to vertebral fractures resulting from vitamin D deficiency with compensatory hyperparathyroidism (Sato et al . , 2011). Supplementation with vitamin D may reduce the risk of stooped postures.

Non-Motor Symptoms

Many symptoms can be treated with medicine or physical therapy that is necessary. No one can predict what symptoms an individual patient may encounter, and the severity of the symptoms often varies among patients. None of these symptoms are fatal but affect life quality (Jankovic, 2008).

Emotional changes. Some people with PD get anxious and insecure. Maybe they don't want to travel or socialise. Some are losing their motivation and becoming apathetic and dependent on family. Others can become pessimistic or uncharacteristically irritable. Loss of memory and slow thinking may occur, but the ability to reason remains intact. Whether people are actually suffering from intellectual loss or PD dementia is still a controversial area under study.

Dysphagia. In later stages of the disease, muscles used for swallowing can function less efficiently. Food and saliva may accumulate in the mouth and at the back of the throat, which may cause choking or drooling. Drugs such as levodopa and apomorphine can frequently alleviate these problems.

Dysarthria. About 50 per cent of all patients with PD have speech problems. They can speak too tenderly or in a monotonous voice, hesitate to talk, slur or repeat their words, or talk too quickly. A speech therapist can ease some of these problems.

Urinary problems or constipation. Bladder and bowel problems in some patients can be caused by improper functioning of the autonomic nervous system, which regulates smooth muscle activity, and adverse drug effects. Some patients may become incontinent while others may have difficulty urinating. Constipation may occur because the gastrointestinal (GI) tract functions more slowly; inactivity, consuming a bad diet, or drinking too little fluid may also cause this. It can be chronic, and may be severe enough to require hospitalization in exceptional cases. Patients should not allow constipation to last for more than a couple of days before taking measures to relieve it.

Skin problems. It is normal for the skin of the patient to become oily, especially on the front and on the nose sides. The scalp can get oily too, contributing to dandruff. The skin may in other cases become very dry. Such problems are the result of an adaptive nervous system that is not functioning properly. It could be helped with standard dermatological treatments. Excessive sweating, which is also normal, is typically controllable with PD medications.

Fragmented sleep. Problems with sleep include difficulty staying asleep at night, restless sleep, nightmares and daytime drowsiness. Whether these symptoms are linked to PD or the drugs used for treating PD is uncertain. Patients can never take the sleep aids over-the-counter without consulting a doctor.

Thinking. Bradyphrenia can occur, or a slowing of the ability to think (Hirsch, 2008). Just as it takes more time to step up from a chair, it may take more time for patients to reply intelligently. Information processing takes longer, and this can lead to disappointment for patients and carers alike. Bradyphrenia may be misinterpreted as deliberate behavior, lack of interest, or even stubbornness, but it is vital to understand that the condition is triggered by changes in the brain.

Pressing on an adult who has cognitive issues causes tension and typically makes matters worse. Patients may find it hard to think about other ways of doing things or move from one subject to another. These alterations in cognition may be mistaken as intentional, and may label the individual as rigid or inflexible. A portion of the brain involved in this sort of thinking may be affected in some patients.

Language. Substantial changes in language are uncommon in PD but subtle changes can occur. Talking also is slower, and it eliminates spontaneous expression. Patients cannot participate in conversation as much as they do, if at all. Such adjustments can be misinterpreted as being insensitive and lead to poor communication.

Cognitive Changes and Dementia. Some PD-patients shift their mood and cognitive abilities. The most common improvements include the slow thought and information processing. There may be a reduction in the capacity to produce new ways of solving problems. While memory changes are less frequent, some people with PD forget where and when they got the information but remember the information itself. In certain cases, dementia occurs, and age progression is a risk factor. In these patients depression is often under-diagnosed. Regardless of the type of cognitive changes encountered, if symptoms are to be handled accurate assessment is important.

Alterations may occur in one's ability to think, reason, and remember, and several factors may contribute to these differences (Hirsch, 2008). Cognitive changes can affect the everyday lives of patients just as much as, and sometimes more, than the physical (motor) effects of PD (Marsh, 2008). Although the importance of addressing cognitive and other non-motor symptoms is increasingly recognized by physicians, many still focus primarily on treating physical symptoms and cognitive changes may remain undertreated or untreated. An objective evaluation of cognitive changes is required to develop a suitable plan for care.

A small number of patients may experience severe and drastic changes in memory, reasoning ability, language, and attention (Marsh, 2008, Galvin, 2006). As people age, there is an increased risk of a progressive decline in their ability to think and remember. When dementia occurs, patients require better treatment and supervision.

Depression. Depression is an additional potential cause of cognitive changes in PD patients, and is more severe in these patients than in the general population; within one year of the onset of PD symptoms, 25 percent of PD patients experience depression (Hirsch, 2008). Depressive condition progression is unlikely to be due to problems adapting to the disorder on its own. Some PD symptoms are similar to depression symptoms (e.g., lack of interest in activities, exhaustion, weight shift and social withdrawal). This similarity will lead to depression in those with PD being undertreated. In addition, patients may not even acknowledge being depressed. On a more optimistic note, depression can be managed and controlled by combining antidepressant medications with cognitive-behavioral therapy. Depression can have serious negative consequences if left untreated, interfering with cognition and, consequently, quality of life.

Adverse Drug Reactions

There are several forms of treatment available for managing PD symptoms. Managing PD symptoms, however, is becoming more complicated as the disease progresses. Developing adverse effects and improvements in the steady reaction to medications present various problems for patients, their families and health care providers. Alterations in cognitive ability can unfortunately be a potential side effect of all drugs used to treat PD. Hence, patients need to know which side effects are associated with the drugs they take. If there is a cognitive decline a health care provider should be immediately notified.

Natural history and prognosis

Treatments currently available are symptomatic and don't stop neurodegeneration. Although pharmacological therapy provides good symptom control in the initial stages of the disease, some levodopa-resistant symptoms (such as falls and freezing, dysarthria, dysphagia and choking, dementia, hallucinations, daytime sleepiness and urinary incontinence) appear in the later stages of the disease, leading to increased disability in advanced PD. Additionally, complications associated with pharmacological treatment add additional difficulties in managing the advanced PD stages.

Parkinson's disease caused serious impairment or death in 25 percent of patients within 5 years of diagnosis, 65 percent within 10 years, and 89 percent within 15 years before levodopa was introduced. Parkinson's disease mortality rate was 3-fold that of the general population balanced for age, sex, and ethnic origin. The mortality rate decreased by approximately 50 percent with the introduction of levodopa, and longevity was extended by many years. It is believed to be attributed to the symptomatic effects of levodopa, since there is no strong evidence to indicate that levodopa impedes the disease's progressive development (Frank et al., 2006; Thobois et al., 2005).

Parkinson's disease patients experience gradual loss in motor and cognitive function and increased mortality. Risk factors for a faster decrease in motor function include older age at diagnosis, and prominent bradykinesia and diagnostic rigidity. Prominent diagnostic tremor can predict slower progression of the disease (Suchowersky And et al., 2006). Dementia incidence increases with Parkinson's disease patient age and duration, with 60 per cent of patients having the disease developing dementia within 12 years of diagnosis (Buter et al., 2008). In a Dutch longitudinal cohort of 6,969 men and women, the relative mortality rate was 1.8 (de Lau et al., 2005). In a community-based cohort in Norway, men with Parkinson's disease at age 70 had eight years of median life expectancy, and women with Parkinson's disease at age 70 had 11 years of median life expectancy (Buter et al., 2008).

For Parkinson's disease, life expectancy declines (odds ratio 2.56, i.e. mortality risk is 2.56 times greater than comparable age-groups without Parkinson's disease), and medical therapies do not tend to change mortality or postpone the onset of non-motor symptoms) Clarke, 2010). Although progression is slower in early-onset disease patients and there is longer absolute survival, this occurs at the expense of increased years of loss of life (11 years lost in early-onset disease v. 4 years in late-onset illness). (Ferguson and others, 2016). Late-onset Parkinson's disease is associated with quicker development of the disorder and cognitive impairment (Reid et al , 2011), which could be due to a lack of cell death compensatory strategies (Ferguson et al, 2016). Long-term outcome data are lacking in the older population (Logroscino, 2016).

The American Academy of Neurology states that the following clinical characteristics can help predict the risk of Parkinson's disease progression (Suchowersky et al., 2006):

• Older age at onset and initial rigidity/hypokinesia can be used to predict (1) a more rapid rate of motor progression in those with newly diagnosed Parkinson disease and (2) earlier development of cognitive decline and dementia; however, initially presenting with tremor may predict a more benign disease course and longer therapeutic benefit from levodopa
• A faster rate of motor progression may also be predicted if the patient is male, has associated comorbidities, and has postural instability/gait difficulty (PIGD)
• Older age at onset, dementia, and decreased responsiveness to dopaminergic therapy may predict earlier nursing home placement and decreased survival

Conclusion

Parkinsonism and PD are frequent in older patients. In the differential diagnosis of patients who have falls. Family physicians should consider parkinsonism, when symptoms show general functional decline. Functional declines are normal among older vulnerable patients. The functional deterioration differential diagnosis is broad and involves side effects of the drug, congestive heart failure, unrecognized dementia or depression, and other common and uncommon diseases.

Parkinson's disease (PD) and parkinsonism sometimes have an unspecific history, and experienced physicians may initially miss the PD's physical characteristics unless considered in the differential diagnosis. Idiopathic PD is the most common form of parkinsonism but recognizing other causes of parkinsonism is important for family physicians. This paper aims to examine the diagnostically relevant features of PD and to explain certain causes of parkinsonism.

PD is associated with an increased risk of death from all causes and a reduction in life expectancy and serious disability. In the advanced phase of the disease, the majority of patients lose autonomy; levodopa-resistant symptoms are the most accurate predictors of nursing home placement and mortality.

Table. 1 Criteria of the UK Parkinson's Disease Society Brain Bank for diagnosing Parkinson disease

Bradykinesia and at least one of the following:

- **Rigidity**
- **Resting tremor (4–6 Hz)**
- **Postural instability not caused by primary visual, vestibular, cerebellar or proprioceptive dysfunction**

Exclusion of other causes of parkinsonism

At least three of the following supportive (prospective) features:

- Unilateral onset
- Persistent asymmetry primarily affecting the side of onset
- Resting tremor (hand, leg or jaw; low frequency (4–5 Hz), asymmetric, disappears with action)
- Excellent response to levodopa (70%–100%)
- Progressive disorder
- Severe levodopa-induced chorea (dyskinesias)
- Levodopa response for five years or more
- Clinical course of 10 years or more

Early motor features	Early non-motor features (may precede the diagnosis)	Late features (usually develop 5-10 years after disease onset)	Late non-motor features
• Difficulty turning in bed • Frozen shoulder • Stiffness, numbness or pain in limb • Micrographia • Difficulty with fine finger movements (bradykinesia) • Tremor of hand, jaw, foot • Decreased facial expression • Decreased arm swing, dragging a leg • Soft voice ("Do people ask you to repeat yourself over the phone?")	• Constipation (30%) • REM sleep behavior disorder (50%, often preceding the diagnosis by median of 14 years) • Depression occurs with a prevalence of 35% in Parkinson disease, and 10%-15% will have depression at the time of diagnosis • Olfaction impairment (most consistent non-motor feature predicting Parkinson disease); up to 97% of patients	• Motor fluctuations • Dyskinesia (complication of dopaminergic treatment, more so with levodopa); typically choreiform, involving the neck, head, limbs and trunk • Gait freezing • Falls	• Dysphagia (50% at 15 years) neuropsychiatric symptoms (50% at 15 years), including hallucinations, sleep disturbance and dementia • Autonomic disturbances (70%-80%), including sweating, orthostasis, sialorrhea and urinary dysfunction • Seborrheic dermatitis (usually involving the forehead, with flaky oily skin)

Note: HR = hazard ratio REM = rapid eye movement.
The risk of synucleinopathy (i.e., Parkinson disease, multiple system atrophy, Lewy body dementia) in patients with REM sleep behavior disorder was reported to be 30% at 3 years, rising to 66% at 7.5 years. Advanced age (HR 1.07), olfactory loss (HR 2.8), abnormal colour vision (HR 3.1), subtle motor dysfunction (HR 3.9) and nonuse of antidepressants (HR 3.5) identified higher risk of disease conversion.

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Haemoperitoneum in undiagnosed fundal placenta percreta in a third trimester pregnancy presented in labor: A case report

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Nansi Dari Alfayez et al. Haemoperitoneum in undiagnosed fundal placenta percreta in a third trimester pregnancy presented in labor : A case report. World Family Medicine. 2020; 18(7): 70-75
DOI: 10.5742MEWFM.2020.93837

Abstract

Fundal placenta with abnormal invasion is relatively rare.

Most of fundal placenta with abnormal invasion is difficult to be diagnosed in the antenatal period, and is mostly diagnosed in the postpartum period .

Risk of uterine rupture in fundal placenta with abnormal invasion is one of the most dangerous complications which can lead to hemorrhagic shock and subsequently leads to death.

We report a 32 year old woman who presented to our obstetric emergency room; she was G2p1 by caeserian section due to fetal distress, secondary infertility of 9 years , spontaneous pregnancy, complaining of abdominal pain and with a history of vaginal spotting at 34 weeks gestation.

During caeserian section haemoperitoneum was noticed.

After exploration fundal placenta percreta with omental band adhesion attached to the placental site was found.

Key words: Case report, Haemoperitoneum, fundal placenta percreta,

Introduction

Fundal placenta with abnormal invasion is invasion of placental villi into the myometrium due to defective decidua basalis (1).

Placenta percreta is considered to be a severe degree of the abnormal placentation, where the placenta invades the full thickness of the uterine wall to reach the covering serosa (2).

Little is known about the exact incidence, and risk factors. Even when the case is highly suspected, no clear guidelines exist concerning the best modality of prenatal management or timing and route of delivery (3,4,5).

Risk factors for myometrial defect are: previous scars such as ceserian section, myomectomy, dilation and curettage, perforation, advanced maternal age more than 35 years, high parity and previous Asherman syndrome and usually high levels of alpha fetoproteins.(6)

One of the most serious and dangerous complication of fundal placenta percreta is ruptured uterus which might end with significant fetal and maternal mortality.

In the antenatal clinic it is difficult to detect elements of invasion in fundal placenta.

High risk groups mentioned earlier have a high suspicion of low lying placenta (previae).

In non previae, fundal placenta with myometrial invasion is mostly diagnosed in the postpartum period after placental removal or retained placenta presented as bleeding.

Fundal placenta with invasion patients may present in signs of shock as did our patient due to bleeding from the placental site causing haemoperitoneum.

Uterine rupture in placenta with abnormal invasion is a serious and life threatening condition which needs urgent intervention and proper management.

The definite diagnosis is based on histopathological study of uterine rupture site and confirmation of the absence of the placenta basal plate and the presence of trophoblastic tissues in the myometrium and the uterine serosa (7).

Case report

A 32 year old female patient G2p1 by caeserian section due to fetal distress, secondary infertility nine years, spontaneous pregnancy.

She is 34 weeks gestation with regular follow up in the clinic, smooth pregnancy course.

Examined during antenatal care in her last visit one week prior to presentation in the clinic .

The fetus was breech, placental site was fundal, measurement goes with 33 weeks and the liquor was adequate.

Our patient presented to our obstetric emergency room with abdominal pain and vaginal bleeding.

On examination patient looks pale and in pain.

The vital signs :
Bp :90\60,pr:110\minute ,tem:37c.

There was generalized abdominal tenderness, rigid.

Bed side ultrasound showed fetus was breech, viable, placenta fundal, measurement went with 34 weeks gestation .

Two intravenous lines were secured.

Blood samples (CBC, PT, INR, kidney function test) taken and sent for laboratory test.

Intravenous fluids started.

Foleys catheter inserted.

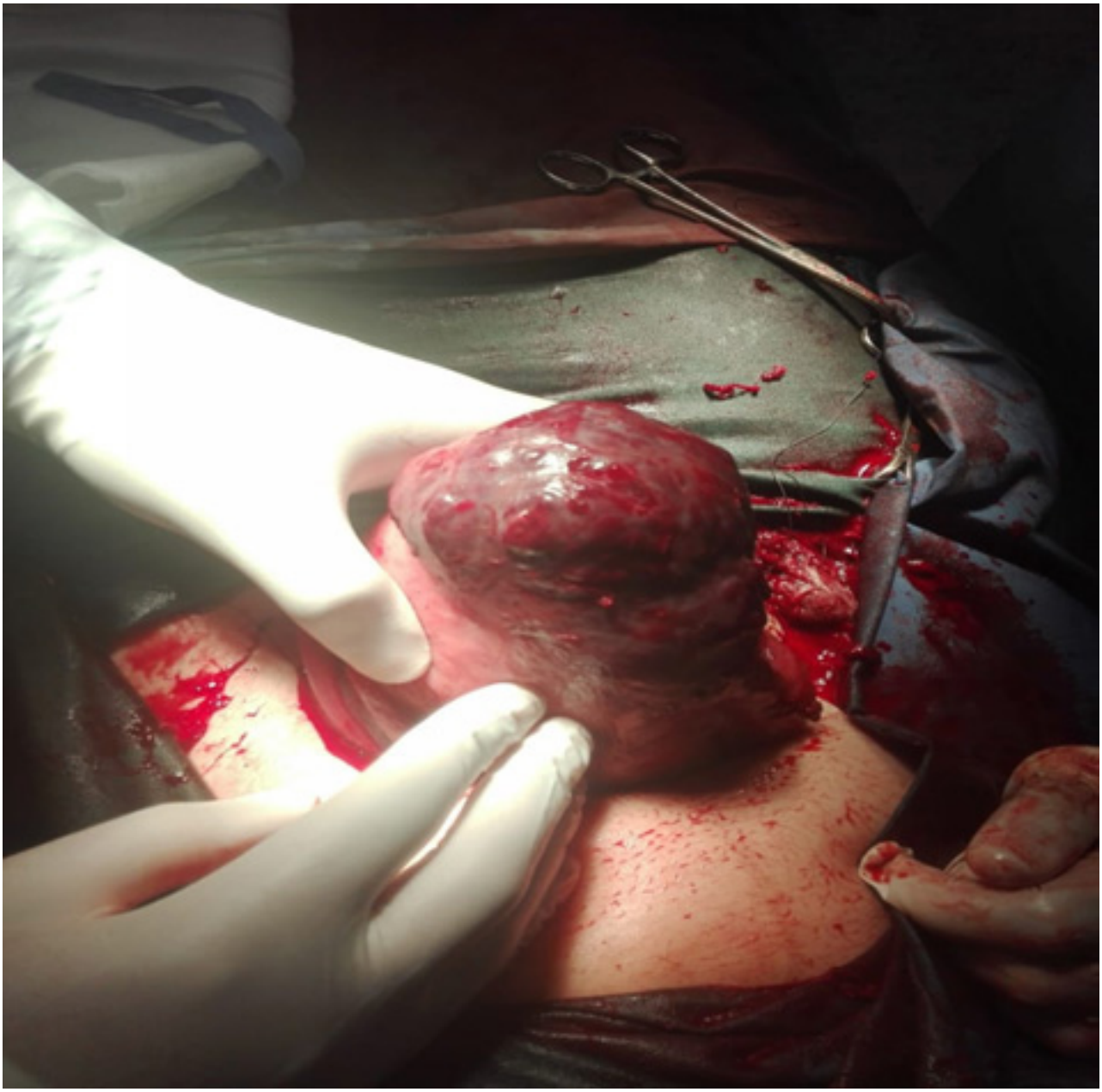
Lab test was :
Hb : 8g\dl., plt : 220, wbcs: 8000.
Creatinine :6.

After rapid assessment we took a decision for urgent caeserian section.

Packed red blood cells and fresh frozen plasma was prepared.
During caeserian section abdominal wall opened in layers smoothly, when peritoneum was incised, the peritoneal cavity was full of blood, around 1000cc blood suctioned and clots removed.

Intra operation we noticed a 5-6cm of placenta protruding from the fundus extended through the serosa and had omental band adherent on placental site seen in Picture 1.

Omental band was ligated and cut by ligasure.



Picture 1:
The uterus was opened in lower uterine segment transverse incision.

Delivered male alive, breech extraction, Apgar score 8\10, fetal weight 1800gm .

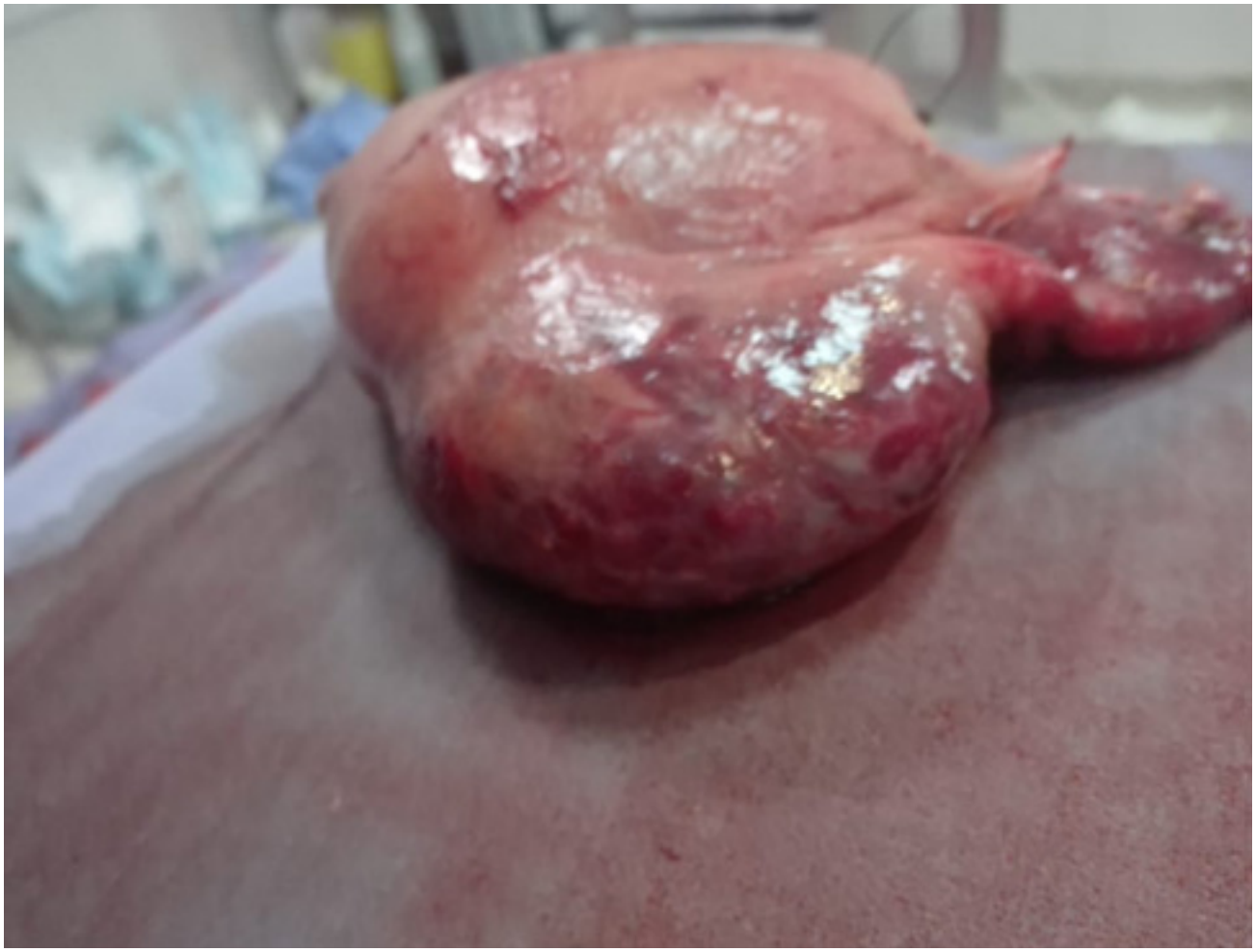
Placenta percreta protruding from the fundus with omental band adherent to the site of placenta.

There was active bleeding from the placental site fundally which was adherent to the myometrium, invading the serosa and protruding as a vascular mass measuring around 5-6 cm, ruptured, causing hemoperitoneum.

Vital signs:
Bp: 60\30, pr: 140\minute .

Decision of hysterectomy to secure hemostasis and life saving for our patient.

The uterus was sent for histopathology (as seen in picture 2).



Picture 2:
Patient received seven units of packed red blood cells, seven units of fresh frozen plazma.

Haemostasis secured .

One drain in the abdomen inserted.

Abdominal walls closed in layers.

Vital signs :
Bp: 120\80, pr: 90\minute.

Urine output was 400cc during the time of surgery which took one hour duration.

Anesthetic recovery was smooth.

Patient then sent to intensive care unit for close monitoring.

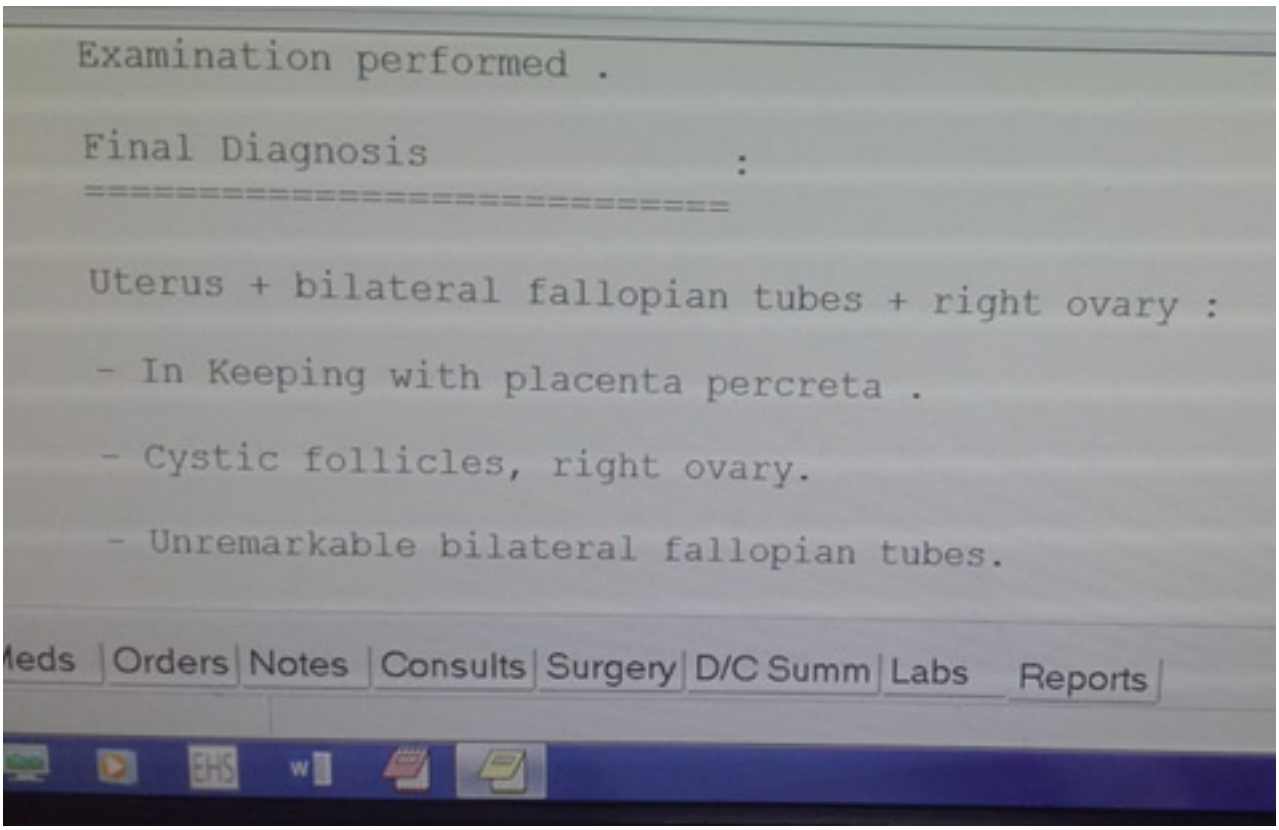
On second day of the operation the patient was transferred to the ward.

The drain was removed in the second day of the operation.

On the fourth day of the operation she was discharged in a good general condition.

Her lab test :
Hb: 11, plts: 187.pt :17, inr : 1.2, creatinine: 8.
Her baby was discharged one week later.

Histopathology result confirmed the diagnosis of placenta percreta as seen in Picture 3.



Picture 3

Discussion

Placenta percreta is rare but is a severe type with major and catastrophic complications.

Placenta accreta occurs approximately in 1 out of 7,000 pregnancies (7). About 75%-80% are placenta accreta, 17% are increta and the remaining are percreta (1%) (8). The abnormal invasion of trophoblast to the myometrium is due to an absence or deficiency of Nitabuchs layer or the spongious layer of the decidua (2).

As we mentioned before, little is known about risk factors of fundal placenta percreta but some risk factors such as advanced maternal age (more than 35 years), previous placenta previae, previous uterine injury, previous caesarean section, myomectomy, manual removal of placenta, hysteroscopy, termination of pregnancy, endometritis, repetitive abortions and uterine malformations(9) can be recognized as risk factors.

Unfortunately most of fundal placenta percreta are not diagnosed prenatally and encountered in the postpartum period as retained placenta and hemorrhage at attempts of manual removal (10).

Conclusion

Fundal placenta with abnormal invasion is rarely diagnosed antenatally.

Most of them are diagnosed in the postpartum period.

They carry risk of haemorrhage and are life threatening.

Little is known about the exact incidence or risk factors.

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Post-stroke Delirium: Meta-analysis of Frequency

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Received: May 2020; Accepted: June 2020; Published: July 1, 2020.
Citation: Saleha Al-Jadidi et al. Post-stroke Delirium: Meta-analysis of Frequency. World Family Medicine. 2020; 18(7): 76-84 DOI: 10.5742MEWFM.2020.93838

Abstract

Objective: To determine the frequency of post-stroke delirium by systematically reviewing original research on this topic.

Methods: MEDLINE, EMBASE, PsychINFO and the Cochrane Database of Systematic Reviews were searched for potentially relevant articles published from 1967 to March, 2014. The bibliographies of relevant articles were searched for additional references. Twelve studies met the inclusion criteria. The validity of included studies was assessed according to criteria derived from Barker et al (Barker et al, 1998). Information about diagnostic criteria for delirium,, diagnostic instruments, length and frequency of screening, population (eligible, enrolled and completed screening), age, gender, time to entering study following stroke, stroke type and location, presence of dementia and medical co morbidity, psycho-active drug use and number of patients with delirium was systematically abstracted, tabulated and synthesized according to the MOOSE guidelines for reporting of meta-analyses.

Results: There was significant heterogeneity in results of the studies of frequency of post-stroke delirium. The proportions ranged from 10% to 48%. The summary proportion was 0.24 (95% CI 0.18, 0.32). The frequency of post-stroke delirium may be related to medical co-morbidity or psycho-active drug use.

Conclusion: Post-stroke delirium may be frequent. Because of significant heterogeneity in the results of studies of frequency, the result of this review must be interpreted cautiously.

Key words: Delirium, post-stroke, incidence, prevalence, confusion

Introduction

Delirium is a neurocognitive disorder characterized by acute onset, fluctuating course and disturbances in consciousness, orientation, memory, thought, perception and behavior (DSMIV-TR). Delirium in older patients has been associated with significant increases in cognitive impairment and functional disability, length of hospital stay, institutionalization and death (Cole/93, Witlox/10).

Delirium may be frequent following stroke but reported rates vary widely. Because knowledge of the frequency of post-stroke delirium may inform decisions to develop special interventions for this disorder and because there are no systematic reviews of frequency, the objective of this study was to determine the frequency of post-stroke delirium by systematically reviewing original research on this topic. The review process, guided by the proposals of the MOOSE group for reporting of meta-analyses of observational studies, involved systematic selection of articles, abstraction of data, assessment of study validity and qualitative and quantitative synthesis of results.

Methods

Selection of articles

The selection process involved four steps. First, 4 computer databases, MEDLINE, EMBASE, PsychINFO and the Cochrane Database of Systematic Reviews were searched for potentially relevant articles published from 1967 to March 2014 using the keywords “poststroke” and “delirium” or “confusion” and “incidence” or “prevalence”. Second, relevant articles (based on independent review of the title and abstract by authors were retrieved for more detailed evaluation. Third, the bibliographies of relevant articles were searched for additional references. Finally, all relevant articles were independently screened by authors to meet the following inclusion criteria: (1) original prospective cohort study; (2) published in English; (3) used acceptable criteria for the diagnosis of delirium and (4); included information about the incidence or prevalence of post-stroke delirium. The final set of included articles was determined by consensus of authors.

Abstraction of data

Information about the study site, inclusion and exclusion criteria, diagnostic criteria for delirium,, diagnostic instruments, length and frequency of screening, population (eligible, enrolled and completed screening), age, gender, time to entering a study following stroke, stroke type and location, presence of dementia and medical comorbidity, psycho-active drug use and number of patients with delirium. Data was abstracted independently by both authors and the data included in the review was determined by consensus.

Assessment of validity

To determine validity, the methods of each study were assessed according to criteria derived from Barker et al (Barker et al, 1998): appropriate population, systemic sample, enrolment rate >75%, use of a reliable and valid diagnostic instrument (Table1). Each study was scored independently by authors with respect to meeting (+) or not meeting (-) each of the criteria. The results of the validity assessment were determined by consensus.

Data synthesis:

Qualitative: All abstracted information was tabulated. A qualitative meta-analysis was conducted by summarizing, contrasting and comparing abstracting data.

Quantitative: For each of the selected studies, the overall incidence of post-stroke delirium was verified or computed if necessary. Incidences for multiple studies were pooled in a binomial meta-analysis (5, 6). We tested study homogeneity and depending on whether homogeneity was accepted or rejected; we used the fixed or the random effect model for meta-analysis in order to calculate an overall incidence and it is 95% CI. We used the Q statistics to test between study homogeneity: homogeneity was rejected when the Q statistic p-value was less than 0.10. The meta-analysis was conducted using the R 3.1 software (7).

Results

Selection of articles:

The search strategy yielded 280 potentially relevant studies; 32 were retrieved for more detailed evaluation; 9 met the inclusion criteria (Sheng et al , 2006, Dostovic et al , 2009, McManus et al , 2009, Dahl et al , 2010, Oldenbeuving et al , 2011, Mitasova et al , 2012, Lees et al, 2013, Naidech et al , 2013, Miu et al , 2013). Twenty three studies were excluded; 6 were clinical reviews, one was a duplicate publication and sixteen did not meet one or more of the inclusion criteria. A search of the bibliographies of relevant studies yielded three additional studies that met the inclusion criteria (Gustafson et al, 1991, Gustafson et al 1993, Caeiro et al , 2004).

Assessment of validity:

All 12 studies had an appropriate population with systematic sample. In six studies, the enrolment rate was greater than 75%. Nine studies used a reliable and valid instrument to diagnose delirium

Data synthesis:

Qualitative analysis: All studies did not report on all the variables of interest (Table 3). The 12 studies were conducted in Europe (n=10), North America (n=1) or China (n=1) and, for the most part, enrolled patients admitted to university stroke units. Sample size ranged from 82 to 535 patients. Mean age ranged from 24 to 101 years. The proportion of men ranged from 46% to 63%. The length of screening ranged from 1 to 28 days and frequency of screening ranged from once during the admission to twice per day. Eight studies included patients with both intracerebral hemorrhage and cerebral infarction; two included only patients with cerebral infarction; one included only those with intracerebral hemorrhage and one study did not report the type of stroke. Eleven studies reported stroke type and location. The number of included

patients with dementia ranged from 8 to 25; two studies reported that 78 patients had cognitive decline. Nine studies reported medical co-morbidities. Four studies reported concurrent psycho-active drug use. Diagnostic instruments included the CAM (n=5), CAM –ICU (n=2), Organic Brain Syndrome Scale (n=2), Delirium Rating Scale (DRS, n=3) and DRS R-98 (n=1). Delirium was diagnosed using different versions of DSM criteria: seven studies used DSM III R; two used DSM IV; two used DSM IV R; one used both DSM IIIR and DSM IV criteria.

The frequencies of delirium varied from 10% to 48%, median 26%. Variation in reported rates could not be explained by most of the above variables. Medical comorbidity and psycho-active drug use, however, may explain some of the variation: study populations with reported high medical comorbidity and psycho-active use appeared to have higher frequencies of post-stroke delirium.

Quantitative analysis

The results of the quantitative analysis are presented in Figure 2. The Q statistic P value was <0.0001, indicating heterogeneity in reported rates of post-stroke delirium. The summary proportion with post-stroke delirium was 0.24 (95% CI 0.18, 0.32).

The frequency of post-stroke delirium may be related to medical co-morbidities and psycho-active drug use in studies that reported co-morbidities and drug use, but the timing of co-morbidity and drug use in relation to the onset of delirium is not clear.

Thus, it is unclear whether the stroke alone was the putative cause of delirium or whether delirium was due to complications of stroke (e.g. aspiration pneumonia, dehydration), other medical conditions or psycho-active drug use. Notably, there was no indication that specific diagnostic criteria, specific diagnostic instruments, greater frequency of screening or longer periods of screening identified more patients with delirium.

This review has five strengths. First, we conducted a systematic search of the literature. Second, only prospective studies were included. Third, the validity of included studies was systematically assessed. Fourth, there was a qualitative and quantitative synthesis of data and examination of study variables to try to account for variability in the study results. Finally, 3 phases of the review process (literature search, assessment of validity, data abstraction,) were conducted independently by authors who met to determine consensus.

This review has three potential limitations. First, the literature search was limited to articles published in English because we did not have the resources to translate articles written in other languages. Second, included studies did not report on all variables of interest. Third, there was significant heterogeneity in the results of the studies; it is arguable that such heterogeneity should have precluded the combining of the results of the studies.

Table 1: Estimated Incidence and weight of individual studies

				Weight of individual studies	
		proportion	95%-CI	%W(fixed)	%W(random)
1	Gustafson et al, 1991a	0.476	[0.3924; 0.5604]	10.03	8.54
2	Gustafson et al, 1991b	0.422	[0.3140; 0.5351]	5.61	8.22
3	Caeiro et al, 2004	0.133	[0.0909; 0.1854]	6.97	8.36
4	Sheng et al, 2006	0.250	[0.1842; 0.3255]	8.11	8.44
5	Dostovic et al, 2009	0.253	[0.1987; 0.3141]	12.22	8.62
6	McManus et al, 2009	0.281	[0.1868; 0.3906]	4.59	8.06
7	Dahl et al, 2010	0.101	[0.0610; 0.1551]	4.49	8.04
8	Oldenbeuving et al, 2011	0.116	[0.0900; 0.1461]	15.2	8.69
9	Mitasova et al, 2012	0.426	[0.3397; 0.5164]	8.75	8.48
10	Lees et al, 2013	0.108	[0.0571; 0.1812]	2.97	7.63
11	Naidech et al, 2013	0.316	[0.2261; 0.4180]	5.88	8.25
12	Miu et al, 2013	0.364	[0.3029; 0.4293]	15.16	8.69

Table 2: Meta Analysis summary: Incidence of Post Stroke Delirium

		Fixed effects model		Random effects model			
Effect	No. of studies	proportion	95% CI	proportion	95% CI	% of variation across studies I^2	Test of heterogeneity (Q^2) p-value
Overall effect	12	0.260	[0.2403; 0.2799]	0.249	[0.1784; 0.3366]	93.9%	< 0.0001

Figure 1: Selection of articles included in the meta-analysis

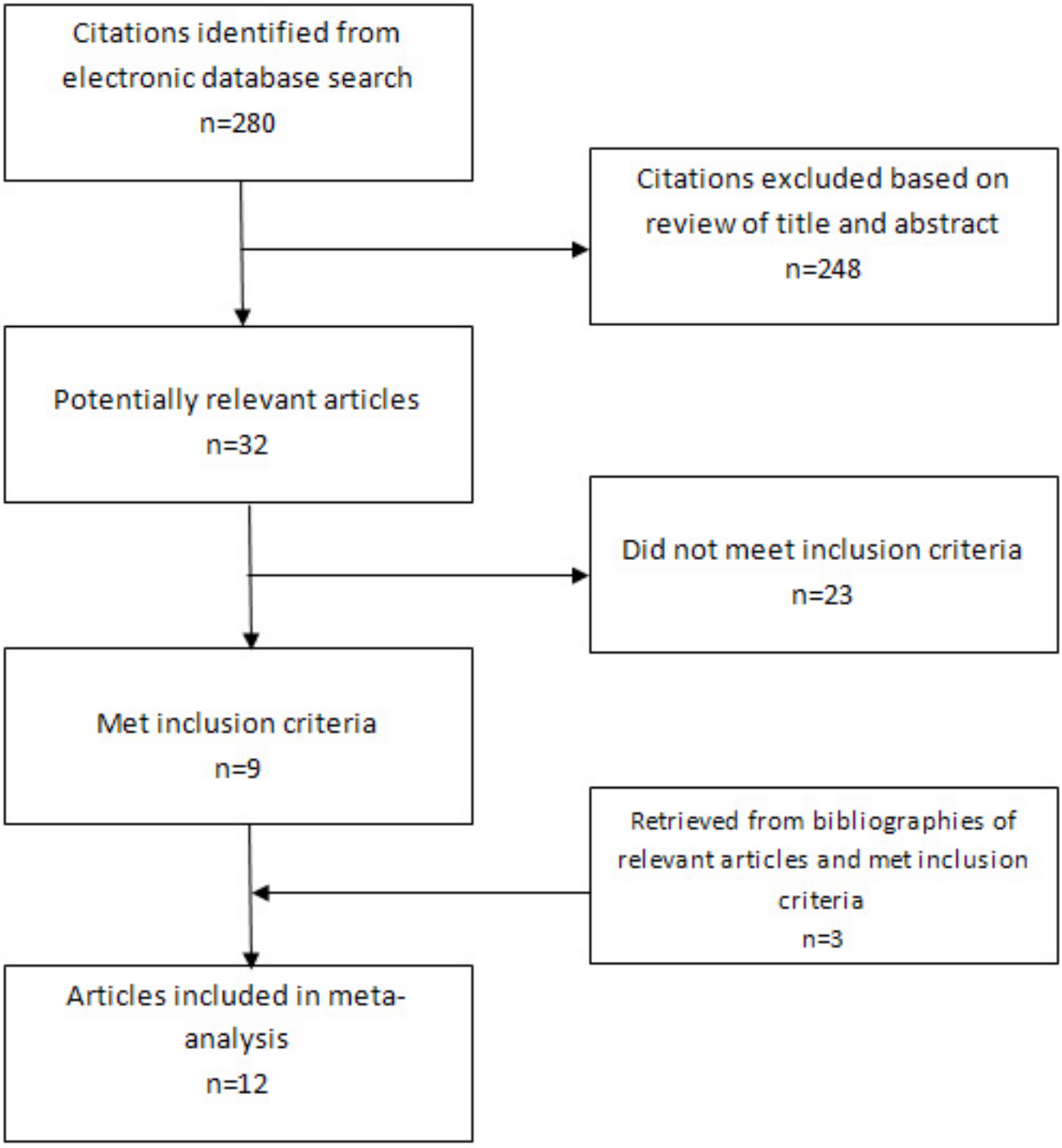

Figure 2: Forest plot of the incidence of post-stroke delirium

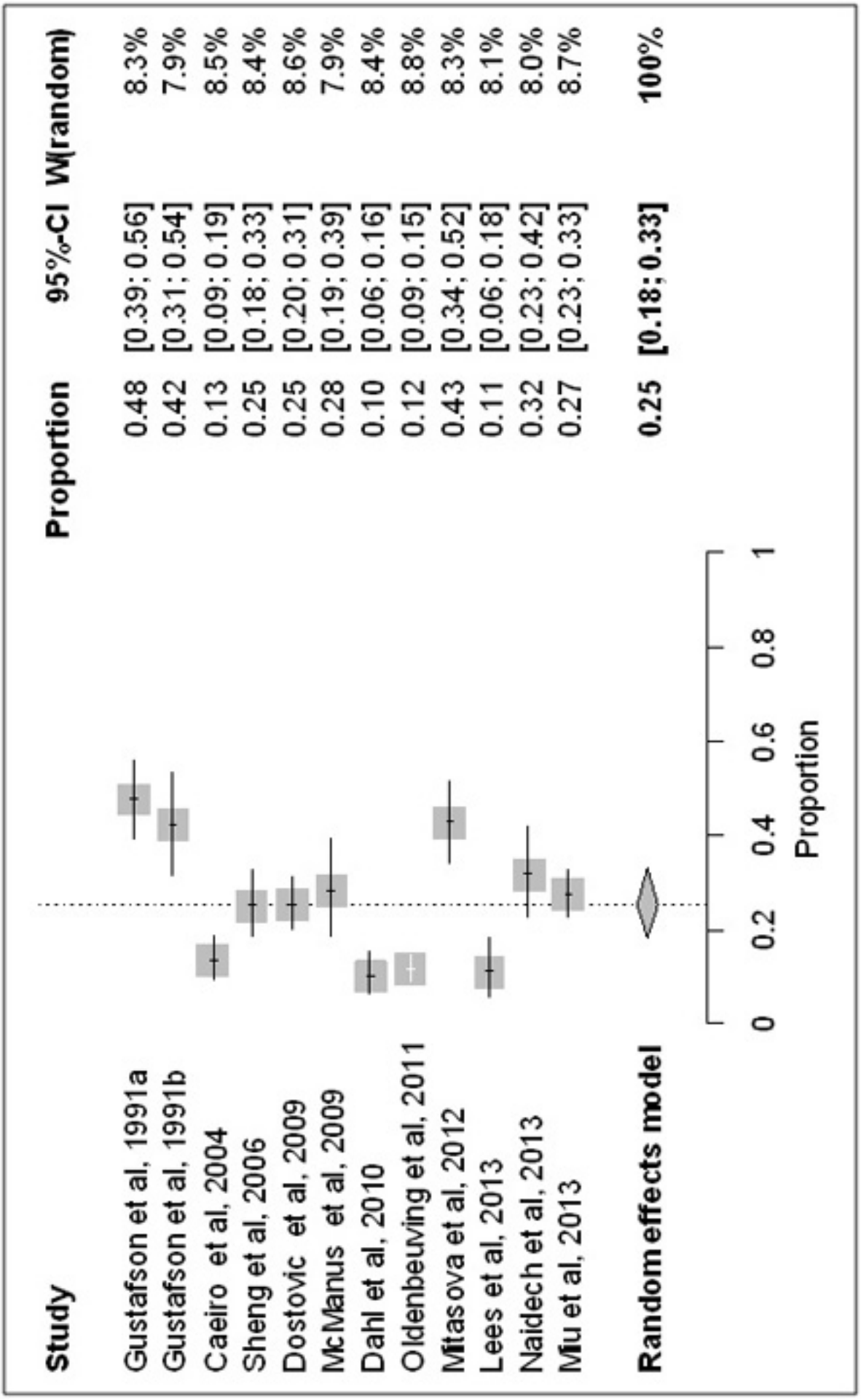

Table 3a: Studies of the Frequency of Post Stroke Delirium

Author /Year	Country	Inclusion Criteria	Exclusion Criteria	Diagnostic Criteria for delirium	Diagnostic Instruments	Frequency of screening	Length of screening (days)
Gustafson et al, 1991	Sweden	IH CI Stroke less than 1 wk prior to	SH Meningitis	DSM III R	OBSS Interview with family and staff	At least twice	7
Gustafson et al, 1991	Sweden	CI	Coma Stupor Fever Renal failure Pituitary insufficiency	DSM III R DRS>10	OBSS Interview	At least once	7
Caeiro et al, 2004	Portugal	IH CI SH	GCS <3	DSM IV TR	DRS	Once	1-4
Sheng et al, 2006	England	IH CI Aged 65+	SH TIA History of severe head injury Cerebral sinus thrombosis Neurosurgery before stroke Stroke due to tumor	DSM IV R		Once on 3rd day of admission	3
Dostovic et al, 2009	Bosnia Herzegovina	IH CI SH	GCS < 3 Recurrent stroke Epileptic seizure at onset of stroke Early stage of dementia Delirium caused by alcohol or other psychoactive substances	DSM IV DRS >16	DRS R-98	Once within 4 days	
McManus et al, 2009	England	IH CI	SH Symptoms <24 hrs GSC<8 TIA Language barrier	DSM III R	CAM DRS	Daily for 4 wks	28
Dahl et al, 2010	Norway			DSM IV DSM III R	CAM MDAS	Twice/day	
Oldenbeuving et al, 2011	Netherlands	IH CI Age 18+	SH TIA Mental Retardation Language barrier	DSM III R	CAM DRS	Between 2-4 days and 5-7 days	
Mitasova et al, 2012	Czech Republic	IH CI	SH Symptoms <24 hrs TIA History of head trauma RASS =/< 4 Tumor	DSM IV	CAM-ICU	Once/day	7
Lees et al, 2013	England	CI		DSM III R	CAM	Once	1-4
Naidech et al, 2013	USA	IH	IH due to trauma Structural lesions CI Other causes than vascular	DSM IV	CAM-ICU	Twice/day	28
Miu et al, 2013	China	IH CI SH Stroke less than 24 hrs prior to admission	Venous thrombosis TIA GSC <3 Neurosurgery Head trauma No informant	DSM III R	CAM	Once/day	1-5

Table 3b: Studies of the Frequency of Post Stroke Delirium

Author /Year	Patients Eligible	Patients Enrolled	Patients Completing Screening	Age range (mean)	M/F	Time to entering in study following a stoke (days)	Stroke Type	Stroke location
Gustafson et al, 1991	155	145		40-101 (73)	90/55	<7 (<1 in most cases)	IH 8 CI 133 TIA 21 Unknown 3	LST 65 RST 47
Gustafson et al, 1991		83		44-89 (75)	52/31	86% <2	CI 83	LH 42 RH 41
Caeiro et al, 2004	220	220	218	65-84 (57)	130/88	<1	IH 48 CI 142 SH 28	LH 71 RH 63 Brainstem-cerebellum 51
Sheng et al, 2006		186	156	65-95 (79)	83/73	3	IH 23 CI 133	CI TAC 19 PAC 45 POC 18 LI 43 Undetermined 8
Dostovic et al, 2009	561	233	233	70		<4		
McManus et al, 2009	110	82	82	24-97 (66)	51/31	<4	IH 15 CI 67	CI TAC 15 PAC 25 POC 10 LI 17
Dahl et al, 2010	200	200	178	73	102/76			
Oldenbeuving et al, 2011	535	535		29-96 (72)	288/239	<1	IH 57 CI 470	LH 272 RH 168 CI TAC 43 PAC 184 POC 87 LI 156
Mitasova et al, 2012	331	151	129	30-93 (71)	72/57	<1	IH 22 CI 107	LH 60 RH 56 IT 13 CI TAC 31 PAC 39 POC 14 LI 33
Lees et al, 2013	138		111	64-85 Median 74	55/56	1	IH 27 CI 84	CI TAC 20 PAC 29 POC 9 LI 26
Naidech et al, 2013	114	114	98	(63)	46/52		IH 114	Subcortical 59 Lober 34 IT 18 Other 3
Miu et al, 2013		314		50-94 (73)	163/151		CI 285	CI PAC 46 PAC 37 POC 14 LI 35

Table 3c: Studies of the Frequency of Post Stroke Delirium

Author /Year	Dementia (n)	Current Medical Co-morbidity	Current Psychoactive Medications Use	Number with delirium (%)
Gustafson et al, 1991	8	Cardiovascular 78 Previous delirium 14 Previous stroke 45 DM 24 Hypertension 62 Infection 12	Antipsychotic 8 Anticholinergic 16 Benzodiazepine 17 Antidepressant 8 Analgesic 21	69 (48)
Gustafson et al, 1991	2	Intercurrent infection 12 DM 12 Previous stroke 17 Previous delirium 4		35 (42)
Caeiro et al, 2004	7	DM 14 Previous stroke 40 Medical complications 47 Alcohol abuse 83		29 (13)
Sheng et al, 2006	12	Hypertension 111 A Fib 49 DM 32 Ischemic heart disease 47 Alcohol abuse 83 Left ventricular failure 13 Infection 25	Anticholinergic 5	39 (25)
Dostovic et al, 2009				59 (25)
McManus et al, 2009		Septicemia 2		23 (28)
Dahl et al, 2010	17	DM 12 Poor vision 19 Cardiac events 17 Infection 30 Urinary retention 18		18 (10)
Oldenbeuving et al, 2011	78 had cognitive decline	Infection 99 Metabolic disturbance 277 Hearing loss 31 Poor vision 21 Alcohol abuse 169		62 (12)
Mitasova et al, 2012	25		Benzodiazepine 10 Antipsychotic 40	55 (43)
Lees et al, 2013	13	Sensory impairment 16		12 (11)
Naidech et al, 2013	2	DM 22 CAD 14 A Fib 10 Hypertension 86 Pneumonia 12 Seizure 5	Benzodiazepine 56 Anticonvulsant 49	31 (32)
Miu et al, 2013	78 had pre-existing cognitive impairment	A Fib 41 Fever 107 UTI 118 Chest infection 140 Urinary retention 108		86 (27)

Legend to Table 3:

A Fib Atrial Fibrillation
BI Barthel Index
CAD Coronary Artery Disease
CAM Confusion Assessment Method
CAM-ICU Confusion Assessment Method Intensive Care Unit
CDT Clock Drawing Test
CI Cerebral Infarction
DM Diabetes Mellitus
DRS Delirium Rating Scale
DRS -R-98 Delirium Rating Scale Revised- 98
DSM Diagnostic and Statistical Manual
FIM Functional Independence Measure
GSC Glasgow Coma Scale
IQ CODE Informant Questionnaire on Cognitive Decline in the elderly
IH Intracerebral Hemorrhage
IT Infratentorial
LH Left Hemisphere
LI Lacunar infarction
LST Left-sided supratentorial
MDAS Memorial Delirium Assessment Scale
MMSE Mini–Mental State Examination
OBSS Organic Brain Syndrome Scale
PAC Partial Anterior Circulation
POC Posterior Circulation
RASS Richmond Agitation –Sedation Scale
RH Right Hemisphere
SH Subarachnoid hemorrhage

Recommendations

• The following recommendations should be considered in the design of new studies to determine the frequency of post-stroke delirium.

• The type(s) of stroke and the criteria for type should be specified as should the time to enrolment following stroke. Perhaps there should be a time limit to enrolment following stroke.

• Standardized instruments to diagnose and measure the severity of delirium would be useful.

• The frequency and length of screening for delirium should be specified.

• The number of patients, who were eligible, enrolled and completed screening should be reported.

• Stroke type and location and stroke size should be reported.

• The putative cause(s) of delirium should be assessed and reported.

• There should be measures of medical co-morbidities and psycho-active drug use that was used in the analysis of frequency of post-stroke delirium. If possible, the timing of the co-morbidity and drug use in relation to the onset of delirium should be specified.

Key points

• Post-stroke delirium appears to be frequent
• Because of significant heterogeneity in the results of studies of post-stroke delirium, the results of this review must be interpreted cautiously

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