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Health System Development
and Mortality Transitions in Libya

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From the Editor

This issue of the journal is rich with various issues including renal failure , education , renal colic, malaria, and health care systems . A paper from Yemen looked at the clinical profile, biochemical parameters and outcome among 64 adult malarial patients complicated with ARF, HD, or both. The age of the patients ranged from 15 to 78 years. Mean duration of febrile illness was 6 days at the time of presentation. 42% (n=27) patients had hepatic dysfunction and 37.5 % (n=24) had acute renal failure (ARF) and 13 patients (20.5%) had both complications according to WHO criteria. 100% of patients with ARF were oligo-anuric and required dialysis support. The authors concluded that although malaria remains a major health problem, malarial hepatic-renal disease has not been reported previously from Yemen. Early initiation of anti-malarial effective therapy, close observation for organ failure and early initiation of dialysis in ARF is instrumental in the recovery of the patient.

A retrospective analysis was done of a series of 21 cases of renal colic due to urinary stones during pregnancy from Jordan to determine the problems related to renal colic due to urinary stones.
Among the deliveries the incidence in this series was 0.13%. Most of them were in third trimester of pregnancy followed by the second trimester and the least were in the first trimester. The most common complaints were flank pain (95.2 %), urinary symptoms (hematuria, dysuria and urgency) in 80.9%, nausea and vomiting in 14.3% and fever in 28.6 %. Spontaneous passing of stones was noted in 19 cases (90.5%) with conservative treatment. The authors concluded that the majority of renal colic due to urinary stones during pregnancy can be safely managed conservatively. The commonest presenting symptoms in our study were flank pain, urinary symptoms (hematuria, dysuria and urgency), and early surgical intervention resulted in safe maternal and fetal outcome.

An observational and prospective study from Yemen looked at incidence of pregnancy related (ARF), clinical spectrum, morbi-mortality of this preventable complication. The total Pregnancy related ARF numbered were 39 patients, 33 (85%) were multipara and 14 (15%) were primigravida. All 39 patients (100%) cases presented to haemodialysis center immediately within (1-3 days) (postpartum). 35 cases (90%) were anuric. Idiopathic ARF was the commonest with 11 patients (28%). Blood loss causing hypotension due to postpartum hemorrhage PPH was the second cause 9 patients (23 %). The authors concluded that pregnancy related acute renal failure is a major health problem and carries very high mortality and morbidity. Poor healthcare facilities and lack of antenatal health care at Postpartum related-acute renal failure mortality, at haemodialysis

A paper from Libya paper attempts to review mortality in Libya through tracing the routes, reviewing underlying factors and examining contribution of Government and other public health institutions. Transition in mortality is an important indication of progress in public health and a precondition for medical interventions and health systems development. The authors make use of national statistics on major mortality indicators viz., crude death rate, infant mortality rate, under 5 mortality rate, maternal mortality rate and expectation of life at birth since 1950. A remarkable change in mortality has been observed which had a clear relation with improvement in health service delivery systems. The authors concluded that these achievements from an experimental people-based health system development have to be treated scientifically through information base for contributing to changes in health delivery systems and also for accelerating progress in the future. Learning from experiences of the previous experimental people's congress oriented health service delivery shall take the system to further health gains.

Study of some non-traditional roles ascribed to vitamin D include immune -modulating effects and anti -inflammatory in sera of Iraqi myocardial infarction patients. A paper from Baghdad showed the non-traditional roles ascribed to vitamin D including immune-modulating as anti-inflammatory agent in different inflammation process. Fasting venous blood samples were taken from 80 subjects collected from Iraqi patients complaining of Myocardial infarction and controls. The authors concluded that their results suggest that vitamin D possesses a crucial role in protection against MI through its property as an anti inflammatory agent by modulating the immune system

A descriptive-analytical study from Iran looked at factors affecting hospital selection decisions (governmental and private) from patients' viewpoint in Iran. Findings show that some factors including referring to hospital by ambulance, physicians' advice, family income, insurance type, hospital quality, employment of family members in hospitals, cost of services provided at hospital and information given to patients about his disease are the factors affecting the hospital selection decision by patients. The authors concluded that although various factors affect the governmental or private hospital selection, high percentage of refereeing to Emam Reza governmental hospital and pervasive role of physicians' advice in selection of hospital due to exclusiveness of physicians in educational-treatment centers caused the patients not to practically have any role in selecting their hospitals and thus role of other factors in selecting hospital was less.

A paper from Baghdad looked at the relation between Students Socio-Economic Status, Internet Use Mode and Attendance on Success Rate in Medical College. A total of 396 students were studied. It was found that socio- economics plays a role in success but no statistical differences were found; those using internet for studying have less failure rate than those who use it for entertainment . This difference was significant . Vision and sleep impairment increase with excessive use of internet . Regularly attending classes leads to success. These results are consistent with many studies. The authors concluded that attending classes and wise use of internet will improve scoring.

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Study of some non-traditional roles ascribed to vitamin D include immune-modulating effects and anti-inflammatory in sera of Iraqi myocardial infarction patients

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Abstract

This study was designed to show the non-traditional roles ascribed to vitamin D include immune-modulating as anti-inflammatory agent in different inflammation processes.

Fasting venous blood samples were taken from 80 subjects collected from Iraqi patients complaining of Myocardial infarction (MI) in the Coronary Center Unit (CCU), Baghdad teaching hospital, and Ibn al-Nafees Hospital and controls. They have been classified into two groups as follows:

A) Patients of Myocardial infarction(MI) group: included (50) patients from both sexes, with age range (35-65) years.
B) Control group : included (30) healthy individual from both sexes, with age range (30-45) years and no previous disease which may interfere with the parameters analyzed in this study.

All the blood samples were analyzed for lipid profile (total cholesterol (TC), triglyceride (TG), high densitylipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein (VLDL), vitamin D3, albumin, C-reactive protein (CRP), Erythrocytes Sedimentation Rate (ESR), immunoglobulin (IgG, IgM, IgA), ceruloplasmin, and alpha1-antitrypsine as well as the Atherogenic indices such as Cardiac Risk Ratio (CRR), Atherogenic Coefficient (AC), and the Atherogenic Index of Plasma(AIP) were calculated.

This study detected a significant increase in TC, TG, LDL-C, VLDL-C, CRR, AC, AIP, IgA, IgG , IgM, ESR, CRP, 1-antitrypsin and CP levels in sera of patients with myocardial infarction compared with controls and a significant decrease in HDL-C, vitamin D3, and albumin levels in sera of patients with myocardial infarction compared to controls.

Also this study demonstrated a significant positive correlation between vitamin D and LDL-C, CRP, ESR, CP, IgA and IgM and a significant negative correlation between vitamin D and AIP, IgG and 1-antitrypsin in sera of patients with myocardial infarction group, and a significant positive correlation between vitamin D and LDL-C, AIP, CRP, ESR, CP and IgM and a significant negative correlation between vitamin D and IgA, IgG and 1-antitrypsin in sera of the control group.

Our results suggest that vitamin D possesses a crucial role in protection against MI through its property as an anti inflammatory agent by modulating the immune system.

Key words: Vitamin D, immune modulating, anti- inflammatory agent

Introduction

Myocardial infarction (MI), commonly known as a heart attack, results from the interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (cholesterol and fatty acids) and white blood cells (especially macrophages) in the wall of an artery. The resulting ischemia (restriction in blood supply) and ensuing oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death (infarction) of heart muscle tissue (myocardium) (1).

Important risk factors associated with an increased risk of myocardial infarction (MI) are high blood levels of certain lipids (total cholesterol, low-density lipoprotein or triglycerides) and levels of high density lipoprotein (HDL) less than 40 mg/dl (2), and atherogenic index of plasma (AIP) calculated as log (TG/HDL-C) (3).

(AIP) inverse relationship between HDL-C and cardiovascular risk has been demonstrated beyond any doubt; the contribution of TGs to cardiovascular risk has been underestimated. This may have been attributable to the high variability of plasma TG concentrations (which decreases the statistical significance of assessments), the lack of information on the role of TG in biochemical mechanisms, or the incessant efforts to find an atherogenic marker independent of other lipids (4). Cholecalciferol is a prohormone that is synthesized in the skin by photochemical conversion of 7-dehydrocholesterol). It is subsequently hydroxylated to 25-hydroxycholecalciferol [25(OH)D3] in the liver and finally to the active metabolite,1,25 didyroxcholecalciferol [1,25(OH)2D3] in the kidney(5).

The active vitamin D metabolites are transported in the circulation by vitamin D-binding protein which has additional effects, including the binding of globular actin and fatty acids and immunomodulation(6).

Vitamin D3 is a steroid hormone shown to regulate 60 genes.(7)

This is accomplished by the translocation of 1,25(OH)2D3 into cells where it binds with high affinity to the vitamin D receptor (VDR), which is a member of the nuclear receptor super family. This complex then interacts with the vitamin D response elements in the promoter region of target genes thereby altering rates of gene expression.

Vitamin D receptors (VDRs) have been identified in dermal capillaries, and cultured endothelial cells appear to express a 1_hydroxylase enzyme, indicating the possibility of a vitamin D micro endocrine system in endothelial cells. (8)

Classically, the action of 1_ ,25(OH)2D3 is to maintain calcium and phosphate homeostasis, with the intestine and bone being key targets. It also acts on a wide range of non classical target tissues, including the heart and arterial wall, The influence of 1,25(OH)2D3 on these tissues could have important implications for vascular function and disease (9).

VDRs are present in vascular smooth muscle cells (VSMCs). There is controversy concerning the action of vitamin D on VSMCs, with some studies reporting stimulation of proliferation and others reporting inhibition of proliferation and a synthetic phenotype being induced by 1,25(OH)2D3.(10)

Macrophages and lymphocytes are other important target cells for vitamin D in the diseased artery wall. (11)

Albumin is synthesized in the liver at a rate that is dependent on protein intake. The molecule contains no carbohydrate. It has a molecular weight of 6600 Dalton (12).

Albumin has a diverse function, playing important roles in the maintenance of the colloid osmotic pressure of the blood, in transport of various ions acids and hormones, and nutrition (13).

Serum albumin level has been linked in clinical practice to several diseases. Low albumin levels can suggest inflammation(14) serum albumin concentration falls (20%) during an inflammatory process (15).

Acute phase proteins are a class of proteins whose plasma concentrations increase (positive acute-phase proteins) or decrease (negative acute-phase proteins) in response to inflammation. This response is called the acute-phase reaction (also called acute-phase response). In response to injury, local inflammatory cells (neutrophil granulocytes and macrophages) secrete a number of cytokines into the bloodstream, most notable of which are the interleukins IL-1, IL-6 and IL-8, and TNF-?. The liver responds by producing a large number of acute-phase reactants. At the same time, the production of a number of other proteins is reduced; these are, therefore, referred to as “negative” acute-phase reactants. As such, increased acute phase proteins from the liver may also contribute to the promotion of sepsis(16).

Immunoglobulin are serum proteins or antibodies subsequently demonstrated to be contained in the third migrating globulin peak (*y*-globulin peak) on electrophoresis (17) Regarding the role of immunologic mechanisms in the development of atherosclerosis, (18) recent evidence indicates that both cellular and humoral immune mechanisms are involved in the development of the atherosclerotic lesions. Thus, they are activated macrophages(19). The serum of patients suffering from myocardial infarction has been found to contain antibodies against phospholipids or phospholipid-binding proteins, which have been considered to play a role in arterial thrombosis. (20) Elevated levels of immunoglobulin classes are associated with myocardial infarction and cardiac death in men with dyslipidemia. For dyslipidemia to cause coronary atherothrombosis, an immune response reflected by elevated levels of these immunoglobulin classes is an important determinant. (21) Serum

immunoglobulin (Ig) concentration may increase in various vascular diseases such as myocardial infarction. (22)

The objective of this study is to highlight the non-traditional roles ascribed to vitamin D which include immune - modulation effect and anti - inflammatory in acute myocardial infarction patients through demonstrating that myocardial infarction disease is an inflammatory disease that contributes to alteration in level of vitamin D which could be related to some inflammatory markers such as acute phase protein , immunoglobulin and erythrocyte sedimentation rate and statistical correlation between these indicators and the vitamin D level was studied.

Sampling

During the period from October 2011 to April 2011 blood samples were collected from patients complaining of Myocardial infarction (MI) Coronary Center Unite (CCU), at Baghdad teaching hospital, and Ibn al-Nafees Hospital, and controls. They have been classified into two groups as following:

1) Patients of Myocardial infarction group: included (50) patients from both sexes, with age range (35-65) years.
2) Control group : included (30) healthy individuals from both sexes, with age range (30-45) years and no previous disease which may interfere with the parameters analyzed in this study.

Specimen Collection and Preparation

Ten millilitres (ml) disposable plastic syringes of 21 G needles were used to draw eight ml of venous blood from each patient and controls after 12 hours fasting. The blood samples were divided into two tubes:

1. Two ml of blood samples were transferred into plastic tubes containing Ethylene Diamine Tetra Acetic acid (EDTA) and left for 20-30 minutes at 37C. The blood was later used for the determination of ESR.
2. The second part of blood samples were transferred into plastic plain tubes, no anticoagulant ; blood was left to clot for 20-30 minutes at 37C. Serum was obtained by centrifugation for 10 minutes at 3000 rpm and was divided into small eppendorf tubes of capacity 1.5 ml and kept at -20C until time of analysis. The separated serum was later used for the determination of the levels of lipid profile (Triacylglycerol TG, Total cholesterol TC, High density lipoprotein cholesterol HDL-C, Very low density lipoprotein cholesterol VLDL-C, and Low density lipoprotein cholesterol (LDL-C), vitamin D3, C-reactive protein (CRP), Albumin, 1-antitrypsin, Ceruloplasmein and Immunoglobulin (IgM; IgG; IgA).

Laboratory Analysis

Serum total cholesterol (TC), HDL- cholesterol (HDLC) and triglyceride (TG) were assayed enzymatically with commercial test kits (Randox Laboratories, England). (23),(24)(25) Serum LDL-cholesterol was calculated using the Friedewald equation (26) as follows :
LDLC= TC-HDLC-TG/2.2
VLDLC=TG/2.2

The Atherogenic indices were calculated as follows:
Cardiac Risk Ratio (CRR)=TC/HDLC
Atherogenic Coefficient (AC)=(TC-HDLC)/HDLC

Atherogenic Index of Plasma (AIP)=log(TG/HDLC)(27) Vitamin D3 was measured using high performance liquid chromatography (HPLC) technique according to (28) method and this method can be summarized by the following:

The alcoholic extract of D3 was done by mixing 1 ml of pure ethanol with 1 ml of serum, then centrifuged for 15 minutes at 15000 rpm, then filtered by 0.45 μ m disposable filter; 20 µl was injected on HPLC system according to the following optimum condition :

Column : flc (fast liquid chromatographic column), 3 µm particle size (50 - 4.6mml.D) STRODS-M column
Mobile phase : water : methanol (1:20 v/v)
Detection : uv set at 240 nm
Temperature : 40 degrees C
(See table at bottom of page)
Concentration of sample =
Area of sample x conc. Of standard x dilution factor
Area of standard

The separation occurred on liquid chromatography Shemadzu 10AV -LC equipped with binary delivery pump model Shemadzu 10AV -LC, the eluted peaks were monitored by UV - VIS 10A-SPD spectrophotometer.
Albumin level was determined in serum samples of all studied groups according to (29) methods.
CRP was measured in serum samples of all studied groups according to (30) methods.
Erythrocyte Sedimentation Rate (ESR) was determined in whole blood samples of all studied groups according to (31) method.

Immunoglobulines (IgM; IgG; IgA); ceruloplasmin and 1-antitrypsin were determined in serum samples of all studied groups according to (32) methods.

Statistical Analysis

Data presented were the means and standard deviation Student's t-test was used to compare the significance of the difference in the mean values of any two groups, P value less than 0.05 was considered statistically significant.

Seq.	Subject	Retention time Minute	Area	Concentration
1	cholescalciferol (D3)	2.12	86792	50 ng/ml

Results and Discussion

Table 1: lipid profile and Atherogenic indices in sera of two studies groups

Parameter	Control N=30	Patients N=50	P
TC(mg/dl)	141.2±10.2	235.87±44.09	P≤0.05
TG(mg/dl)	82.1±11.7	195.7±30.6	P≤0.05
HDL(mg/dl)	57.4±5.2	30.41±6.66	P≤0.05
LDL(mg/dl)	67.4±8.34	166.3±16.5	P≤0.05
VLDL(mg/dl)	16.4±2.2	39.1±6.6	P≤0.05
CRR	1.43±0.33	6.42±0.97	P≤0.05
AC	0.43±0.33	5.42±0.97	P≤0.05
AIP	0.15±0.02	0.80±0.08	P≤0.05

Table 2: vitamin D3, Albumin, CRP, ESR ,Immunoglobulin (IgG, IgM, IgA),CP& α1-AT

Parameter	Control N=30	Patients N=50	P
Vitamin D3 (ng/ml)	47.26 ±1.02	12.43 ±2.58	P≤0.05
Albumin (g/dl)	4.11 ±0.19	3.35±0. 53	P≤0.05
CRP(mg/dl)	0±0	2.1 ±0.57	P≤0.05
ESR(mmol/hr)	10.3 ±1.65	34.5±4.57	P≤0.05
IgG(mg/dl)	1328.9 ±307	2024.4±168.7	P≤0.05
IgM(mg/dl)	8.75±474	209±48.2	P≤0.05
IgA(mg/dl)	251.9±65.52	578.8±95.63	P≤0.05
CP(mg/dl)	40.02 ±7.9	81.04±9.30	P≤0.05
α1-AT(mg/dl)	150.7±34.06	255.2±21.5	P≤0.05

Data in these tables above, (1) and (2) shows that a significant increase in level of TC, TG, LDL, VLDL, CRR, AC, AIP, CRP, ESR, IgG, IgM, IgA, CP and α1-AT in sera of myocardial infarction patient group compared with controls with ($P \leq 0.05$), while there was a significant decrease in level of HDL, vitamin D and albumin in sera of patients compared with control group with ($P \leq 0.05$) .

Coronary heart diseases are the most important factor of death. Patients with MI showed significant change in lipid profile when compared to healthy controls. (33) There was no significant alteration in triglyceride levels reported. (34)

it showed that triglyceride levels diminished slowly from the second hour after myocardial infarction. Some studies showed that there are correlations between the occurrence of AMI and abnormality of lipid profiles (35).

Other studies showed that there was an increase in serum triglycerides during MI. (36)

Study of (37) revealed significantly high levels of triglycerides and low levels of HDL-cholesterol in AMI patients compared to control subjects.

In our present study, serum triglyceride levels showed significant increase in MI patients when compared with control subjects. This result was in agreement with previous studies (37) which suggest the elevation of TG level.
A different mechanism has been suggested about elevation of triglycerides after MI. It is reported that elevated triglyceride levels may depend on genetic basis. (38) Nutritional habits (39) and Triglyceride levels may be changed because of inherited abnormality of very low density lipoprotein. It maybe that it happens because of increased flowing of fatty acids and impaired elimination of VLDL from the plasma (40).

The result of the present study revealed significant change in total cholesterol serum levels after acute myocardial infarction. This is in agreement with other researchers who found an increase. (41)

Some results stated that elevated serum cholesterol has depended on elevated consumptions of fat. (42)

LDL carries the most cholesterol in the plasma and increasing of LDL depends on increasing of total cholesterol level.(43)

Reduction of HDL concentration in our findings disagrees with the other studies that show increased HDL. (44)

Several studies have supported that the ratios of LDL-cholesterol/HDL-cholesterol and total cholesterol /HDL-cholesterol show the atherosclerotic injury of the wall of the vessels, (45) (46) which suggests that LDL-Ch level is increased in MI patients which supports our result. It has been claimed the LDL cell surface receptors cleaned LDL from the circulation. These receptors may change as a result of coronary heart disease, thus uptake of LDL is decreased (47). On the other hand, increasing of LDL is possibly as a result of excessive production of VLDL and /or decreasing of VLDL remnants (Low activity of LDL receptors which has been reported (37).

Hyperlipidemia is an elevated concentration of lipids in the blood. The major plasma lipids of interest are total cholesterol and the triglycerides. When one or more of these major classes of plasma lipids is elevated, this means that hyperlipidemia exists. (48)

The association between hypertriglyceridemia and IHD events may be related to the presence of atherogenic, triglyceride rich particles in plasma such as LDL and VLDL. (49)

Atherogenic Index of Plasma (AIP) log (TG /HDL) may be an important tool for analyzing the results of clinical trials. The association of TG and HDL-C in this simple ratio theoretically reflects the balance between risk and protective lipoprotein forces, and both TG and HDL are widely measured and available. A lot of work has been done on the relationship between TG and HDL-C, and it has been shown that the ratio of TG to HDL was a strong predictor of myocardial infarction. (50)

Vitamin D insufficiency defined as serum 25-hydroxyvitamin D [25(OH)D] levels < 75 nmol/l [to convert to ng/ml, divide by 2.5]) is associated with the development of CVD in the general population. (51)

It has been reported that vitamin D insufficiency is associated with decreased arterial compliance (52) and increased carotid IMT. (53) Strikingly, vitamin D insufficiency is associated with a two-fold increased risk of developing an initial cardiovascular event in previously healthy asymptomatic individuals. (54) This association between vitamin D and incident CVD remained significant after adjustment for several confounders associated with CVD including age, sex, systolic blood pressure, diabetes, total to high-density lipoprotein cholesterol ratio, body mass index and tobacco use. Proposed mechanisms of vitamin D's role in CVD development to its effects on inflammatory cytokines (55), its direct effects on the vasculature (56) and inhibition of the renin-angiotensin II-aldosterone system (57) in addition to some non-traditional roles ascribed to vitamin D include anti-inflammatory and immune-modulating effects. These effects have led to possible implications in the pathophysiology of immune-mediated diseases including multiple sclerosis (MS) and inflammatory disease (58)

(59) suggested that osteoregulatory mechanisms related to bone development may affect calcification in the vasculature. Levels of 1,25-dihydroxyvitamin D have been shown to be inversely associated with vascular calcification, (60) suggesting that vitamin D may affect myocardial infarction risk through its effects on vascular calcification. Other mechanisms could account for, or contribute to, the association between 25(OH)D and MI risk. Vitamin D deficiency, possibly combined with low calcium intake, has been associated with impaired fasting glucose and possibly risk of type 2 diabetes mellitus.

Vitamin D deficiency has also been associated with a cytokine profile that favours greater inflammation (e.g. higher C-reactive protein and interleukin 6 levels and lower interleukin 10 levels) which could predispose to heightened risk. (61)

Seasonal respiratory tract infections, particularly influenza, have been proposed to account for the winter increase in mortality due to CVD,(62) and hypo vitaminosis D could contribute to these infections. (63)

In addition, vitamin D has long been known to play an important role in immune function. Vitamin D receptor expression is found in monocytes, stimulated macrophages, dendritic cells, natural killer cells, T cells and B cells. Additional evidence shows that vitamin D modulates the adaptive immune system as well, through direct effects on T-cell activation and on the phenotype and function of antigen-presenting cells. (64) Evidence showed that in vitamin D effect on the immune system, it is reasonable to consider a link between HIV-related factors, such as CD4+ T-cell count and inflammation, which then may indirectly also affect an individual's CVD risk. Few studies have investigated vitamin D status and HIV-related health effects, but a recent study showed that low vitamin D status appears to have a negative effect on HIV disease progression and mortality. (65)

Another study found a positive relationship between vitamin D dietary intake and CD4+ T-cell counts. (66)

Despite some conflicting data, Vitamin D insufficiency appears to be widespread in HIV- infected adults (67) and may contribute to the already increased CVD risk in this population. To date, no study has examined the relationship between 25(OH) D levels and carotid IMT or proinflammatory cytokines and endothelial activation marker levels known to be associated with CVD among HIV-infected individuals. They hypothesized that vitamin D status plays a role in CVD risk in HIV-infected adults by affecting levels of inflammatory markers. Likewise, given vitamin D's effect on inflammation and the immune system, the researchers

D's effect on inflammation and the immune system, the researchers hypothesized that vitamin D status is related to HIV-related factors, such as $CD4^+$ T-cell count. (68)

Albumin normally makes the largest single contribution to plasma total protein. Since a fall in albumin may roughly be balanced by a rise in immunoglobulin levels. This is quite a common combination. Most individual proteins, other than albumin, make a relatively small contribution to total protein; quite a large percentage change in the concentration of one of them and may not be detectable as a change in total protein. (69)

Of constituent proteins, only low albumin levels are of clinical importance (70). A low plasma albumin level, despite a normal total body albumin, may be due to dilution by an excess of protein - free fluid, or to redistribution into the interstitial fluid due to increased capillary permeability. There may be true albumin deficiency due to a decreased rate of synthesis, or to an increased rate of catabolism or loss from the body. The slight fall in the albumin level found in even mild acute illness may be due to a combination of the above two factors (71). Reduction in albumin concentration was reported in inflammatory processes, including acute-phase response and chronic inflammatory disorders and in neoplastic diseases .(72)

Coronary artery disease (CAD) which frequently becomes manifest as myocardial infarction (MI), continues to exact an enormous toll in Western society. Despite progress in its prevention, detection and treatment, it continues to be the leading cause of death. (73)

Several risk factors for coronary heart disease have been well documented, including hyperlipidemia, hypertension, smoking, diabetes, a positive family history, obesity and lack of exercise. However, these factors explain only part of attributable cardiovascular disease. It is clear that other and unknown factors are involved (74).

A growing body of evidence supports the concept that local and systemic inflammation plays a role in the initiation and progression of atherosclerosis and its complications. (75)

C-reactive protein (CRP) is an acute-phase reactant marker for underlying systemic inflammation. CRP has been reported to be elevated in patients with acute ischemia and MI.(76) CRP was subsequently shown to predict risk of recurrent ischemia in patients with unstable angina. Subsequent MI in patients with angina (77)CRP was shown to be a risk predictor for future MI or stroke over a period of at least 6 years in apparently healthy men in a case-control sub-study of the Physicians' Health Study. (78)

The inflammatory signals driving immunologic activity in CAD are unknown. They may be non-antigenic or antigenic but of non-infectious origin. Oxidized low density lipoprotein (LDL) and hypertension represent proposed non-infectious stimuli. Finally, they may include an infectious, antigenic source. A distant infection might generate circulating cytokines, or persistent local infectious (as well as non-infectious) sources within plaque may provide the ongoing stimulus. (79)

CRP is associated with endothelial cell dysfunction and progression of atherosclerosis, possibly by decreasing nitric oxide synthesis (80)

The complex of CRP and LDL is opsonized by macrophages, resulting in the generation of foam cells (Libby P and Aikawa M 2003) and to facilitate thrombogenesis through stimulation of tissue factor biosynthesis by macrophages. This suggests that high CRP plasma concentrations and the extent of its deposition in the atherosclerotic plaque are associated with plaque vulnerability and the occurrence of acute thrombotic events. (81)

It is therefore conceivable that CRP not only acts as a marker but also is involved in the initiation and progression of atherosclerosis (82)

The immune system has emerged over the last few years as a key factor in the development of atherosclerosis. Modified lipoproteins, and especially oxidized LDL (ox-LDL), have been the focus of much research. Ox-LDL may be a key antigen in the atherogenic process, by stimulating monocytes to infiltrate into the vessel intima; these then differentiate into macrophages, which produce cytokines, oxygen radicals and heat-shock proteins, and form foam cells. (83)

Inflammation has been postulated to play an important role in the development of atherosclerosis. (84) In addition, increased levels of antibodies against ox-LDL were predictive of MI. (85)

Elevated levels of anti-myosin and anti-actin antibodies have been reported in various heart diseases, and a direct relationship between the levels of these antibodies and extent of post-cardiac injury syndrome has been found.(86)

Adaptive immunity is recognized to play an important role in atherosclerosis. Oxidized low-density lipoprotein (oxLDL) is immunogenic and the immune response against oxLDL is considered as a crucial and modifiable event in atherogenesis. (87)

The concept of oxLDL as an important auto antigen in atherosclerosis is supported by the findings showing that (i) T-cells cloned from human lesions respond to oxLDL in an MHC class II-dependent manner, (ii) both plasma and lesions contain high levels of antibodies recognizing various epitopes of oxLDL, and (iii) hypercholesterolaemic animals with genetic deficiencies in the adaptive immune system develop less atherosclerotic disease. (88)

Infections stimulate the immune system and may result in increased immunoglobulin levels. (89)

An inflammatory pattern indicating an inflammatory condition is seen when there is a decrease in albumin

and an increase in the α1-globulins (α1-acid glycoprotein, α1-antitrypsin), α2-globulis (Ceruloplasmin and haptoglobin), β-globulin blood and C - reactive protein. (90)

Correlation relation:
The correlation coefficient (r) test is used to describe the association between the different studied parameters P<0.05 was considered statistically significant.

1. Correlation relation between vitamin D and LDL-C:
Figures (1A) and (1B) showed a significant positive a correlation between vitamin D and LDL-C with P.0.05 for control group and myocardial infarction with correlation coefficient value r (0.06), (0.18) respectively.

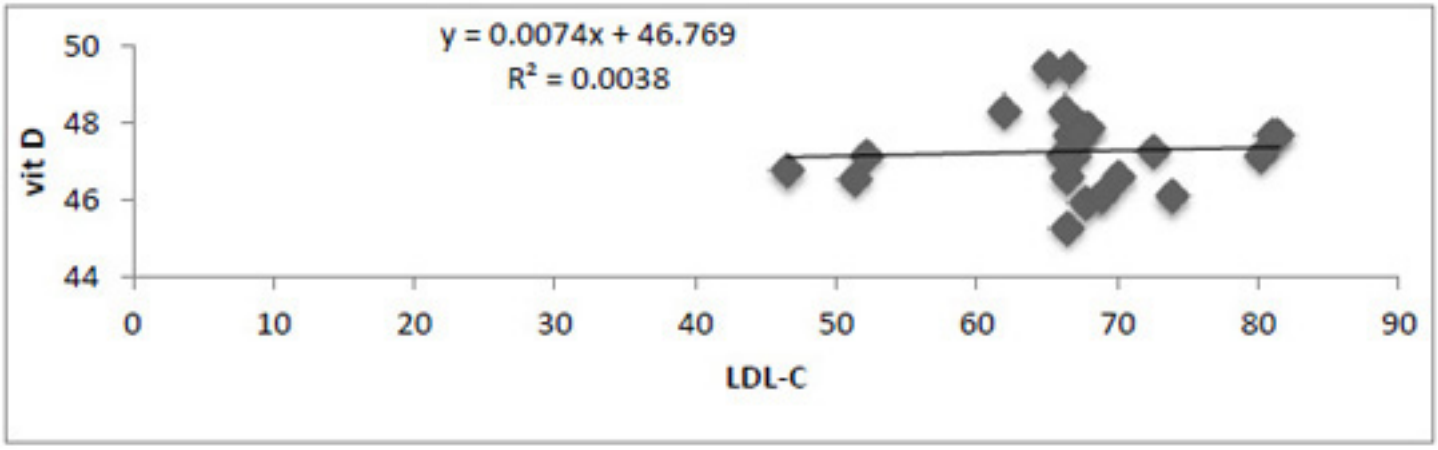

Figure 1A: Correlation relation between vitamin D and LDL-C in control group

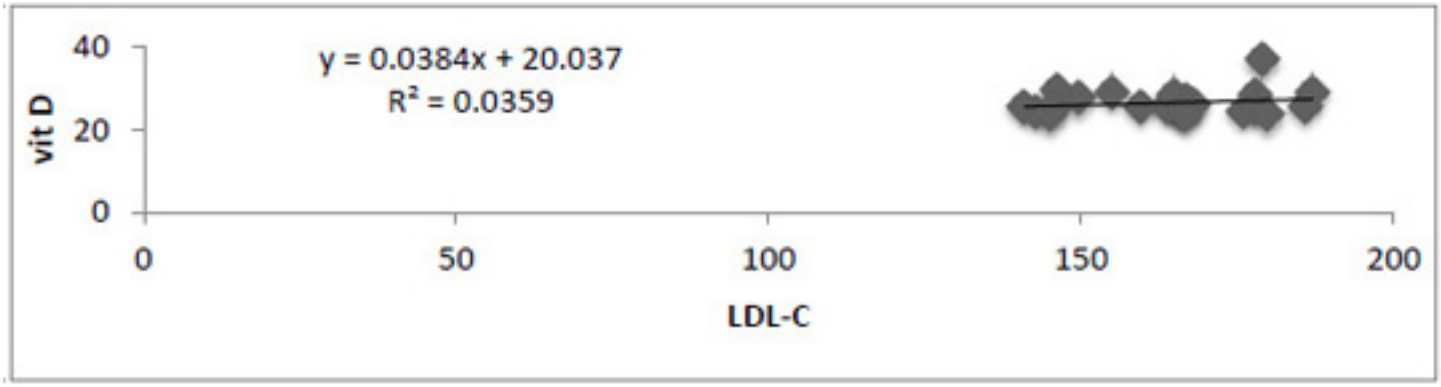

Figure 1B: Correlation relation between vitamin D and LDL-C in myocardial infarction patients group

2. Correlation relation between vitamin D and AIP:
Figures (2A) and (2B) showed a significant positive correlation between vitamin D and AIP with P ≤ 0.05 for control group with correlation coefficient value (0.07) while showing a significant negative correlation between vitamin D and AIP with P < 0.05 for myocardial infarction group with r value (-0.43).

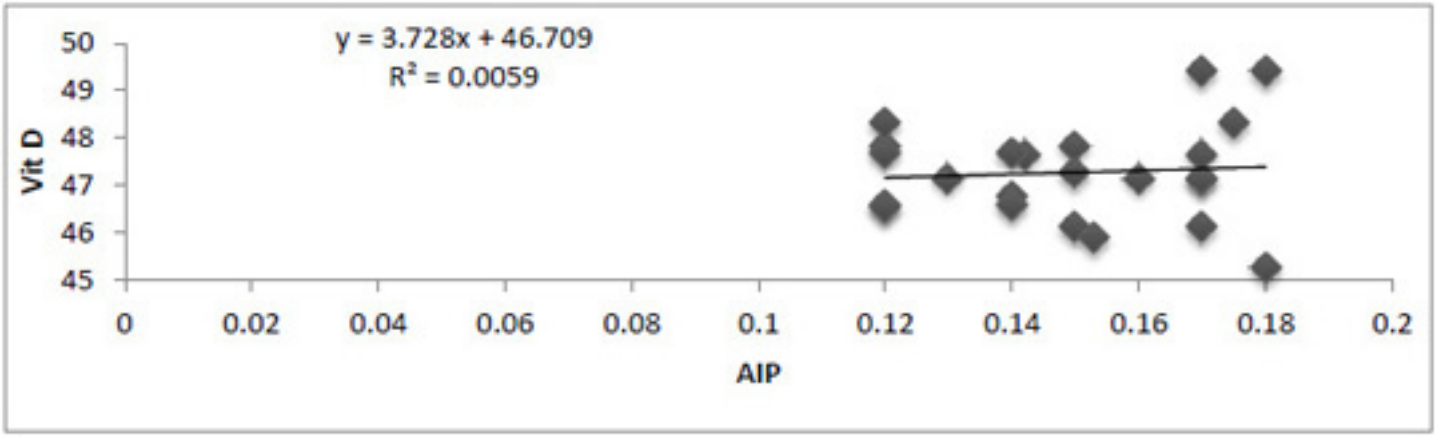

Figure 2A: Correlation relation between vitamin D and AIP in control group

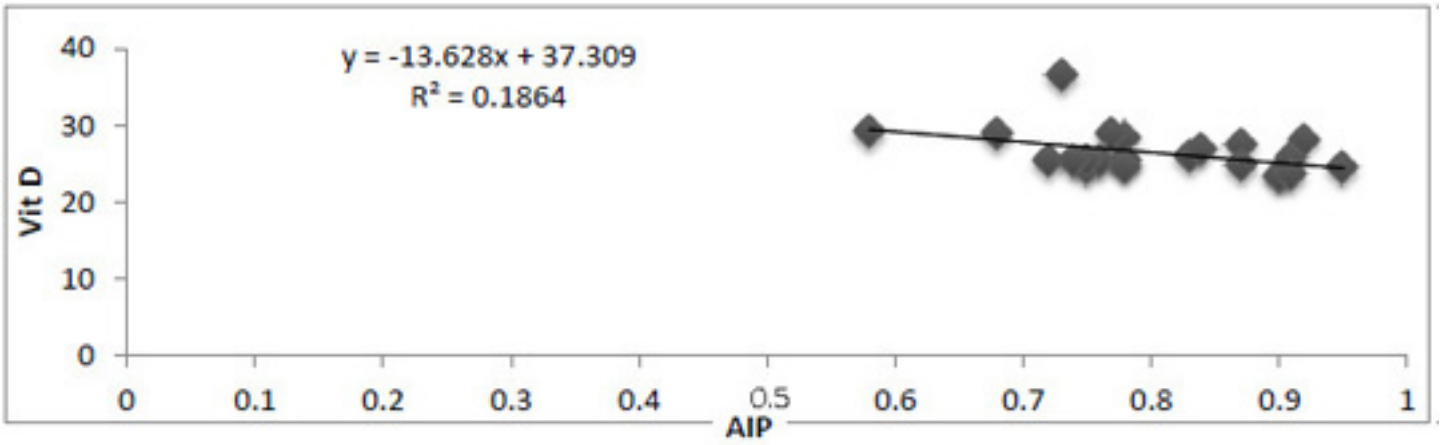

Figure 2B: Correlation relation between vitamin D and AIP in myocardial infarction patients group

3 .Correlation relation between vitamin D and CRP:
Figures (3) showed a significant positive correlation between vitamin D and AIP with P ≤ 0.05 for myocardial infarction with correlation coefficient value (0.009) while showing no significant positive correlation between vitamin D and AIP with P < 0.05 for control group with r value(0).

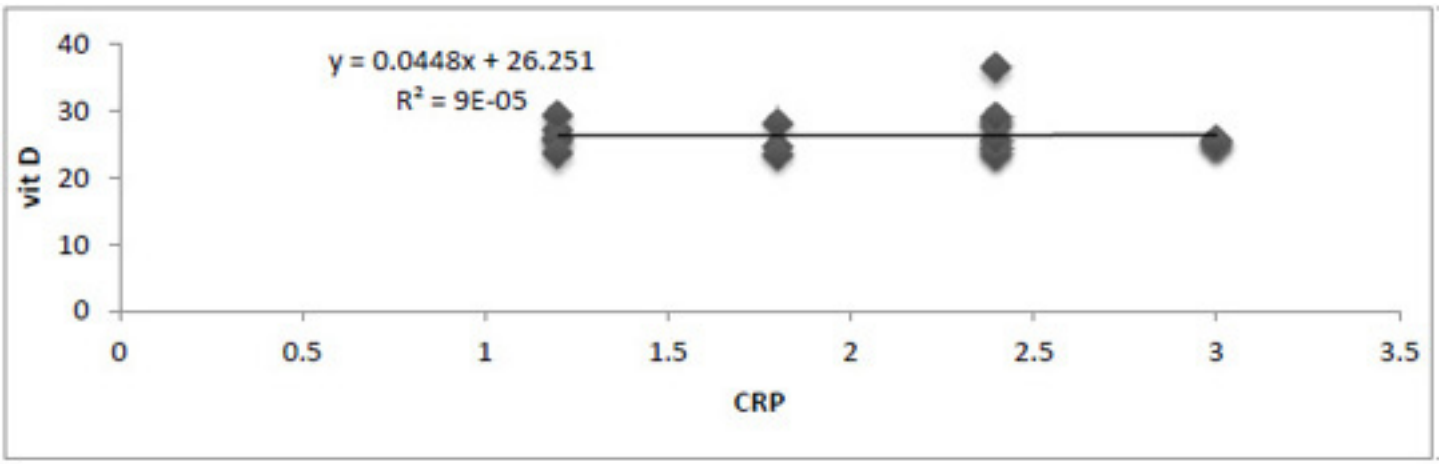

Figure 3: Correlation relation between vitamin D and CRP in myocardial infarction patients group

4. Correlation relation between vitamin D and ESR:
Figures (4A) and (4B) showed a significant positive correlation between vitamin D and ESR with P ≤ 0.05 for control group and myocardial infarction with correlation coefficient value r (0.21), (0.05) respectively.

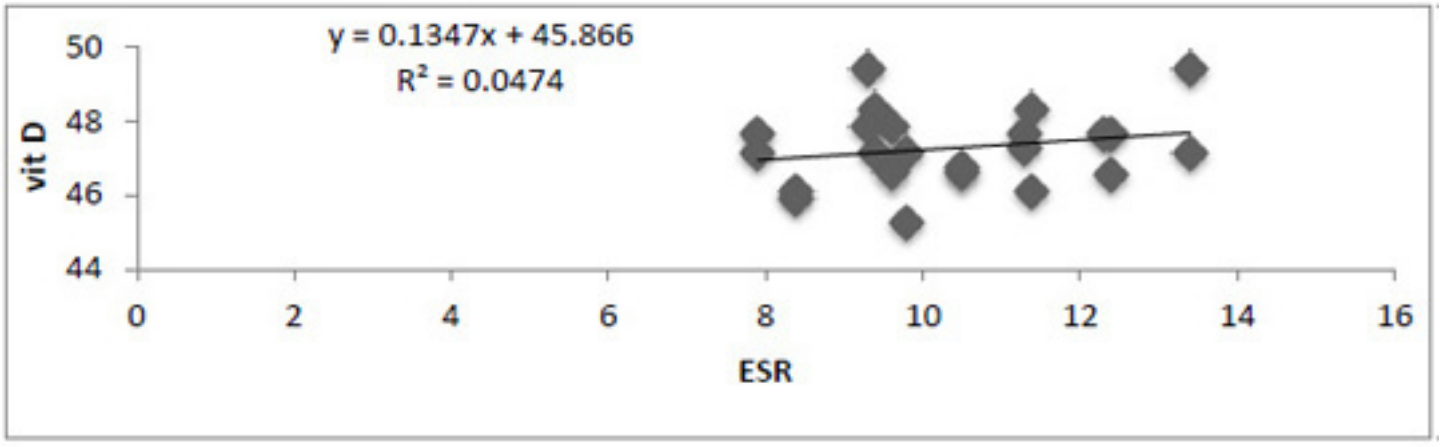

Figure 4A: Correlation relation between vitamin D and ESR in control group

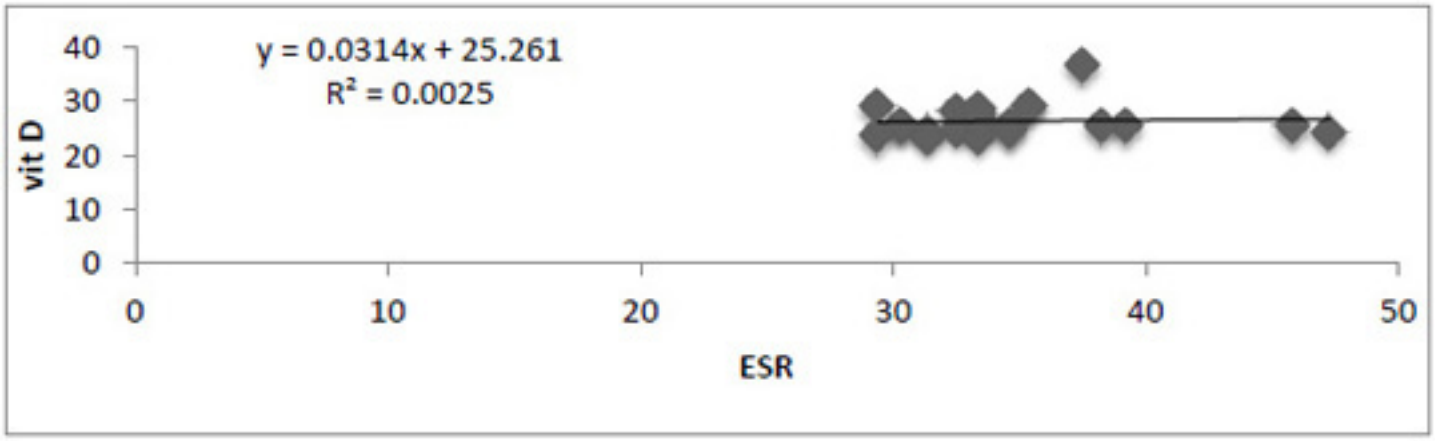

Figure 4B: Correlation relation between vitamin D and ESR in myocardial infarction patients group

5. Correlation relation between vitamin D and α1AT:
Figures (5A) and (5B) showed a significant negative correlation between vitamin D and α1AT with P≤0.05 for control group and myocardial infarction with correlation coefficient value r(-0.12), (-0.05) respectively.

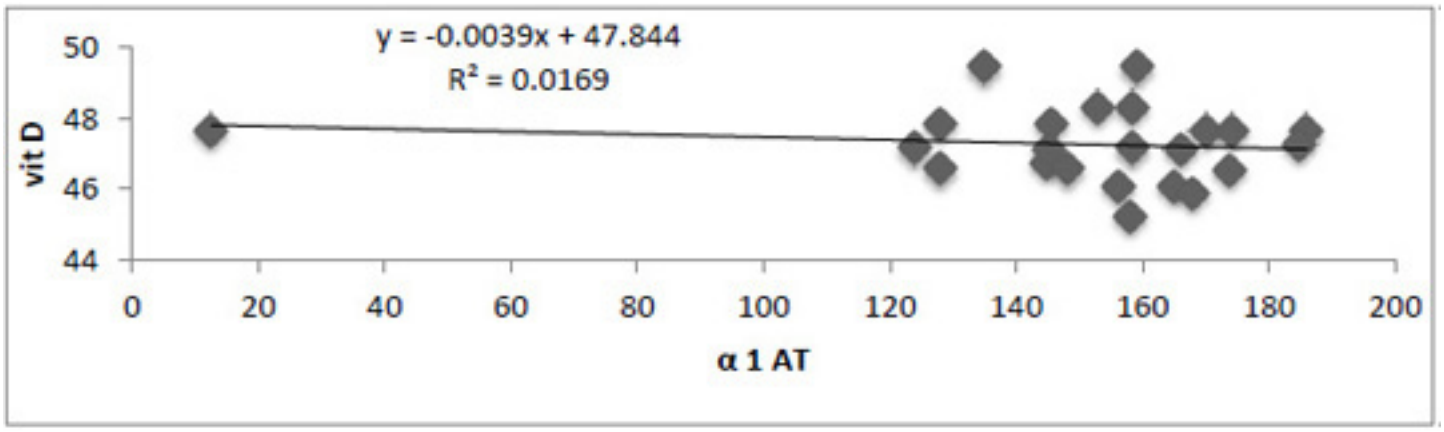

Figure 5A: Correlation relation between vitamin D and α1AT in control group

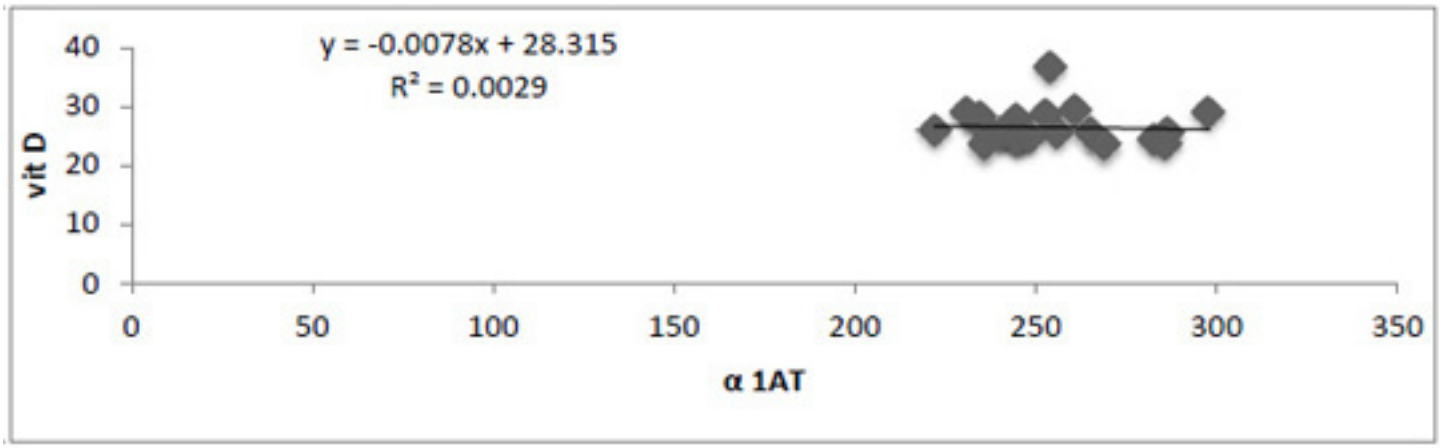

Figure 5B: Correlation relation between vitamin D and α1AT in myocardial infarction patients group

6. Correlation relation between vitamin D and CP:
Figures (6A) and (6B) showed a significant positive correlation between vitamin D and CP with P≤0.05 for control group and myocardial infarction with correlation coefficient value r (0.27), (0.17) respectively.

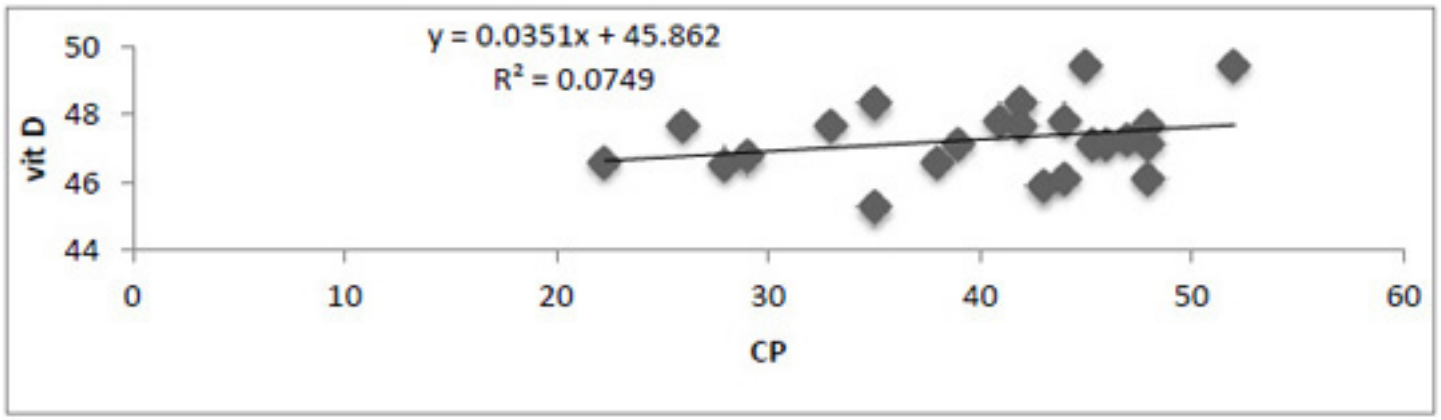

Figure 6A: Correlation relation between vitamin D and CP in control group

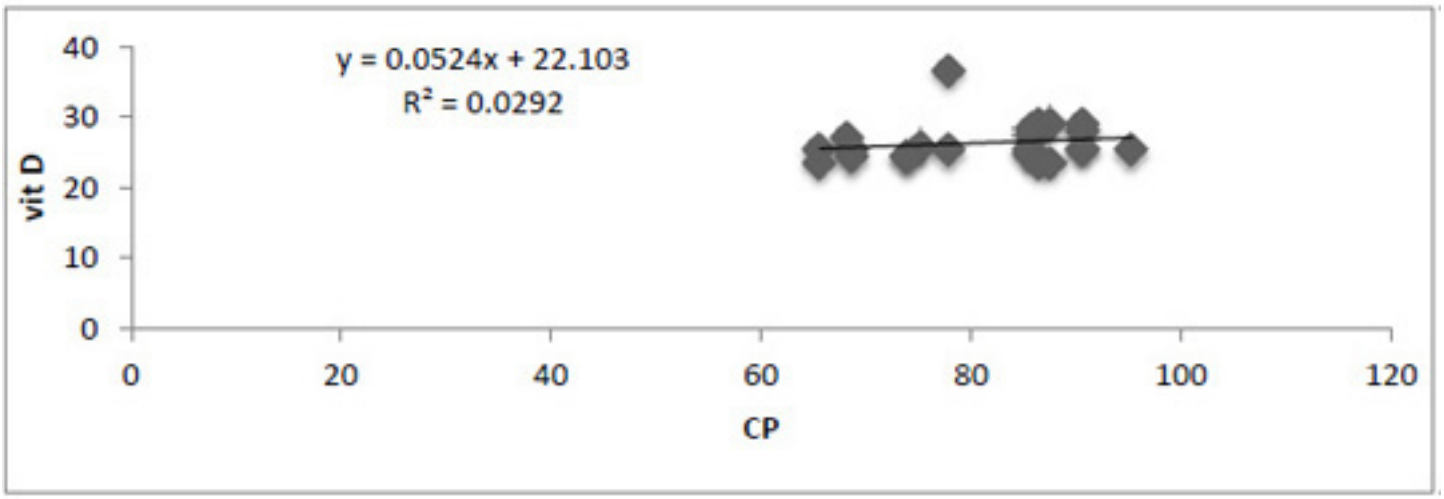

Figure 6B: Correlation relation between vitamin D and CP in myocardial infarction patients group

7. Correlation relation between vitamin D and IgA:

Figures (7A) and (7B) showed a significant negative correlation between vitamin D and IgA with P≤0.05 for control group with correlation coefficient value (-0.04) while a significant positive correlation between vitamin D and IgA with P≤0.05 for myocardial infarction group with r value(0.24).

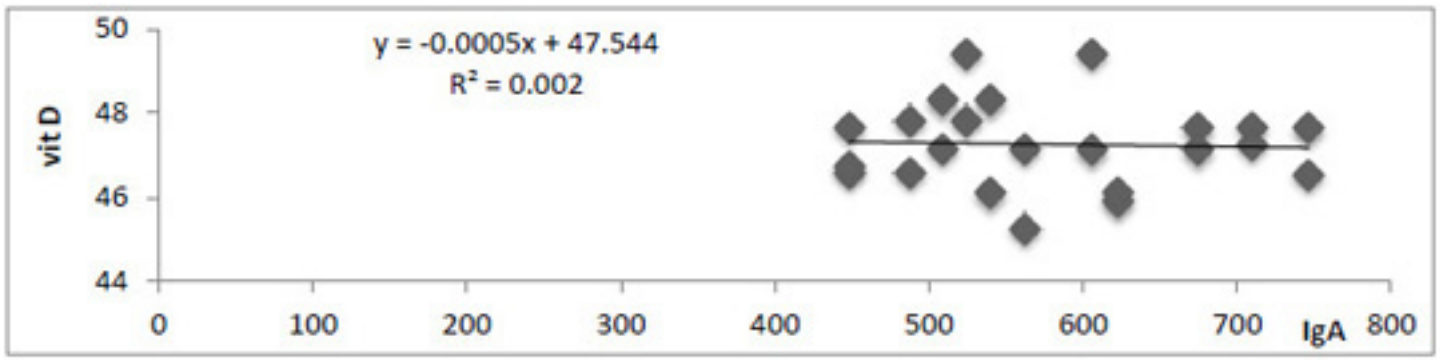

Fig (7A): Correlation relation between vitamin D and IgA in control group

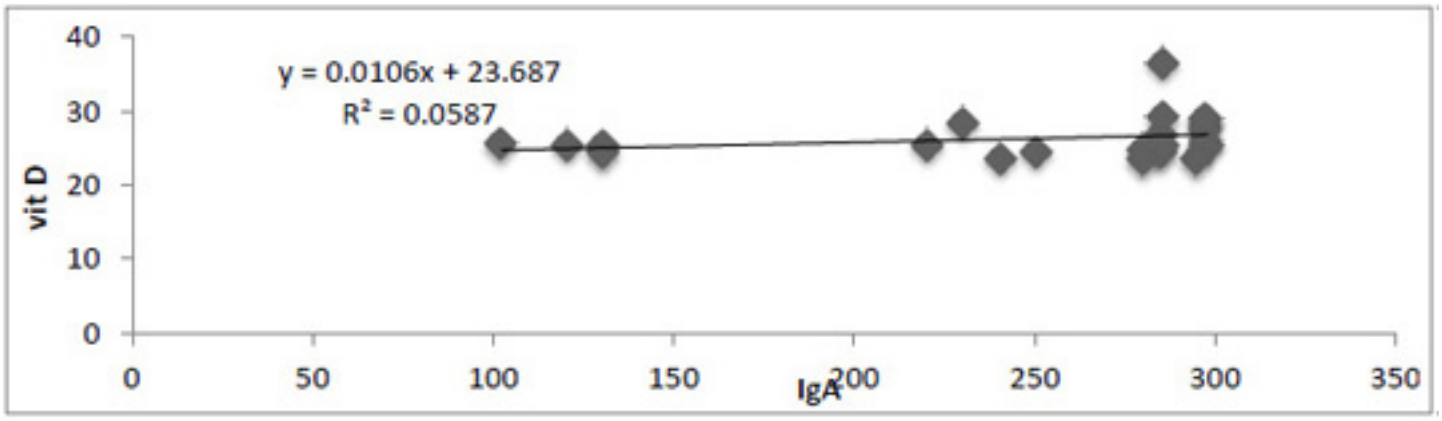

Figure 7B: Correlation relation between vitamin D and IgA in myocardial infarction patients group

8. Correlation relation between vitamin D and IgG:
Figures (8A) and (8B) showed a significant negative correlation between vitamin D and IgG with P≤0.05 for control group and myocardial infarction with correlation coefficient value r (-0.23), (-0.25) respectively.

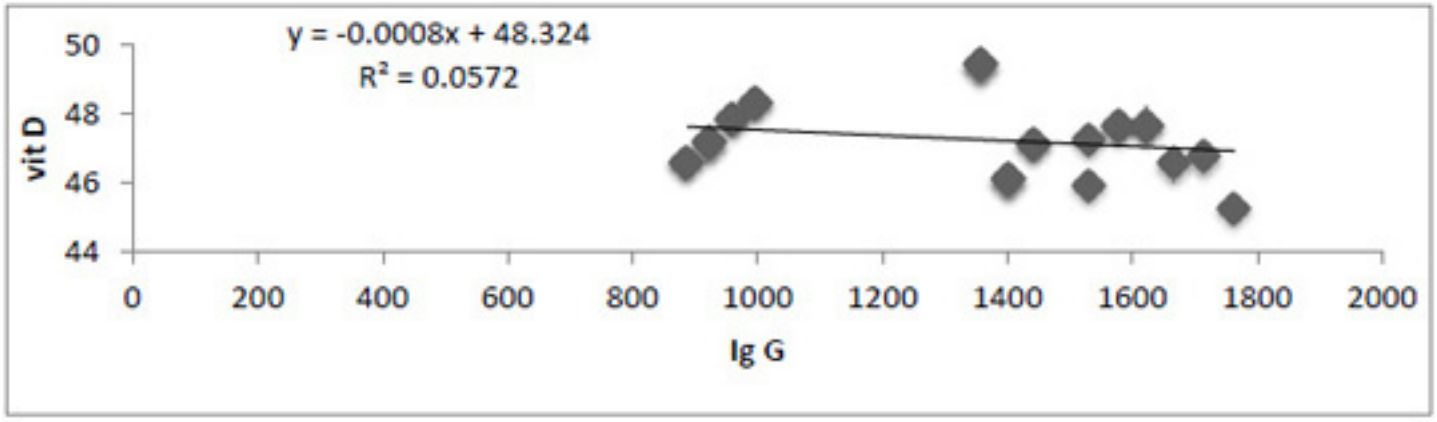

Figure 8A: Correlation relation between vitamin D and IgG in control group

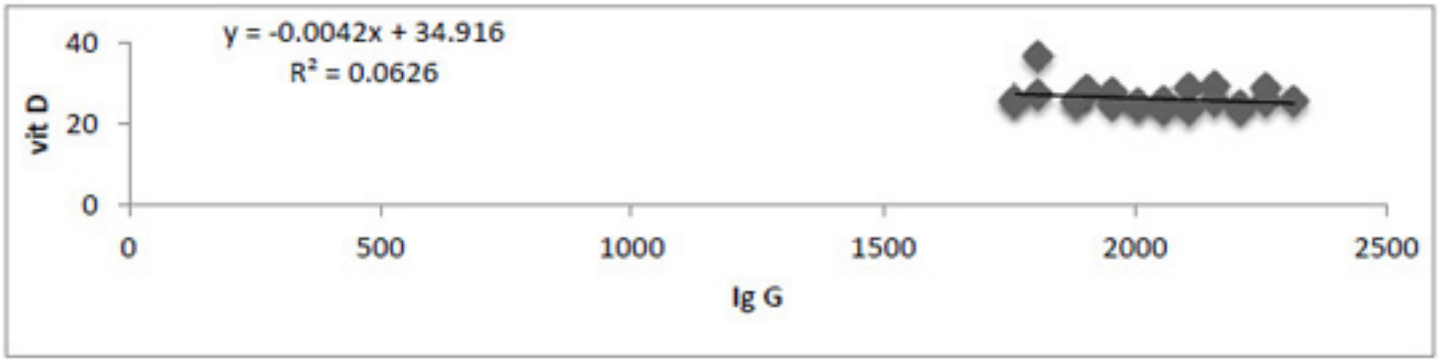

Figure 8B: Correlation relation between vitamin D and IgG in myocardial infarction patients group

9. Correlation relation between vitamin D and IgM:
Figures (9A) and (9B) (top of next page) showed a significant positive correlation between vitamin D and IgM with P≤0.05 for control group and myocardial infarction with correlation coefficient value r (0.23), (0.15) respectively.

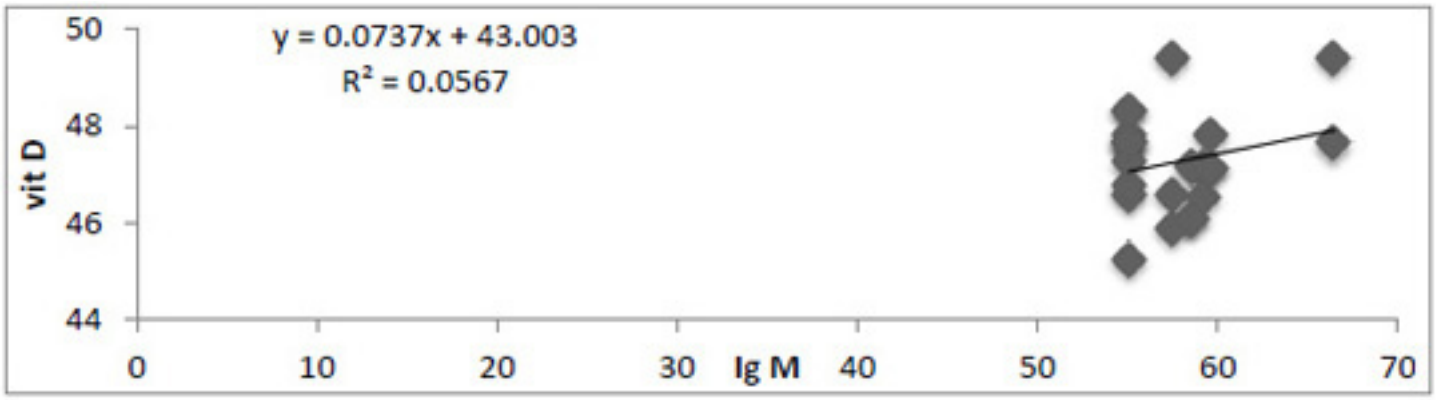

Figure 9A: Correlation relation between vitamin D and IgM in control group

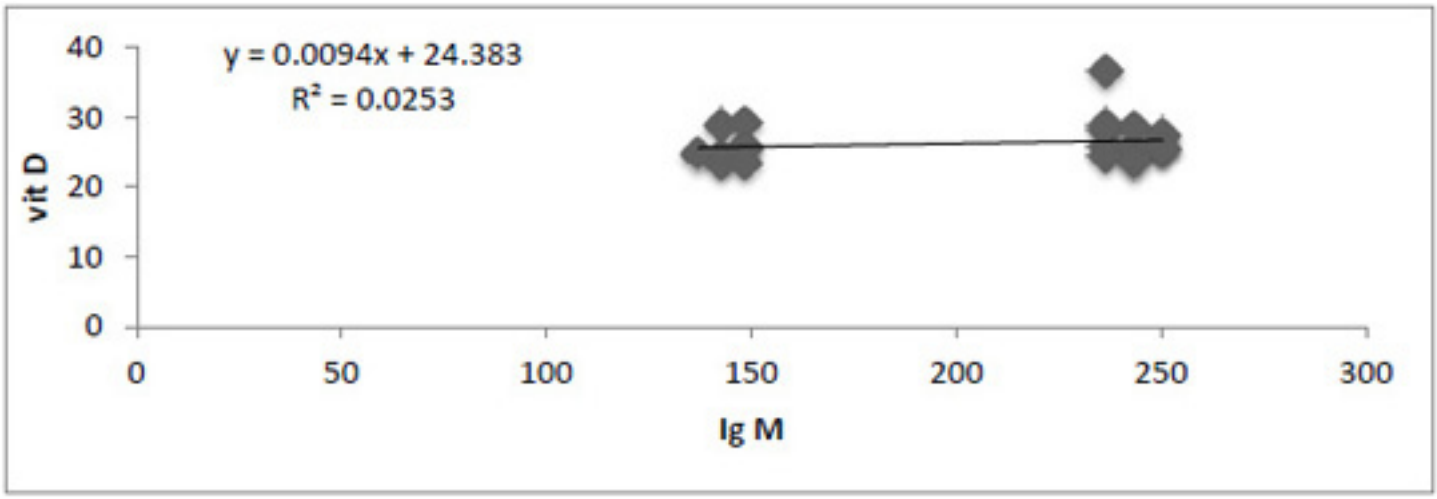

Figure 9B: Correlation relation between vitamin D and IgM in myocardial infarction patients group

References

1. Mallinson, T. "Myocardial Infarction". Focus on First Aid 15: 15 (2010)
2. Bax L, Algra A, Mali WP, Edlinger M, Beutler JJ and van der Graaf Y. Renal function as a risk indicator for cardiovascular events in 3216 patients with manifest arterial disease; Atherosclerosis ,200 (1): 184-90(2008)
3. Tan MH, Johns D and Glazer NB. Pioglitazone reduces atherogenic index of plasma in patients with type 2 diabetes; Clin Chem, 50:1184-1188 (2004).
4. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor to cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population based prospective studies. J Cardiovasc Risk;3:213-9(1996).
5. Holick M. Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. Curr Opin Endocrinol Diabetes;9:87-98(2002)
6. Norman A, Bishop J, Bula C, Olivera C, Mizwicki M, Zanello L, Ishida H, Okamura W. Transduction responses initiated by 1,25(OH)2-vitamin D3; Steroids, 67:457- 466 (2002).
7. Omdah J, Morris H and May B. Hydroxylase enzymes of the vitamin D pathway: expression, function and regulation; Annu Rev Nutr, 22: 139-166 (2002).
8. Merke J, Milde P, Lewicka S, Hugel U, Klaus G, Mangelsdorf D, Haussler M, Rauterberg E and Ritz E. Identification and regulation of 1,25-dihyroxy vitamin D3 receptor activity and biosynthesis of 1,25-dihyroxyvitamin D3. Studies in cultured bovine aortic endothelial cells and human dermal capillaries; J Clin Invest, 83:1903-1915 (1989).
9. Brown A, Dusso A and Slatopolsky E. Vitamin D; Am J Physiol, 277: (157-175) (1999).
10. Tukaj C and Wrzolkowa T. Effects of vitamin D on aortic smooth muscle cells in culture; Toxicology In Vitro, 10:701-711 (1996).
11. Shioi A, Katagi M, Okuno Y, Mori K, Juno S, Koyama H and Nishazawa Y. Induction of bone-type alkaline phosphatase in human vascular smooth muscle cells: roles of tumor necrosis factor-alpha and oncostatin M derived from macrophages; Circ Res, 91:9 -16 (2002).
12. Tietz, N.W., Fundamentals of clinical chemistry W.B. Saunders Co. Philadelphia, P.A. p. 940 (1987).
13. Poteres T Jr, The plasma Protein, NewYork, AcademicPress Inc(4th ed) pp.133-181(1975)
14. Sesmilo G et al; Ann Intern Med, 133(2):111-22 (2004).
15. Danesh J, Collins R and Appleby P. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies; JAMA, 279: 1477-1482 (1998).
16. Herpers B L, Endeman H, de Jong B A W, de Jongh B M, Grutters J C, Biesma D H, and van Velzen-Blad H. Acute-phase responsiveness of mannose-binding lectin in community-acquired pneumonia

is highly dependent upon MBL2 genotypes. Clin Exp Immunol;156(3):488-94 (2009).
17. Kabat, E.A., Wu, T.T., Bilofsky, H., Reid-Miller, M., and Perry, H. Sequences of Proteins of Immunological Interest, NIH Publication Annu Rev Immunol; 1:1 (1983).
18. Libby P and Aikawa M. Effects of statins in reducing thrombotic risk and modulating plaque vulnerability; Clin Cardiol, 26:I11-I14 (2003).
19. Moreno PR, Falk E, Palacios IF, Newell JB, Fuster V and Fallon JT. Macrophage infiltration in acute coronary syndromes: implications for plaque rupture; Circulation, 90:775-778 (1994).
20. Baker WF Jr and Bick RL. Antiphospholipid antibodies in coronary artery disease: a review; Semin Thromb Hemost, 20:27-45 (1994).
21. Petri T., Kovanen MD, Matti Mänttäri MD, Timo Palosuo MD, Vesa Manninen MD and Kimmo Aho MD. Prediction of Myocardial Infarction in Dyslipidemic Men by Elevated Levels of Immunoglobulin Classes, MD Arch Intern Med. 158(13):1434-1439(1998) .
22. Szczeklik A, Sladek K, Szczerba A and Dropinski J. Serum immunoglobulin response to myocardial infarction; Circulation ,77:1245-49 (1988).
23. Richmond.W. Preparation and Properties of a Cholesterol Oxidase from Nocardia sp. and Its Application to the Enzymatic Assay of Total Cholesterol in Serum, Clinical Chemistry . 19 (12): 1350-1356(1973)
24. Burstein, M., H. R. Scholnick, and R. Morfin.. Rapid method for isolation of lipoproteins from human serum by precipitation with polyanions. J. Lipid Res.11: 583-595.(1970)
25. Fossati, P. and Principle, L: Clin. Chem; 28: 2077 (1982).
26. Friedwald, W.T., Levy, R.I., and Fredrickson, D.S.: Clin. Chem; 18: 499-502, (1972).
27. Dobiášová M, & Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER HDL). Clinical Biochemistry 34: 583-588,2001
28. AL-Dulaimy W.Y. Study of some non-traditional roles ascribed to vitamin D include immuno-modulating effects and anti - inflammatory in sera of myocardial infarction in Iraqi patients. Thesis Submitted to the college of education for pure science Ibn Al-Haitham, University of Baghdad in partial fulfilment of the requirement for the MSc. Degree of Science in Biochemistry 2012
29. Doumas BT, Watson WA, Biggs HG. Albumin standards and measurement of serum albumin with bromcresol green. Clin Chim Acta;31: 87-96(1971)
30. Young D.S., Effect of drugs on clinical laboratory tests (4th ed). AACC press. (1995).
31. Bick, R.L., .Haematology clinical and laboratory practice. 1st Mosby, Baltimore , p.253.(1993)
32. Berne G.H. Detection of total IgG; Clin Chem, 200: 61-89 (1974).
33. Bitla AR, Pallavi M, Vanaja V, Suchitra MM, Reddy Seshadri V, Prabhakar Reddy E, Srinivasa Rao P.V.L.N. Acute Myocardial Infarction in a Southeast Indian Population: Comparison of Traditional and Novel Cardiovascular Risk Factors Research Journal of Medicine and Medical Sciences; 4(2): 202-206. (2009)
34. Berlin R, Oldfelt CO, Vikrot O. Acute myocardial infarction and plasma phospholipids levels. Acta Med. Scand, 185, 439-442.(1969).
35. Pocock SJ, Shaper AG, Philips AN, Walker M, Whitehead TP. High density lipoprotein cholesterol is not a major risk factor for ischemic heart disease. British Medical Journal 292: 515-519 (1986).
36. Goldstein JL, Hazzard WR, Schrott HG : Hyperlipidemia in coronary heart disease. J Clin Invest, 52:1533-1543. (1973)
37. Salahuddin, Karira KA, Shah SMA, et al. Serum homocysteine in patients with acute myocardial infarction. Pakistan J Cardiol, 11: 93-99(2000)
38. Watts GF, Jackson P, Mandalia S. Nutrient intake and progression of coronary artery disease. Am J Cardiol, 73: 328-332(1994).
39. Fredrikson GN, Hedblad B, Berglund G, Alm R, Ares M, Cercek B, Chyu KY, Shah PK and Nilsson J. Identification of immune responses against aldehyde-modified peptide sequences in apoB associated with cardiovascular disease; Arterioscler Thromb Vasc Biol, 23:872-878 (2003).
40. Dyerberg J, Bang, H.O. and Neilsen, J.A. Plasma lipids and lipoproteins in patients with myocardial infarction and in a control material. Acta Med. Scand, 187: 353-359(1970).
41. Bjorntrop P, Malmcrone R. Serum cholesterol in patient with myocardial infarction in younger ages. Acta Med Scand, 168: 151-155. (1960)
42. Hargreaves AD, Logan RL and Thomson M: Total cholesterol, LDL-Ch and HDL-Ch and coronary heart disease. BMJ: 303.678 (1991).
43. Natio HK. The association of serum lipids, lipoproteins and apolipoproteins with coronary artery disease assessed by coronary arteriography. Ann. N.Y. Acad. Sci: 454, 230-238(1985).
44. Heldenburg D, Rubenstein A, Levtov 0, Berns L, Werbin B, Tamir L. Serum lipids and lipoprotein concentrations during the acute phase of myocardial infarction. Atherosclerosis:35. 433-437(1980
45. Zampogna A, Luria MH, Mancibens SJ, Luria MA. Relationship between lipids and occlusive coronary disease. Arch. Intern Med, 140:1067-1069(1980).
46. Sandkamp M, Funke H and Schulte H : Lipoprotein (a) is an independent risk factor for myocardial infarction. Clin Chem; 36: 20-23(1990).
47. Kromhout D: Body weight, diet and serum cholesterol in middle aged men during 10 years follow up. Am J Clin Nutr: 38: 591-598 (1983).
48. Lawrence A. Kaplan, Amado J. Pesce and Steven C. Kazmierczak. Coronary artery disease and disorders of lipid metabolism. Clinical chemistry: theory, analysis, correlation. Mosby Inc., St Louis, USA. ISBN 4th ed pp(610-615) (2003).
49. Katwan OJ: Study of the relationship between lipid peroxidation and serum trace elements, lipid profile and tissue damage in patients with acute ischemic heart disease. Msc thes: Ibn Al-Haitham College, University of Baghdad. 1999

50. Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL and Buring JE. Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction.; Circulation, 96:2520-5 (1999).
51. Judd SE and Tangpricha V. Vitamin D deficiency and risk for cardiovascular disease; Am J Med Sci,338: 40-44 (2009).
52. London GM, Guerin AP and Verbeke FH. Mineral metabolism and arterial functions in end-stage renal disease: potential role of 25-hydroxyvitamin D deficiency; J Am Soc Nephrol,18: 613-620 (2007).
53. Targher G, Bertolini L and Padovani R. Serum 25-hydroxyvitamin D3 concentrations and carotid artery intima-media thickness among type 2 diabetic patients; Clin Endocrinol (Oxf),65: 593-597 (2006).
54. Wang TJ, Pencina MJ and Booth SL et al. Vitamin D deficiency and risk of cardiovascular disease; Circulation, 117: 503-511 (2008).
55. Schleithoff SS, Zittermann A, Tenderich G, Berthold HK, Stehle P and Koerfer R. Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: a double-blind, randomized, placebo-controlled trial; Am J Clin Nutr, 83: 754-759 (2006).
56. Rahman A, Hershey S, Ahmed S, Nibbelink K and Simpson RU. Heart extracellular matrix gene expression profile in the vitamin D receptor knockout mice; J Steroid Biochem Mol Biol,103: 416-419 (2007).
57. Li YC, Qiao G, Uskokovic M, Xiang W, Zheng W and Kong J. Vitamin D: a negative endocrine regulator of the renin-angiotensin system and blood pressure; J Steroid Biochem Mol Biol : 89-90: 387-392 (2004).
58. Lappe J.M., Travers-Gustafson D., Davies K.M., Recker R.R. and Heaney R.P., Vitamin D and calcium supplementation reduces cancer risk: Results of a randomized trial; Am J Clin Nutr ,85: 1586-1591 (2007) .
59. Watson KE, Abrolat ML, Malone LL et al. Active serum vitamin D levels are inversely correlated with coronary calcification; Circulation, 96(6):1755 1760 (1997).
60. Maghbooli Z, Hossein-Nezhad A, Karimi F, Shafaei AR and Larijani B. Correlation between vitamin D3 deficiency and insulin resistance in pregnancy; Diabetes Metab Res Rev, 24(1):27-32 (2008).
61. Zittermann A, Dembinski J and Stehle P. Low vitamin D status is associated with low cord blood levels of the immunosuppressive cytokine interleukin-10; PediatrAllergy Immunol, 15(3):242-246 (2004).
62. Reichert TA, Simonsen L, Sharma A, Pardo SA, Fedson DS and Miller MA. Influenza and the winter increase in mortality in the United States; Am J Epidemiol, 160(5):492-502 (2004).
63. Aloia JF, Li-Ng M. Re: epidemic influenza and vitamin D; Epidemiol Infect, 135(7):1095-1096 (2007).
64. Kamen DL, Tangpricha V. Vitamin D and molecular actions on the immune system: modulation of innate and autoimmunity; J Mol Med,88: 441-450 (2010).
65. Mehta S, Giovannucci E and Mugusi FM. Vitamin D status of HIV-infected women and its association with HIV disease progression, anemia, and mortality; PLoS ONE,5: 8770 (2010).
66. De Luis DA, Bachiller P and Aller R. [Relation among micronutrient intakes with CD4 count in HIV infected patients]; Nutr Hosp,17: 285-289 (2002).
67. Arpadi SM, McMahon D, and Abrams EJ. Effect of bimonthly supplementation with oral cholecalciferol on serum 25-hydroxyvitamin D concentrations in HIV-infected children and adolescents; Pediatrics,123: 121-126 (2009).
68. Mueller NJ, Fux CA and Ledergerber B. High prevalence of severe vitamin D deficiency in combined antiretroviral therapy-naive and successfully treated Swiss HIV patients; AIDS,24: 1127-1134 (2010).
69. Ziliva J.F. Clinical chemistry in diagnosis and treatment 4thed. Lloyd-Luke (medical books) LTD London, p.337 (1984).
70. Zilva P.M. and Philip D.M."Clinical chemistry in diagnosis and treatment" 6th ed. pp. 159-160 (2002).
71. Ryffel B., Car B.D., and Woerly G. Long-term interleukin-6-administration stimulates sustained thrombopoiesis and acute- phase protein synthesis in a small primate-the marmoset; Blood, 83: 2093-2102 (1994).
72. Keating K., Smith T., Gehan E., Merdie K., Bodey G., and Freireich E. A prognostic factor analysis for use in development of predictive models for response in adult acute leukemia; Cancer, 50: 457-465 (1982).
73. National Heart, Lung, and Blood Institute Fact Book. US Department of Health and Human Services Monograph. pp(30- 52) (1995).
74. Farmer JA and Gotto AM Jr. Dyslipidemia and other risk factors for coronary artery disease. In: Braunwald E, editor. Heart Disease: A Textbook of Cardiovascular Medicine. 5th ed. Philadelphia: WB Saunders, pp1126- 160 (1997).
75. Maseri A; Inflammation, atherosclerosis, and ischemic events-exploring the hidden side of the moon; N Engl J Med, 336:1014-6 (1997).
76. Pietila K, Marmoinen A, Hermens W, Simoons ML, Van de Werf F and Verstraete M. Serum C-reactive protein concentration in myocardial infarct patients with a closed versus an open infarct-related coronary artery after thrombolytic therapy; Eur Heart J, 14:915-9 (1993).
77. Thompson SG, Kienast J, Pyke SDM, Haverkate F and van de Loo JCW. Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris; N Engl J Med,332:635- 41 (1995).
78. Ridker PM, Cushman M, Stampfer MJ, Tracy RP and Hennekens CH. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men; N Engl J Med, 336:973-9 (1996).
79. Grayston, J. T., Aldos, M. B., Easton, A., Wang, S.-P., Kuo, C.-C, Campbell, L. A., Evidence that Chlamydia pneumoniae causes pneumonia and bronchitis. Journal of Infectious Diseases 168: 1231-5 (1993).
80. Libby P and Aikawa M. Effects of statins in reducing thrombotic risk and modulating plaque vulnerability; Clin Cardiol, 26:I11-I14 (2003).
81. Pepys MB, Hirschfield GM. C-reactive protein: a critical update; J Clin Invest, 111:1805-1812 (2003).
82. Van DM, I, De Maat MP, Hak AE, Kiliaan AJ, Del Sol AI, Van Der Kuip

DA, Nijhuis RL, Hofman A and Witteman JC. C-reactive protein predicts progression of atherosclerosis measured at various sites in the arterial tree: the Rotterdam Study; Stroke, 33:2750 -2755 (2002).
83. Hansson G. K. Cell-mediated immunity in atherosclerosis; Curr. Opin. Lipidol, 8: 301-311 (1997)
84. Ross R. Atherosclerosis an inflammatory disease; N Engl J. Med, 340: 115-126 (1999).
85. Puurunen M., Masnttas M. and Manninen V. Antibody against oxidized low-density lipoprotein predicting myocardial infarction. Arch. Intern. Med. 154, pp 2605-2609 (1994).
86. De Scheerder IK, De Buyzere M, Delanghe J, Maas A, Clement DL and Wieme R. Humoral immune response against contractile proteins (actin and myosin) during cardiovascular diseases; Eur Heart J,12:88-94 (1991).
87. Hansson GK and Libby P. The immune response in atherosclerosis: a double-edged sword; Nat Rev Immunol. 6:508-519 (2007).
88. Fredrikson GN, Hedblad B, Berglund G, Alm R, Ares M, Cercek B, Chyu KY, Shah PK and Nilsson J. Identification of immune responses against aldehyde-modified peptide sequences in apoB associated with cardiovascular disease; Arterioscler Thromb Vasc Biol, 23:872-878 (2003).
89. Weatherland, D, Clegg, J, Higgs, D and Wood, W., The hemaglobinopathies in: The metabolic basis of inherited disease ; 8thed. Mc. Graw-Hill, pp. 4000-4656(2000)
90. Michael. L. Bishop, Edward, P., Fody, Larry Schoeff., “Clinical chemistry, principle, procedures, correlation” fifth edition. Lippincott Williams and Wilkins pp. (194-195), pp:270-286 (2005) .

The Relation between Students' Socio-Economic Status, Internet Use Mode and Attendance on Success Rate in Medical College

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Abstract

Background: Success is an important indicator in the college; many factors influence it.
Objective: To find out the effect of Internet use, socioeconomic status and attendances upon success in the medical college in 2012.

Students and Method:
Students: 396 from Al-kindy College of Medicine.
Type of study: Ambi-directional cohort.
Method: Four classes of college students were asked about mode of use of internet and socio-economic status; then attendance rate, sleep, visual problems and final degree score of the two years, were reviewed.
Study period: 15th December 2010- 30th to May 2012.
Statistical analysis: Microsoft excel 2007, Minitab program, the significance level was P<0.05.

Results and Discussion:
Socio-economics play a role in success but no statistical difference was found; use of internet for studying had less failure rate than those who used it for entertainment. This difference was significant. Vision and sleep impairment increases with excessive use of internet. Regularly attending classes lead to success. This result isin consistent with many studies.

Conclusion: attendance and wise use of internet will improve scoring.

Key words: Success rate, attendance rate, internet use, socio-economic status

Introduction

As university academics most of us would agree that there is a link between socio-economics, mode of use of internet and student attendance at classes and eventual success. What is less clear however, is how strong is that association? (1)

Internet has been used as one of the most universal tools for communication, information, chatting, sending emails, downloading files and music, etc (2). While time spent on the Internet can be hugely productive for studying (3), some students use Internet for long periods, causing a decrease in hours of studying leading to decline in students' marks, and it also may lead to loss of concentration and may cause dry eyes (4-5-6).

It is clear that a Medical student's life is not an easy one; also they may come from different socioeconomic levels, or classes, and of course the time he/she spends for studying takes the biggest share of available time. All of the research reviews support the hypothesis that student performance depends on socio-economic, psychological, and environmental factors.(7)

Lifestyle modality may affect student performance; recent findings indicate that short sleepers (less than 7 hours per day), as compared to long sleepers (9 hours and more per day), were more psychologically maladjusted, anxious, less creative, more neurotic, and more prone to hallucinate (8).
And this may play a negatively association with educational performance. (9)

It is obvious that class attendance is the best teaching method for any student, to improve communication, obtain new current knowledge and information, and hear comments especially in medicine. The students who had missed a lecture because they did not 'think it was worth going to had lower efficiency and passing rates (10).

This Study was conducted to uncover some factors that may affect success.

Students and Method

Students: 396 students from four different classes at Al-kindy College of Medicine, were enrolled in the study.
Type of study: Ambi- directional cohort.
Study period: 15th December 2010-30th May 2012.
Methods: After agreement from the scientific and ethical committee. well defined college students were assessed in the beginning of the study and then followed for two academic years. Base line data was obtained when study started and there was another review after the end of the second academic year.

Base line data included:
Questionnaire adapted and approved from the community department in Al-Kindy College of Medicine, University of Baghdad for the area of the study. Also approval of the ethical and scientific committee of the college was taken.

1. Measuring socioeconomic status: a questionnaire was distributed among the students; the questionnaire was taken from the WHO site, which divides the socioeconomic status into 3 categories.
- High, middle and low (through measuring the parent's level of education and occupation).

2. Measuring internet use and mode, questions regarding internet use
- For studying.
- For entertainment.

The respondents were classified according to the hours spent on internet the previous year or who did not use it.
- Occasionally (7 hours weekly or less).
- Commonly (more than 7 hours per week).

3. Measuring sleeping hours.
- Positive effect means (sleeping less than 6 hours per day)
- No effect means (sleeping more than 6 hours per day).

The second look at the cohort includes the following data:-
1. Measuring attendance, (regular and irregular).
- Regular attendance means no absenteeism from attending the classes throughout the academic year.
- Irregular attendance means the rate of absenteeism more than 5%)

2.Measuring impairment of vision by asking if he/she wears or changes his/her glasses.
3. Measuring the success: the students were divided according to their grades (succeeded and failed).
- Failed: means the final score was less than 50%
- Succeed: means the final score was more than 50%.
- 1-20 rank means the first 20 successful students according to their marks.

4. This information was taken from the registration unit of the college.

Statistical analysis: Microsoft excel 2007, Minitab v.17 program were used, the significance level was set at $P<0.05$.

Results

Success	Rank 1-20		Passed		Failed		Total	
SES	no	%	no	%	no	%	no	%
High	59	15	87	22	40	10	186	47
Middle	36	9	79	20	55	14	170	43
Low	12	3	20	5	8	2	40	10
Total	107	27	186	47	103	26	396	100

P = 0.074
Table 1: Classification of students according to socioeconomic status and success

Success	Rank 1-20		Passed		Failed		Total	
Internet use mode	no	%	no	%	no	%	no	%
Internet use for studying	67	17	95	24	24	6	270	68
Internet use for Entertainment	40	10	91	23	79	20	126	32
Total	107	27	186	47	103	26	396	100

P=0.001
Table 2: Relationship between Internet use mode and success

Internet use	Effect on vision					
	yes		no		total	
	no	%	no	%	no	%
occasionally	22	18	105	82	127	32
commonly	122	45	147	55	269	68
Total	144		192		396	100

P = 0.012; * Wear glasses during the study period

Table 3: Internet effect on vision*

Internet use	Effect on sleep					
	yes		no		total	
	no	%	no	%	no	%
occasionally	66	52	61	48	127	32
commonly	199	74	70	26	269	68
total	265		131		396	100

P = 0.028

Table 4: Internet effect on sleep

Internet use	Gender					
	Male		Female		total	
	no	%	no	%	no	%
occasionally	66	52	61	48	127	32
commonly	159	59	110	41	269	68
total	195		171		396	100

P = 0.081

Table 5: Comparison between Males and Females regarding Internet use

Success	Succeeded *		failed		total	
attendees	no	%	no	%	no	%
regular	269	68	103	26	372	94
irregular	24	6	0	0	24	6
total	293	74	103	26	396	100

P =0.012

*Mean rank 1-20 and pass

Table 6: The relationship between attendance and success

Discussion

Medical students face numerous stressors; of course medical study is difficult, and socioeconomic status (SES) adds to these factors which may implicate more troubles for some of them.

It seems that SES plays a role concerning students' success. This finding comes with consistence with other studies that concluded that there is a direct and indirect effect of SES on academic output (11))(12)(13)(14). This study shows that effect: high SES students earn higher scores; compared to low SES, but this difference is not statistically significant. This can be explained by higher education being free in Iraq (Iraqi constitution 2004). The students and families pay nothing for all academic courses, free books, housing to students; further some students may obtain some economic help from their colleges (15). These incentives may play a role in decreaseing the effect of SES;, conversely some studies agree that there is no effect of SES (16).

Almost the majority of studies conclude that internet use has a direct effect on decrease or increase of student's success.

The bi-phase of its use (17, 18).

In this study and for better understanding the real effect of internet use, we classify the use mode into two parts. Firstly use for studying which seems to have a positive and statistically significant effect on success rate as seen in Table 2, (18) and it can be called Internet-enriched teaching and learning.

On the other hand faulty use may impair success rate as seen in Table 3, but there is but no statistically significant relationship (19).

In this study we throw a light on the indirect effect of internet use which seems that it effects on sleep pattern and vision with a highly significant result (Tables 4,5) (pathological effect). This result is consistent with a lot of studies (20-21). These results are strong evidence of the indirect effect of internet use, which consequently may impair success.

Regarding gender difference, it seems that Iraqi students follow the Asian pattern, in which there are no clear differences between both sexes (22). But Shu suggested in his study that boys were more addicted to Internet than girls (with there being three male addicts for each female addict). (23).
Some medical class attendance is not mandatory (24), but there is an overall agreement that regular attendance will definitely improve academic performance. This study runs parallel with this theory with a high statistical significance p=0.001, missing classes consequently decreases success rate (25).

Crone also stated “As we noted in past reports, there is a direct correlation between attendance and academic achievement. Students who go to class invariably do better in school and maximize their chances for success down the road.” (26, 27).

In conclusion success in Iraqi medical college needs good SES environment, attendees, and wise use of internet, enough sleeping hours, which will definitely improve academic performance.

References

1- Nicola Hughes (The link between attendance and Foundation Year success). A journal for international foundation programmed professionals, Manchester university Learning and Teaching in Action. LTiA vol 8 Issue 1(April 2009).
2- Essay on Internet Addiction by Andrew Wamae. Centre for Internet Addiction. A Growing Epidemic. Retrieved on 29th September 2011 from http://www.netaddiction.com/.
3- Joanna Saisan, M.S.W., Melinda Smith, M.A., Lawrence Robinson, and Jeanne Segal, Ph.D. Internet addiction treatment and self-help. Association for Behavioral and Cognitive Therapies January 2012.
4- Anna Cocke : May 29, 2010 http://www.livestrong.com/article/134688-internet-addiction-health-effects/.
5- Scherer, K. (College life online: Healthy and unhealthy Internet use). Journal of College Student Development, (1997). 38(6), 655-665
6- Choi K, Son H, Park M, Han J, Kim K, Lee B, Gwak H. (Internet overuse and excessive daytime sleepiness in adolescents). Psychiatry Clin Neurosci. 2009;63:455-462
7- Syed Tahir Hijazi and S.M.M. Raza Naqvi, Mohammad Ali Jinnah (FACTORS AFFECTING STUDENTS’ PERFORMANCE A Case Of Private Colleges)., Pakistan. Bangladesh e-Journal of Sociology. Volume 3. Number 1. January 2006.
8- Kelly, William E. (Sleep-Length and Life Satisfaction in a College Student Sample). College Student Journal, College Student Journal v. 38 no ,. 3 (September 2004) p. 428-30, 2004.
9- John Deweys (concept of student) Canadian journal of education26,3(2001):183-200.
10- J. Esteban Fernández Rico, Samuel Fernández Fernández, Alberto Álvarez Suárez, Pablo Martínez Camblor. (The Importance of University Lecture Attendance). The Annual Teaching Survey for the 2003/2004 academic year
11- Christenson, Sandra L.; Rounds, Theresa; Gorney, Deborah (Family factors and student achievement: An avenue to increase students’ success). School Psychology Quarterly, Vol 7(3), 1992, 178-206.
12- Paul DiMaggio. Cultural Capital and School Success: The Impact of Status Culture Participation on the Grades of U.S. High School Students. American Sociological Review. Vol. 47, No. 2 (Apr., 1982), pp. 189-201.
13- Anthropology & Education Quarterly Volume 21, Issue 4, pages 358-377, December 1990
14- Erik Porfeli, Chuang Wang, Robert Audette, Ann McColl ,Bob Algozzine. Influence of Social and Community Capital on Student Achievement in a Large Urban School District. Education and Urban Society November 1, 2009 42: 72-95
15- Iraqi constitution 1980.
16- John Jerrim, John Micklewright, Institute of Education, University of London. Children’s education and parents’ socio-economic status: distinguishing the impact of mothers and fathers. August 2009 1:
17- Shields, N., & Kane, J. (2011). Social and Psychological Correlates of Internet Use among College Students. Cyberpsychology: Journal of Psychosocial Research on Cyberspace, 5(1), article 1.
18- Hong, K.-S., Ridzuan, A. A., & Kuek, M.K. (2003). Students’ attitudes toward the use of the Internet for learning: A study at a university in Malaysia. Educational Technology & Society, 6(2), 45-49, (ISSN 1436-4522).
19- Aryn Karpinski; “Does the Facebook site affect the students’ academic work”, Education department at Ohio State University, 2009
20- Unnikrishnan B, Kulshrestha V, Saraf A, Agrahari A C, Prakash S, Samantaray L, Parida A. Pattern of computer and internet use among medical students in Coastal South India South East Asian Journal of Medical Education Volume: 10 Issue 2: May 2, 2007 . P18-22.
21- Dr. Fatih Bayraktar and Zübeyit Gün. CyberPsychology & Behavior. Incidence and Correlates of Internet Usage Among Adolescents in North Cyprus . April 2007, 10(2): 191-197..
22- Nai Li A, Gill Kirkup, Gender and cultural differences in Internet use: A study of China and the UK. Computers & Education 48 (2007) 301-317
23- Shu Ching Yang, Chieh-Ju Tung. Comparison of Internet addicts and non-addicts in Taiwanese high school Graduate Institute of Education, National Sun Yat-sen University, 70 Lien-hai Road, Kaohsiung, 80424. Taiwan, ROC. Available online 27 April 2004.
24- Medicine From The Trenches Theme: Andreas04 by Andreas Viklund. Blog at WordPress.com.

19 January, 2011 Posted by drnjbmd | academics, medical school coursework,
25- Gottfried, Michael A. Evaluating the Relationship between Student Attendance and Achievement in Urban Elementary and Middle Schools: An Instrumental Variables Approach. American Educational Research Journal, v47 n2 p434-465 2010 .
26- Crone,-Linda-J.; An Examination of Attendance in Louisiana Schools. Paper presented at the Annual Meeting of the Mid-South Educational Research Association (22nd, New Orleans, LA, November 10-12, 1993).
27- Ziomek-Robert L.; Schoenenberger, William J. Achievement as Related to Program and School Attendance. Elementary-School-Journal; v84 n2 p232-40 Nov 1983

Health System Development and Mortality Transitions in Libya

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Abstract

Introduction: Transition in mortality is an important indication of progress in public health and a precondition for medical interventions and health system development. Developing countries are always said to be lagging behind in terms of demographic transition. This statement undermines experiences of some developing countries, especially those in the Arab Region. Almost all Arab countries have made substantial reduction in mortality. An Arab country located on the north of Africa, The Great People's Arab Libyan Jamahiriya (Libya) sets an ideal example of improved mortality and a health service delivery system among developing countries. Recent political developments have disrupted the health setup, which depended on the Libyan People's Congresses. But a similar setting is emerging in the country with the new political and administrative governance taking lessons from experiences.

Objectives: This paper attempts to review mortality in Libya through tracing the routes, reviewing underlying factors and examining the contribution of Government and other public health institutions.
Methodology: This paper makes use of national statistics on major mortality indicators viz., crude death rate, infant mortality rate, under 5 mortality rate, maternal mortality rate and expectation of life at birth since 1950.

Results: A remarkable change in mortality has been observed, which had a clear relation with improvement in health service delivery systems. A strong political will coupled with stability of governance have contributed to this improvement. A few international organizations and regional and national agencies have also contributed to this trend. Recent events have affected the system, overloading emergency services.

Conclusions and Implementations: These achievements from an experimental people-based health system development have to be treated scientifically through information base for contributing to changes in health delivery systems and also for accelerating progress in the future. Learning from experiences of the previous experimental people's congress oriented health service delivery shall take the system to further health gains.

Key Words: Infant Mortality, Overall Mortality, Life Expectancy, Spatial Distribution, Grass Root Level Planning

Introduction

Mortality trends are the most researched component of population dynamics. An understanding of mortality levels and trends becomes challenging when there are not adequate data to enable comparisons over years and also among different population groups. Disparity in data provided by a single source for a specific region also occurs. Such disparities not only confuse but also create a vacuum in understanding national demographics and lead to difficulties in health planning.

In this paper, an attempt is made to analyze mortality change in Libya in terms of crude death rate (CDR), infant mortality rate (IMR), life expectancy at birth (e00), under 5 mortality rate (<5 MR) and maternal mortality rate (MMR). Statistics on the above indicators have been collected from population surveys, national censuses and vital registrations and also from international databases. Until recently mortality decline occurred against a background of spatial distribution of population, educational improvement and grass root level planning. Gains in population health, were based on policy development and program planning in an experimental people's democracy (with dictatorial leadership) which set in place local level secretariats and peoples' congresses, who planned, organized, directed and controlled health activities. Recent developments in Libya, including political uprising and change in governance - resulted in exacerbated mortality, diseases, disabilities and deprivations, substantially reversing earlier gains. Still, the earlier experiments add value in building not only the future Libyan Health System following democratic (people oriented) governance but also of emerging nations in the Arab World.

Mortality statistics reflecting levels and trends are useful in community health interventions for (i) comparing issues across geographic areas (ii) assessing health needs and fixing priorities to reduce risk (iii) remodeling and strengthening health services (iv) evaluating health programs (v) measuring relative importance of specific diseases leading to death and (vi) assessing efficacy of drugs and clinical and therapeutic trials against fatal diseases. It might also facilitate addressing discrimination in healthcare, as specified by WHO (cited in Krug, 2002) (1), and to institute routine monitoring programs. Statistics relating to population are of use to improve management and quality of healthcare (2).

Mortality transition has a close link with health system performance and the sectors that determine health status and health care of the population. Factors inherent in the health system, namely economics, technology, public health, knowledge about health; all paved the way for unprecedented mortality decline during the last century (3). This paper explores mortality transition and its linkages with health system strategies in Libya.

Mortality Decline

The Libyan Arab Jamahiriya is a nation of large geographical area with a small population and located on the North African shore of the Mediterranean Sea. The country has undergone several changes in the recent years, from a relatively poor desert land having the lowest standards of living in the world to one of the world's leading oil producing nations (4), thereby having an improved standard of living. Recent developments in political governance and freedom from the dictatorship are also of note in this context. Demographic changes in Libya have been dramatic especially after revolution in 1969. The country experienced a rapid increase in population due to the natural increase, which may further accelerate in current independent democratic Libya.

Medical schools and other medical and health related schools were affiliated to general and specialized hospitals, health services institutions and research institutions in order to enhance technical competency of professionals, prior to independence. During the time, social security was guaranteed to all citizens in case of old age, disability, sickness, unemployment, accident, work related illnesses, disasters, maternity etc. Such welfare measures which were aimed at supporting people in need had promoted health status of the population through improving quality of life. Health policies provided frameworks for health strategies and were aimed at delivering services to all citizens to achieve a comprehensive and uniform distribution of health services. National health policy was aimed at 'health for all by all', through creating a society in which every member played an active role both socially and economically. Thus paving the way for implementing primary health care along the lines of the Popular Committee of Health and Environment's vertical programs for TB, school health etc.

As the population carries forward their disabilities and disasters due to recent war, the health system will face immense challenges. The new government, with a focus of democratic freedom, could create a system different from that practiced earlier.

Reducation in Overall Mortality during 1965-2005

Statistics relating to vital events were rarely consolidated which restricted their use for public health interventions. Various national and international attempts reflected a trend of decline in crude death rate from a high of 16 in 1970 to a low of 3.1 in 2005; even though there were differences in estimates given by the National Statistical Group, UNICEF and Libya Forum. Still one can clearly see high mortality till 1970 and its year wise declining trend afterwards.

Mortality rates fluctuated until the 1990s but had stabilized thereafter for a clear decline. There was agreement that it reached a level of around 3 per 1000 population by 2005. That was a remarkable achievement which was commendable in the Arab region.

Crude death rates that consider deaths without any effect of

Year	CDR	Source
1965	4.4	
1967	6.37.3	
1969	8.1	
1974	5.6	
1979	7.0	The Office of Census and Statistics (5)
1984	7.0	
1989	3.3	
1994	3.3	
1999	2.6	
2004	3.1	
2005		
1970	16.0	UNICEF, 2004 (6)
1990	5.0	
2005	4.0	
2002	3.5	Libya Forum 2007 (7)
1973	13.90	
1978	8.99	
1983	5.99	
1988	4.57	US Census Bureau, International Database (8)
1993	3.72	
1998	3.52	
2003	3.49	
2007	3.47	
2000	3.51	
2005	3.48	CIA World Fact Book, 2007 (18)
2011	3.40	
2012	3.41	

Table 1: Crude death rate (per 1000 population) in Libya 1965-2005

deaths without any effect of associated factors, reflect deaths occurring in the total population. Recent developments followed by political uprising caused a rise in mortality rates. Estimates show total deaths of 23,000 during the year, giving rise to a CDR of 3.41, however field-level reports by media show total deaths approximating 50,000 during 2011 as the result of war. While adding this number to that of other deaths, CDR rises to 10 per 1,000.

Infant Mortality Changes during 1960-2006

While infectious diseases continued to be the major cause of infant mortality in developing countries, in Libya birth defects accounted for a significant percentage. Infant mortality had declined noticeably in Libya and had reached a level of around 20 infant deaths per 1000 live births. This decline had been from a high of 159 in 1960. This marked a decline of 87 percent during the last 45 year period. A higher proportion of this decline was achieved before 1990, marking the period 1960-1990 as crucial. The 1960-80 period was the most crucial. The period of 1980-90 witnessed a decline of around 20 points, whereas that in the next decade (1990-2000) was around 17 points. Further during 2000-2005 IMR was fluctuating. There were inconsistencies in IMR reported by various sources. Field level surveys conducted in 2002 found an IMR of 25.0. Third World Institute quoted it at 18.0. UN common database of UNICEF quoted the same at 16.0. The CIA World Fact Book quoted 23.7 as the IMR as in 2006 which declined to 23.0 in 2007. A nationwide survey conducted by PAP (Pan Arab Project) put IMR of Libya as 24.4 in 1995. It can be inferred from the above data that IMR of Libya was around 20 in 2005, which was remarkable.

There was clear evidence of a rapid decline in infant mortality after the Liberation from a high of 119.39 per 1000 live births in 1970-71 to 22.82 in 2007. There was some disparity between male IMR and female IMR, with male IMR higher compared with that of females. The decline in IMR has also been found to be higher in females.

As recent statistics are unclear or unreported, a major impact of recent catastrophe is expected soon as evidenced by the causalities reported. Latest estimates of infant mortality, it seems, did not account for deaths caused due to the 2011 war. An update may give rise to astonishing results. Addressing maternal and child care concerns within house technologies will create a controlled situation.

Improvement in Under 5 Mortality Rate during 1960-2005

As of the available statistics, mortality of children under 5 years (<5 MR) remained high during the pre-liberation period. UNICEF quoted an <5 MR of 270 in 1960, which declined to 22.0 in 1999 as per the same source. Data of WHO also agreed on this latter figure of <5 MR but that given by the General Peoples Committees of Libya had been found to be higher (30.1) than that of other sources. It was the Third World Institute that had quoted a < 5 MR of 41.0 in 1990. So, in brief, it might be assumed that <5 MR declined from 270.0 in 1960 to 41.00 in 1990 to 22.0 in 1999 to 19 in 2005 to 17.0 in 2009. There is no recent update to exemplify the situation born out of man made disaster which resulted in deaths, diseases and disabilities. But the rates are expected to rise.

This achievement over the period of 50 years (1960-2009) was remarkable in view of the extent of reduction from a high of 270 in

Year	IMR	Source
1960	159.0	UNICEF, 2001 (9)
1970	105.0	UN Common database, UNICEF, 2001 (9)
1973	118.0	UNEP, 2002 (10)
1969	58.9	Vital Statistics 82-90 (11) MoH 1976 Annual Statistical Report (12)
1974	63.0	
1984	49.9	
1989	37.0	
1980	55.0	UN Common database, UNICEF, 2001 (9)
1990	35.0	Third World Institute (13)
1995	24.4	PAP Child Survey, 1995 (14)
1999	19.0	UNICEF, 2001 (9)
2000	16.0	WHO, 2004 (15)
2002	25.0	LMICS Survey, 2002 (16)
2002	26.0	Libya Forum 2007 (7)
2002-03	28.0	UNFPA, 2004 (17)
2003	26.8	CIA World Fact Book, 2007 (18)
2004	24.6	
2005	24.6	
2006	23.7	
2009	21.1	
2010	20.9	
2011	20.1	
2005	18.0	Third World Institute (13)

Table 2: Infant mortality rate (per 1000 live births) in Libya 1960-2007

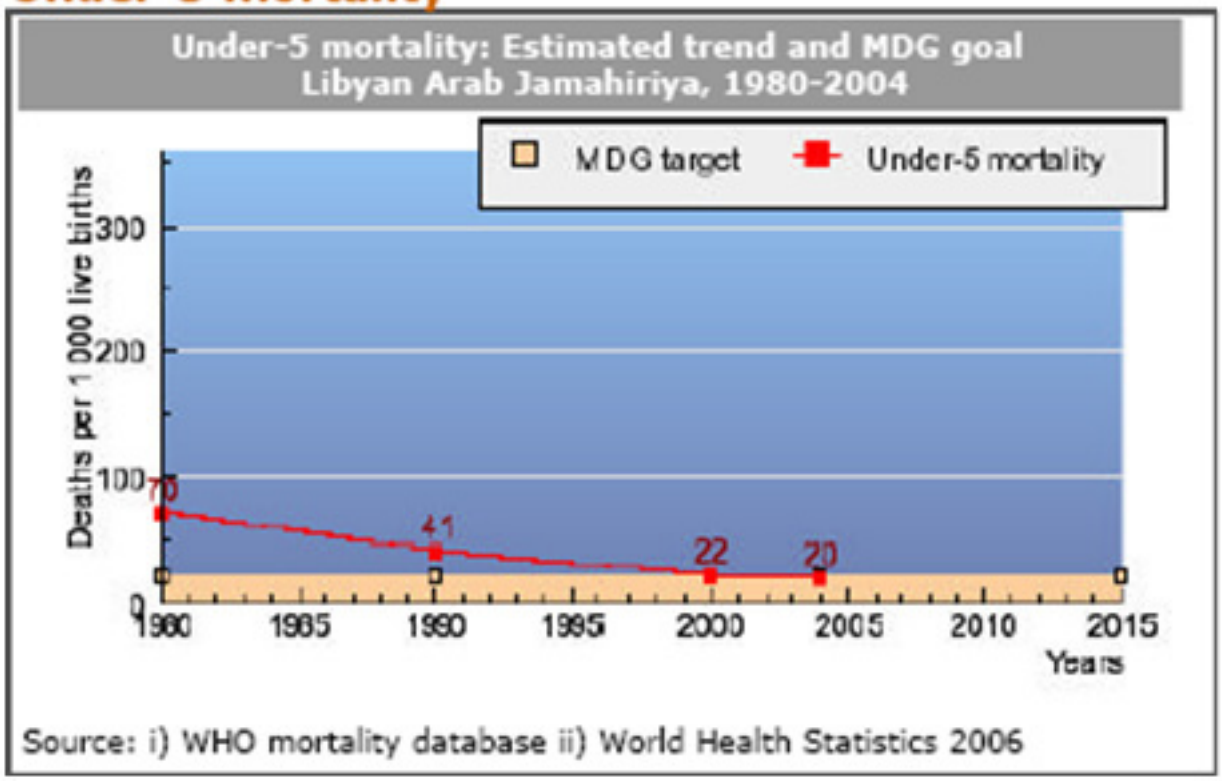
Year	Male	Female	Total	Source:
1970-71	-	-	119.39	U.S. Census Bureau, International Data Base (8)
1974	101.34	91.17	96.38	
1979	77.49	69.37	73.53	
1984	60.73	54.21	57.55	
1989	49.81	44.35	47.15	
1994	40.75	35.75	38.31	
1999	33.85	28.88	31.43	
2004	28.04	23.26	25.70	
2007	25.07	20.47	22.82	
2011				
2000	-	-	30.1	www.exxun.com/Libya/c_pp.html
2005	26.9	22.2	24.6	
2010	23.2	18.8	21.1	
2012	21.3	17.3	19.3	

Table 3: Infant mortality rate (per 1000 live births) in Libya 1970-2007

Year	Under 5 MR	Source
1960	270.0	UNICEF, 2001 (9)
1990	41.0	Third World Institute (13)
1999	22.0	UNICEF, 2001 (9)
2000	20.0	WHO, 2004 (15)
2002	30.1	General People's Committee, 2002 (19)
2004	20.0	WHO, 2006 (20)
2005	19.0	UNICEF 2006 (21)
2009	17.0	CIA World Fact Book, 2012 (18)

Table 4: Under 5 mortality (per 1000 live births) in Libya 1960-2005

Under-5 mortality



1960 to as low as 19 in 2005 or 17 in 2009. Under 5 mortality rate of the country during the pre-liberation period showed symptoms of an underdeveloped health system or poorly organized health system. But within a span of 50 years, the same had been brought to a level showing a developed and well organized health system. This enabled achievement of the Millennium Development Goal of under 5 mortality (20 per 1000) by 2000. As this promising situation reached a status quo, only the future health system can take control over the under 5 mortality scenario. Children, who witnessed emergencies, are gripped with psychosocial trauma in addition to physical injuries and disabilities, which are threatening.

Progress in Maternal Mortality

Maternal mortality rates (MMR) have been debated in Libya as the rates remained high. There were not enough indications to trace out its change since liberation. Available information showed that MMR remained above 75 during the early 1990s which reached nearly 40 by 2005. Available data did not show any large decline in MMR, which might be due to the effect of other demographic variables or health technologies.

The current situation of maternal mortality is unreported even though a hike may be assumed. Maternal health care services offered by national agencies and also by international agencies shall focus on curbing further increase in the coming years. The anxieties and phobias developed during the recent violence affected the new mothers and expected mother's health.

Life Expectancy

One of the greatest achievements of Libya's demography and public health was the expectation of life at birth. Life expectancy had improved from 42.7 years in 1950 to 76.9 years in 2007. Life expectancy improved to 51.0 in 1970; 68.0 in 1990; 69.0 in 2002 and 74.0 in 2005. There was a consensus that life expectancy was low during the pre-revolution period (below 50 years). It was a period of calamities due to political instability and poor overall conditions including economic and social backwardness. Infectious diseases dominated the health scenario during that period, till liberation in 1964.

The liberation and the revolution that followed (during the1960s) paved the way for improving the stability of the governance system. Efforts made by the public sector in making provisions to people in improving living arrangements and also accessing health care services paved the way for reducing infections and infectious diseases. It might be assumed that the administrative system in the country had contributed immensely in improving life expectancy of the population, even though the approach was dictatorial.

Progress in national demography, especially in terms of mortality in the country had been routed through the reforms in administration and health delivery systems. The country had made landmark achievements in administrative aspects in terms of spatial distribution and grass root level planning, to mention a few, during the Gaddafi Regime period. New democratic government with its innovative approaches and people orientation have a long way to build a system that supports health of the general public while bringing their participation.

Year	MMR	Source
1995	77	PAP Child, 1995 (14)
1998	75	Libya Forum, 2007 (7)
2000	97	WHO, 2004 (15)
2002-03	75	UNFPA, 2004 (17)
2005	40	EMRO (22)
2008	64	CIA World Fact Book, 2012 (18)

Table 5: Maternal mortality (per 100,000 live births) in Libya 1995-2005

Year	Expectation of life at birth			Source
	Male	Female	Persons	
1950	-	-	42.7	UNFPA, 2002 (23)
2000	-	-	71.6	
2002-03	68.3	72.2	-	
1970	-	-	51.0	UNICEF, 2007 (24)
1990	-	-	68.0	
1995	68.0	71.0	-	UNEP, 2002 (10)
2002	68.0	71.0	69.0	NCID, 2002 (2)
2002	70.4	73.8	72.6	WHO, 2004 (15)
2004	70.0	75.0	72.0	WHO, 2006 (19)
2005	-	-	74.0	UNICEF, 2007 (24)
1974	-	-	59.10	
1979	-	-	65.01	
1984	-	-	69.25	
1989	-	-	71.99	US Bureau of Census, 2007 (8)
1994	-	-	74.05	
1999	-	-	75.21	
2000	-	-	75.45	
2004	-	-	76.28	
2005	-	-	76.50	
2007	74.60	79.20	76.90	
2009	-	-	77.26	
2010	-	-	77.47	
2011	-	-	77.65	
2012	75.5	80.27	77.83	www.exxun.com/Libya/c_pp.html

Table 6: Improvement in life expectancy in Libya 1950-2007

Spatial distribution of Population

Libya's population is mainly distributed on the Mediterranean coast where there was favorable temperature, rainfall and water. Population increased during the two inter-census periods viz., 1973-84 and 1984-95 showing trends of urbanization. Large towns grew rapidly with an average of 7.8 percent growth annually. Urban centres that experienced rapid population growth, according to 1973, 1984,1995, censuses were Tobrug , Derna, Beida, Benghazi, Sirte, Missrata, Tripoli, Zawia, and Ziwara. This urbanization was a result of the fast industrialization and modernization characterized by commercial construction and industrial and governmental activities that created employment opportunities. Libya was considered to be one of the most rapidly growing urbanizing regions in North Africa as nearly 97.5 percent of the population lives in urban centers along the coast. Recently, due to war and fear of its after effects, the population distribution has been disrupted. The Mediterranean coast was affected more critically than the other areas. As a result a massive displacement took place in the country. While migrant workers, including health workers, fleed to their own native lands, the indigenous Libyan population migrated to their safe haven. Time is running out to stabilize the situation for a democracy while the elections, formation of new governments, ministries of health; all on the way of formation. Population settlement and stabilization are expected after these processes.

National efforts, prior to the 2011 revolution, had concentrated on redistributing population across the country by encouraging people to stay in rural inhabitations. Provisions of rural livelihood were ensured

in cases of people living in rural settings and also for those who were willing to move back to rural areas. Infrastructure development and provisions like transport, electricity and water were major areas of concern in cases of urban to rural return migrations. Government facilitates cottage industries and agriculture and livestock based livelihoods in rural areas. Service provisions for education and health care were also being made to a large extent. These efforts control urbanization to an extent and created balance of resources, environmental hygiene and thereby healthy living.

Following the 2011 revolution, by international attention, efforts are being made to create pockets of population based on familiarities with location, likeminded people around or any other criterion. It is expected soon in the national policy on population redistribution.

Grass Root Level Planning

People oriented planning in Libya started with the revolution through five year plans. Such plans progressed from industrial development to economic and social development, to introducing base for heavy industry, to improvement of women's participation in labor force. Basic infrastructure services such as roads, electricity, housing, sewage and water facilities were restored and investments were made in the development of infrastructure namely electricity, water and communication as well as social welfare services such as education and health. Sectors allied to health, namely livelihood options, were opened through construction of road networks, ports and harbors. Environmental policies focusing on solid waste management and industrial air quality pollution control were made, which facilitated achievements in health status.

The health sector received attention of total allocated national budgets and there was significant proportional allocation for the sector. Reform in education started in 1984 with the new educational system introduced by the Popular Committees of education. Focused on developing human potential, the program created new special secondary schools with specified fields of studies that equip early entry into the job market or enrolment in higher education. During the 2011 war, health facilities were damaged seriously. In addition, many foreign health workers fled the country. Efforts at bringing them back, trained doctors and nurses, particularly in remote and rural areas is the challenge for the health system at present.

The country could be divided into seven regions - Al-jabal Al-Akhdar, Al-jabal Al-Gharbi (mountainous areas), Khalij-Sirt, Sabha (desert areas), Sahel Benghazi, Tripoli and Al-Zawia (coastal regions) each have urban and rural areas (14). For administrative purposes the country was divided into 33 municipalities (Shabiats). Libya had one of the most politically decentralized systems ever known, in principle, even though lead by a dictator. Municipalities (Shabiat) and communes (Mahallat) were the decision making and executing units and were governed through local people. The grass-roots democracy existed in the country provided an open minded political course where local People's Committees constituted the basic instrument of government and were the direct representation of the people - Libyan citizens. This process of decentralization emphasized capacity building to support healthcare services at municipality level. In theory, the country planned to eliminate all central government functions and decentralize power to the 380 Popular Congresses, in principle. All functions of administration and execution including handling local affairs were run within Shabiat. These administrative reforms had impacted heavily on the health status of people due to the high levels of public orientation and commitment.

The most important highlights of governance that contributed to health development of Libya were decentralization, health legislation, health manpower development strategies, social security systems and health policies. Local Popular Congress determined public services to be implemented regionally. Health service planning and implementation were affairs of Local Popular Congress and it made health care a basic right of every individual. Legislation was made simple to avoid hindrance to organizational performance or creating complexity of administrative procedures. Capacity building in the health sector was aimed through developing local manpower to carry out key tasks of health care administration.

The National Health System in Libya was three tiered with primary healthcare providing basic preventive, curative and promotional services through to health care centres and polyclinics offering services of specialized physicians, laboratory and radiology and other basic services like health education, MCH and school health and general hospitals and specialized hospitals. However, primary health care was equipped to deal with health and all medical problems of locals were offered a network of referrals to other levels of care. The national health strategy aims at providing health for all and the achievement of high quality and uniform distribution of health services among the people. Basic health care had been given a high priority by creating the Department of Primary Health Care at all levels.

The national health plan was studied by the Popular Congress and the Health Secretariat from a technical point of view and then executed by Popular Health Committee in each municipality. Primary health care strategies in Libya included mental health, school health, occupational health and social and health care of the elderly. Moreover, the decree promised to integrate health development with overall socioeconomic development and to streamline the entry to health care through family practice. A hierarchy of health care delivery existed in the country; however it was not well-defined with a fixed division of

Indicators	Libya	Egypt	Saudi Arabia	Tunisia
Percent urban	85	43	85	65
CBR	20.3	25.8	25.3	16.8
CDR	2.6*	6.4	3.8	6.0
TFR	5.2	3.1	3.7	2.0
Adult literacy	86	61	-	78
Immunization (One year old)				
BCG	100	98	96	98
DPT	98	98	96	98
OPV	98	98	96	98
Measles	97	98	97	96
Hepatitis B	97	98	97	97
Life expectancy				
Total	76.9**	71.4	73.6	73.4
Males	74.6	69.2	72.5	71.4
Females	79.2	73.6	74.7	75.3
Infant mortality rate	16.0***	20.5	19.1	20.6
Under 5 mortality rate	20.0****	26.2	27.0	30.0
Maternal mortality rate	40.0	62.7	12.0	48.0
Morbidity				
Cholera	0	0	12	0
Malaria	12	23	1059	38
Poliomyelitis	0	0	0	0
Measles	292	110	373	22
Pulmonary Tuberculosis	1622	8516	2192	915
Diphtheria	0	0	7	0
Tetanus	2	213	32	2
Neonatal Tetanus	0	44	22	0
AIDS	50	39	63	28
Meningococcal meningitis	119	154	18	287

Source:
* (5) ** (8) *** (15) **** (19)
WHO country profiles (21)

Table 7:
A Comparison of Four Major Arab Countries in terms of Demographic and Health Characteristics (2005)

functions and strict referral routes between health care facilities. It was the Health Secretariats at the municipal level that were responsible for all health issues within a given geographical area.

A comparison of health statistics with neighboring Arab countries shows Libya to compare well with them. All the vital statistics (except MMR), immunisation levels and morbidity prevalence appeared at an advantage in favor of Libya. CDR was as low as 2.6; IMR was as low as 16; <5MR was as low as 20.

This was a phase of administrative reforms, population distribution, building capacity in medical, public health, educational and public services areas that the country had gone through during the last five centuries, despite the dictatorial leadership. Complementarily, demographic change and epidemiologic transition had taken place. It was this hypothesis of a people oriented democracy and its impact on demographic transition, which was the core of this paper.

Recent Developments since the Uprising

The Libyan health system collapsed with the emergence of the freedom movement that rose up against the dictatorial leadership of Colonel Maumar Al Gaddafi. Starting from the eastern city - Benghazi; the freedom struggle spread all over the country, which witnessed destruction and demolition of public utilities and government sector enterprises. The country's health system shattered, and the new ministry swiftly took up the reconstruction challenge of the destroyed primary health care system, general and specialized hospitals. Emergencies during the period from the beginning of uprising (17 February, 2011) till the end (20 October, 2011) was massive, unmanageable and burdening. Deaths, amputations, wounds and psychic trauma dominated the scenario (25). Conflict-related injuries were followed by non-communicable diseases and mental health needs prioritizing as at least 50,000 people were wounded (20,000 seriously); one third of the population was directly or indirectly exposed to the conflict, needing provisions of psychosocial support (26). Primary health care facilities

functioned all over the country but were disrupted over the period due to their ineffectiveness to contribute to public concerns. In other words, the primary health care system failed to evolve as a point of contact to offer care to people affected by war either physically or mentally. During the war period, the United Nations inter agency rapid assessment mission conducted a need assessment in the eastern part to identify public health risk of migrants.

Similar to other sectors, the Libyan health sector also had a foreign workforce at executive functions - surgical, laboratories and caring roles; their absence affected not only the primary health care functions but also the secondary and tertiary care. Poor policies towards foreign labor force and casual attitude towards bringing previous labor force shall create wear on regaining the lost strengths of the health system. Added to this are the fact of reemergence of episodes namely infections, disabilities and handicaps and psychic trauma. Rehabilitation of those affected by the war and resettlement of population dispersed shall take a lion share of health sector efforts. Lack of tertiary care services within the national health system emerged as another hurdle - huge investments to seek care outside the country.

The Libyan National Health System (LNHS) will face after-effects and threats from (i) wounds, injuries and emergency surgical car (ii) water, sanitation and hygiene related and food borne diseases (iii) diseases related to crowding - acute respiratory infection, influenza, meningococcal disease and tuberculosis (iv) vaccine preventable diseases - measles, diphtheria, pertussis, polio, tetanus (v) vector borne diseases - malaria, dengue, rabies and plague and (vi) public health issues - reproductive health, non communicable diseases, mental health (psychosocial trauma), malnutrition, environmental risk and toxic agents and chemicals (27).

In Libya, the government has changed from dictatorial to democratic. The new Ministry of Health in place, moved swiftly to tackle daunting reconstruction in collaboration with WHO. Ministry of Health in consultation with WHO shall focus on (i) scaling up primary health care (ii) improving key aspects of health service organization (iii) strengthening laboratory services (iv) improving radiology services (v) enhancing drug supply management and (vi) increasing the pool of trained nurses. Reconciliation, consensus building and reengineering are major challenges to provide a fresh start to create an equitable, accessible and people oriented health system shall be in place soon (25).

There are a number of Libyans currently receiving health care abroad (30), creating extra burden on health financing. To address this critical situation, the newly formed National Transitional Council calls for a forum bringing stake holders, consumers and health authorities in Libya to come together in a way of reconciliation and consensus building and agree on the most immediate priorities for reengineering the health system to provide equitable and accessible services that are centered around people's needs and expectations.

The public health sector interventions of importance in this context are (i) health sector priorities, namely access to surgical and emergency obstetric care,
(ii) referral systems (iii) maintenance and continuity of treatment for chronic diseases
(iv) public health surveillance and response including preparedness for epidemic prone cases
(v) maternal and child health
(vi) health communications and
(vi) non health sector priorities impacting health namely provisions of sufficient safe water, provisions of sanitation and hygiene and provisions of safe food and shelter (27).

Conclusions and Recommendations

The above exploration brought us to four points. First, there was a very remarkable improvement in the mortality situation in the country over the past 40 years. Statistics regarding such an improvement were neither readily available nor were there efforts to collate them comprehensively. National and international sources of vital statistics vary, but they all converged to the low level of mortality that the country experienced recently. There was also agreement about higher levels of mortality that the country experienced before 1969.

Mortality indicators, in particular the CDR, IMR and MMR registered their remarkable decline over the 40 year period while that of MMR required further evaluations. The achievement in terms of expectation of life at birth in Libya appeared to be highly appreciable.

Changes in the mortality level had implications on health sector planning and management. There was a remarkable difference in mortality levels in the country, which meant otherwise, that there was a remarkable improvement in health status. It was also advisable to look at changes in population structure and characteristics of the country over a period of 40 years. It was also advised to fine tune the health system in order to match with the current health status and population structure of the country.

Finally, it is wise to look back and evaluate Libyan progress in terms of effort, resources and contributions comparing the existing system with that of neighboring countries in the Arab region. We hope that the new democratic government not only takes leads from these experiences but also make the national health system more efficient in the future.

Health system based on Popular Congresses and People's Committees has disrupted. The new democratic political order that builds a modern, efficient health care system based on international order shall devote a major emphasis on rehabilitation and reconstruction. Let the global community of public health and healthcare support and guide this effort.

References

1 Krug, H.N., Health and freedom from discrimination: Durban 2001, The Lancet, 2002, 359, January 12 pp 163.

2 Boerma, J.T., and Stansfield S.K., Health Statistics now: are we making the right investments? The Lancet, 2007, 369, March 3, pp 779-786.

3 The World Bank, World Development Report 1993: Investing in Health, New York, Oxford University Press Inc. 1993.

4 UNEP, Indicators for Sustainable Development in the Mediterranean Coastal Regions: National Report of Libya, Plan Bleu Sophia Antipolis, November 2002.

5 The office of Census and Statistics, Census of Libya, The Secretariat of People's Committee for Planning, 2006.

6 UNICEF, State of the World's Children 2004, New York, United Nations Children's Fund, 2004.

7 Libya Forum, 2007, Encyclopedia of the Nations: Africa - Libya Health, Advameg Inc. (an internet publication)

8 US Bureau of Census, International Data base, www.cenus.gov/cgi-bin/ipc/idbsprd, accessed on Feb. 2008.

9 UNICEF, State of the World's Children 2001, New York, United Nations Children's Fund. 2001.

10 UNEP, Indicators for Sustainable Development in the Mediterranean Coastal Regions, National Report of Libya, Sophia Antipolis, Plan Bleu, Regional Activity Centre, 2002.

11 Vital Statistics 82-90, The Libyan Arab Jamahiriya, National Corporation for Information and Documentation, 1990.

12 MoH Annual Statistical Report, Tripoli, Ministry of Health, 1976.

13 The Third World Institute, Social Watch Country by Country, Extended Data of Libya, http://www.socialwatch.org, accessed on Feb. 2008.

14 The General People's Committee for Health and Social Affairs and League of Arab States, Arab Libyan Maternal and Child Health Survey - 1995, Cairo, Pan Arab Project for Child Development, 1997.

15 WHO, World Health Report 2004, Geneva, World Health Organization, 2004.

16 UNICEF, Libyan Multi Cluster Indicator Survey, Amman, United Nation's Children's Fund, 2002.

17 UNFPA, State of World Population - 2004, New York, United Nation's Population Fund, 2004.

18 CIA, World Fact Book - 2007 and 2012, Libya Infant Mortality Rates, (http://www.cia.gov), Accessed on Feb. 2008 and March 2012.

19 General Public Committee, Statistical Report Summary on the main health indicators, The Libyan Arab Jamahiriya, Health Services Affairs, 2002.

20 WHO Mortality Database, World Health Statistics, cited in World Health Organization - Mortality Country Fact Sheet, 2006, WHO, 2006.

21 UNICEF, State of World's Children, New York, United Nation's Children's Fund, 2006.

22 EMRO Database, Country Profiles (www.emro.who.int), Accessed on Feb. 2008 .

23 UNFPA, Libyan Arab Jamahiriya, Demographic, social and Economic Indicators, Amman, Country Technical Services Team for Arab States (http://www.cstamman.org.jo), 2002, Accessed on Feb.2008.

24. UNICEF, At a glance, Libyan Arab Jamahiriya Statistics, UNICEF (an internet based data source), 2007, Accessed on Feb., 2008.

25. WHO . Rebuilding the Libyan health system, post-revolution. www.who.int/features/2012/ libya_health_syste/en/index.html. Accessed on 2012 Feb.

26. WHO. Partners supporting the provision of essential health care in Libya. http://www.who.int/ hac/crises/lby/en/index.html. Accessed on 2012 Feb.

27. WHO. The Libyan Arab Jamahiriya: Civil Unrest - Public health Risk assessment and interventions. World Health Organization. March 2011. Accessed on 2012 Feb.

28. Libya People 2012. www.theodora.com/wfbcurrent/libya/libya-people.html Accessed on March 2012

29. www.exxun.com/libya/c_pp.html Accessed on March 2012

30. Benamer, H. Health Care System in Libya - Factual Report 2012. www.scribd.com/doc/77356124/Libya-Health-Report-2012. Accessed on Feb. 2012.

Postpartum related acute renal failure mortality, at haemodialysis, Aden Yemen

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Abstract

Background: Acute renal failure ARF in pregnancy can be induced by any of the disorders leading to renal failure, such as acute tubular necrosis. Early in pregnancy, they commonly are resulting from a septic abortion, preeclampsia, postpartum bleeding and idiopathic postpartum ARF. **Objective:** To determine the incidence of pregnancy related (ARF), clinical spectrum, morbimortality of this preventable complication. **Methods:** It was an observational and prospective hospital based study, done at hemodialysis HD center-Aden

Results: The Pregnancy related ARF numbered were 39 patients, 33 (85%) were multipara and 14 (15%) were primigravida. The majority 25 (64%), receiving antenatal care 28 (72%) were from rural areas and had not received any antenatal care. All 39 patients (100%) cases presented to the haemodialysis center immediately within (1-3 days) (postpartum). 35 cases (90%) were anuric. Idiopathic ARF was the commonest cause, 11 patients (28%). Blood loss causing hypotension due to postpartum hemorrhage (PPH) was the second cause, 9 patients (23 %). Sepsis in general including septicemia in 6 cases, and eclampsia in 7 (18%) cases. (67%) patients received haemodialysis, 13 of these patients died during HD and 2 patients (5%). The commonest probable clinical diagnosis was acute tubular necrosis (ATN) in 22 (56%) cases with complete recovery. 13 patients were HD.

Conclusion: Pregnancy related acute renal failure is a major health problem and carries very high mortality and morbidity. Poor healthcare facilities and lack of antenatal healthcare clinics compound this problem.

Keywords: ARF; Haemodialysis; Acute tubular necrosis, Acute cortical necrosis; idiopathic ARF; ARF; Eclampsia; postpartum; antenatal

Introduction

Pregnancy related acute renal failure is one of the most common causes of acute renal failure (ARF). Acute renal failure may be defined as a sudden decrease in renal function which is usually reversible, over a period of several hours to days sufficient enough to result in retention of nitrogenous waste products (i.e. Blood urea nitrogen (BUN) and creatinine) in the body. Acute renal failure has become a rare complication with pregnancy in industrialized countries. The differential diagnoses include pre-renal, vascular and post-renal causes, as well as deterioration of pre-existing renal failure. In pregnancy it can occur during antenatal or postnatal periods. Over the last six decades several important causes of pregnancy induced ARF and its pathophysiological mechanisms have been described. The important causes of obstetric ARF are divided into (i) causes in early pregnancy which include septic abortion leading to septic shock and acute renal failure, the mortality is high if the causative organism was clostridium(1) (ii) Causes in late pregnancy i.e. after 34 weeks of gestation and immediate puerperium are Ante-partum hemorrhage (abruptio-placentae) (APH), postpartum hemorrhage (PPH), pre-eclampsia/eclampsia, haemolytic uraemic syndrome (HUS), puerperal sepsis and haemolysis, elevated liver enzymes, low platelets (HELLP syndrome).(1-3) Acute tubular necrosis (ATN) is the most common pathological lesion and has good prognosis as compared to other pathological lesions associated with disseminated intravascular coagulation DIC, HUS, severe eclampsia, and HELLP syndrome in which glomerular involvement is predominant.(1,3) It is postulated that all these diseases are manifestations of thrombotic microangiopathy caused by endothelial injury, due to deficiency of NO-dependent

endothelial relaxing factors.(4) The prognosis of pregnancy induced HUS, HELLP syndrome and severe form of eclampsia is not good; most of the patients require chronic dialysis or survive with markedly reduced renal functions.(1,3) Another bad prognostic lesion seen in obstetric induced ARF is acute bilateral renal cortical necrosis (ABCN). It is rarely seen in industrialized nations.(5) The incidence of cortical necrosis is still very high in developing countries; in India it is about 24% as reported by Parkash et al (6) and 13% reported in Pakistan by Ramzan et al (7) It is frequently seen after ante-partum hemorrhage and prolonged retention of dead foetus.(1,2,8) There is also incomplete (patchy) cortical necrosis followed by a variable improvement of renal function and a stable period of moderate renal insufficiency over a few years, and in some cases it may progress to end stage renal failure a few years later.(5) Acute renal failure is one of the most serious complications of pregnancy. ARF that is severe enough to require dialysis is quite rare in industrialized nations; its incidence is 1:20000 or less of all gestations.(1,3) These statistics show significant improvement as compared to the situation in the 1950s and 1960s when as many as 22% of all cases of acute renal failure were of obstetrical origin with mortality rate ranging from 20% to 48%.(9) This achievement in industrialized nations is most likely due to liberalization of abortion laws, improved pre-natal care and better management of maternal complications potentially leading to ARF.(2) The incidence of obstetrics related ARF in developing countries like Pakistan has not changed significantly. There is no such local data available in the past to compare with, only a few scanty available articles which showed pregnancy related ARF 7-10%.(10) Mortality in Obstetric ARF depends on underlying renal lesion and associated complications. It is high when associated with HELLP syndrome, severe PET, acute fatty liver of pregnancy, HUS, sepsis, DIC and cortical necrosis. Preeclampsia typically develops in the third trimester, with only a few percent of cases developing in the postpartum period, usually in the first one to two days.

Thrombotic thrombocytopenic purpura almost always occurs antepartum; many cases begin before 24 weeks but the disease also occurs in the third trimester. The aim of this study was to highlight the magnitude of the problem leading to high mortality and morbidity. Pregnancy related acute renal failure is a challenging health problem of Yemeni women especially of rural areas. Therefore effective measures are needed to prevent this preventable complication of pregnancy. Most obstetric patients who develop bacteremia do not develop sepsis. Conversely, bacteremia is not necessary to develop sepsis because local infection can initiate an inflammatory response. (11,12) The microbiology of sepsis is distinct in pregnancy; endotoxin-producing Gram-negative rods such as E. coli are common etiologic agents.(13,14) Pyelonephritis, caused in part by the reduction in renal concentrating ability, bladder flaccidity, and ureteral dilation during pregnancy, is a frequent precipitating illness, and urosepsis in pregnancy can be fatal. The most common risk factor for maternal sepsis is cesarean delivery.(10) Diagnosis of sepsis during labor can be particularly challenging, since heart rate and respiratory rates increase significantly with exertion and the stress of labor.(10) Most obstetric patients who develop bacteremia do not develop sepsis. Conversely, bacteremia is not necessary to develop sepsis because local infection can initiate an inflammatory response.(11,12) The microbiology of sepsis is distinct in pregnancy; endotoxin-producing Gram-negative rods such as E. coli are common etiologic agents, whereas Gram-positive bacteria are common culprits in non-pregnant patients with sepsis.(11,12) In many cases, polymicrobial causes are identified, for example E. coli.

Objective

To determine the study of postpartum related acute renal failure (ARF), clinical spectrum, morbidity and mortality of this preventable complication of pregnancy.

Patients and Methods

It was an observation based study, conducted in the hemodialysis HD center at Al Gamhouria Teaching Hospital, Aden, Yemen, during November 2005 till October 2007. During this period 97 patients suffering from acute renal failure were admitted to the HD center, central hospital or ICU; they arrived in Casualty in serious condition. Out of these, 39 patients were mortal-induced ARF. All these women were previously healthy and were shifted to the ward when they developed deranged renal functions. Some of the patients were referred from other hospitals and others were from other governorates.

The patients suffering from postpartum (peripartum, is the term we can use here) fatal-ARF were enrolled and chosen in the study after their death. Their clinical history, physical examination and intake/urine output was recorded in a separate sketched Performa. Routine laboratory investigations were done related to each case and specialized investigations like, hematology, biochemistry, blood catheter and renal ultrasonography and renal biopsies were not performed because of lack of facilities. Conservative treatment included all therapeutics modalities available as management of fluids, electrolytes, blood transfusion and antibiotics. Haemodialysis was done as a part of treatment when indicated. Central catheterization of jugular or subclavian was inserted on arrival. Recovery from ARF was declared when renal function returned to normal range (diuresis >1000ml), anuria (<200cc).

Daily follow up was instituted for urine output, blood pressure, and evaluation for possible gynecological infection or bleeding. Partial recovery due to patchy cortical necrosis was suspected when renal functions showed improvement but did not return to normal even after 12 weeks. Cortical necrosis was diagnosed when the patient remained anuric

for >3 weeks and renal ultrasound showed bilateral increased echogenicity with small size kidneys and scattered renal cortical calcification and the patient remained dialysis dependent. Renal angiography, a gold standard technique for diagnosis of cortical necrosis, could not be done due to lack of facilities.

Results

Out of these 97 patients, 39 (40%) were of obstetrical related ARF. The ages of the patients were between 17-43 with the Majority 25 years (64%). 33 (85%) were multipara and 4 (15%) were primigravida. No acute renal failure occurred in the early part of their pregnancy (first trimester) nor the later period of pregnancy i.e. 3rd trimester. All ARF occurred at the puerperium postpartum. 11 patients (28%) were from Aden city, with a past history of receiving antenatal care. 28 (72%) were from rural areas mainly from Lahj province, and other rural areas had not received any antenatal care and there was a history of traditional birth attendants assisting in home delivery. All 39 patients (100%) cases presented to the haemodialysis center immediately within (1-3 days) after delivery (postpartum). 35 cases (90%) were anuric. Only 28 (72%) patients had not received any antenatal care at any stage of pregnancy and had undergone traditional birth attendant assisted home delivery, from Aden. 11 (28%) patients had delivered in the hospital but with antenatal care.

There were 6 (15%) patients who had undergone major surgical procedures like C-section or caesarian hysterectomy where 33 patients (85%) had vaginal deliveries. 28 (59%) cases were from Lahj and Abyan. 11 (28%) were residents of Aden, Hawta and Little Aden cities. Anuria was observed in 20 (51%) cases; the remaining 19 (49%) patients presented with normal urinary volume or oliguria. Hemodialysis HD was done in 26 (67%) patients and 2 of those patients (5%) maintained renal replacement therapy for life (HD). 13 (33%) patients were not dialyzed, as they recovered normal renal functions with conservative treatment. Blood loss due to APH causing hypotension was the commonest cause of ARF in our study. Sepsis, Disseminated intravascular coagulation, intra uterine death, HELLP syndrome (Hemolysis, elevated liver enzymes, and low platelets) and pre eclampsia were also the commonest causes in order of frequency. Clinical spectrum of pregnancy related ARF showed that the idiopathic ARF was the commonest cause of ARF in 11 patients (28%). Blood loss causing hypotension due to postpartum hemorrhage (PPH) was the second cause, with 9 patients (23 %). Sepsis in general including septicemia and septicemia was found in 6 (15%) cases, and preeclampsia / eclampsia in 7 (18%) cases. The commonest clinical diagnosis was acute tubular necrosis ATN in 22 (56%) cases with complete recovery. 14 patients developed bilateral cortical necrosis due to PPH, sepsis, septicemia and DIC. More than 20 patients were in need of HD (46%), 13 patients died while they were on HD.

Discussion

Obstetrical acute renal failure is now a very rare entity in the developed countries. Its incidence is less than 1:20000 of all gestations(15,16). The situation in some of the developing countries, like South Africa, India, and Turkey has shown improvement. Chugh et al(17) from India reported declining incidence from 22% in 1965-1974 to 9% in 1981-1986. In South Africa incidence of pregnancy induced ARF has declined from 25% in 1978 to less than 16% in 1992(12,17). But in our data presented in this study on pregnancy related acute renal failure the incidence was (39%) in a 2 year period; it was an alarming result, but this is the reality.

In Turkey the situation has also improved from 17% in early 80% to 13% in 1997(13). Strata et al(14) quoted the incidence of obstetrical ARF to decrease from 43% (1956-1967) to 0.5% with respect to total ARF cases (1988-1994) and no case of maternal death or irreversible renal damage was observed in last eight years. The reported data from various studies of the country showed very high incidence of mortality, 18% to 23%) and morbidity (13% to 26%) related to obstetrical ARF(10,15).

One striking feature of our study indicated that the pregnancy related ARF is more commonly seen (60%) in patients who had not received any kind of antenatal care and their deliveries were carried out at home. In the hospital it is also reported that the women delivered there also had not received antenatal care and were more prone to developing ARF 16 (30%). This figure indicates the importance of antenatal care in the prevention of pregnancy related ARF. In 2008, Ansari et al(16) reported 36% obstetrical ARF from Hyderabad and interior Sindh province with overall morbidity of 19% and mortality of 26%. In 1996, Naqvi et al (15) reported 18% obstetrical ARF from Karachi city with 23% mortality and 26% morbidity. If we compare our data with the rest of the countries it indicates an alarming high frequency of pregnancy related ARF-death in the Yemeni population, about half of the cases. The reported data from various studies of the country showed very high incidence of mortality (18% to 23%)(18) and morbidity (13% to 26%) related to obstetrical ARF.(10, 19) This indicates the failure of health care facilities, especially antenatal care in the interior of the province or in Yemen as a whole.

Conclusion

Our study shows that obstetrical ARF is one of the most common causes of acute renal failure, which is now a rare entity in developed and some developing countries. This calls for an improvement in the existing healthcare facilities and public awareness programs and better care in the public sector hospitals as well as rapid diagnosis for those affected and immediate and near therapeutic methods especially renal replacement therapy. It is also a dangerous complication of pregnancy which has a very high mortality and morbidity. This calls for an improvement in the existing

Main Features	No. of Patients	%
Pregnancy with ARF	39	--------
Age (mean/range) in years	(25)/ 17-43	--------
Parity:		
Primigravida	4	(10%)
Multipara	35	(90%)
Mode of onset		
Postpartum	39	--------
Type of ARF:		
Oligo-anuric	35	(90%)
Normal or Pyloric	4	(10%)
Thrombocytopenia		
<100,000 platelets/mm3	4	(10%)
Renal sonography		
Cortical necrosis	14	(36%)
Tubular necrosis	22	(56%)
Chronicity with HD	3	(8%)
Causes of mortal ARF n=39	**No.**	**%**
Hemorrhage	9	(23%)
Severe preeclampsia	6	(15%)
Sepsis, septicemia , DIC	7	(18%)
Hemolysis, low platelets,	1	(3%)
Uterine hemorrhage	3	(8%)
Miscellaneous	2	(5%)
idiopathic ARF	11	(28%)
Total	39	(100%)

Table 1: Clinical, Paraclinical and Causes of death in ARF Patients Postpartum N= 39

Therapeutics	survived		died		Change to ESRD		P
	No.	%	No.	%	No.	(%)	
Receive HD therapy	10	(26%)	13	(33%)	3	(8%)	0.001*
Conservative therapy	13	(33%)	0	(0%)	0	(0%)	
Total	23	(59%)	13	(33%)	3	(8%)	

*there is a Significant difference in the outcome among ARF pregnant patients according to the type of therapy received (p value < 0.05)

Table 2: Outcome of ARF Pregnant Patients n=39

health care facilities, transport facilities, earlier referral and public awareness programs, and better care in the public sector hospital. If we compare our data with the rest of the country it indicates an alarmingly high frequency of obstetrical ARF in the Yemeni population, particularly in Aden and surrounding provinces, Abyan, Lahj, and Dahle. This indicates the failure of healthcare facilities, especially antenatal care there.

References

1. Schrier RW. Diseases of kidney and urinary tract. Philadelphia: Lippincott Williams and Wilkins, 2001.Pertuiset N, Grünfeld JP. Acute renal failure in pregnancy. Baillicres Clin Obstet Gynaecol 1994; 8: 333-51.

2. Lindheimer MD, Katz AI. Renal functions and disease in pregnancy. Philadelphia: Lea & Febiger 1977, pp 146-187.

3. Schrier RW. Diseases of Kidney & Urinary Tract. Philadelphia: Lippincott Williams & Wilkins, 2001.

4. Sibai BM, Kustermann L, Velasco J. Current understanding of severe preeclampsia, pregnancy associated hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, hemolysis, elevated liver enzymes and low platelets and postpartum acute renal failure: different clinical syndromes or just different names? Curr Opinion

Nephrol Hypertens1994:3; 436-45.
5. Madias NE, Donohoe JF, Harrington JT. Postischemic acute renal failure. In: Brenner BM, Lazarus JM, eds. Acute renal failure. 2nd ed. New York: Churchill Livingstone, 1988; pp :251.
6. Parkash J, Tripathi K, Pandey LK, Gadela SR, Usha. Renal cortical necrosis in pregnancy-related acute renal failure. J Indian Med Assoc. 1996; 94:227-9.
7. Ramzan M, Sameeh JK, Ghiasuddin. One year renal outcome of pregnancy related kidney failure. J Pakistan Inst Med Sci 2004; 15:834-8.
8. Lindheimer MD, Katz AI. Renal physiology in diseases and pregnancy. In: Seldin DW, Giebisch G, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2000: pp 2597.
9. Grunfeld JP, Pertuiset N. Acute renal failure in pregnancy. Am J Kidney Dis 1987; 9:359-62.
10. Ali A, Zafar S, Mehmood A, Nisar A. Obstetrical acute renal failure from Frontier Province: A 3 years prospective study. J Postgrad Med Inst 2004; 18:109-17.
11. Guinn D, Abel D, Tomlinson M. Early goal directed therapy for sepsis during pregnancy. Obstet Gynecol Clin North Am 2007;34:459-79
12. Maupin R. Obstetric infectious disease emergencies. Clin Obstet Gynecol2002;45:393-404
13. Winn H. Group B streptococcus infection in pregnancy. Clin Perinatol2007;34:387-92
14. Stratta P, Besso L, Canavese C, Grill A, Todros T, Benedetto C, et al. Is Pregnancy related acute renal failure a disappearing entity? Ren Fail. 1996; 18: 575-84.
15. Naqvi R, Akhtar F, Ahmed E, Shaikh R, Ahmed Z, Naqvi A et al. Acute renal failure of obstetrical origin during 1994 at one centre. Ren Fail 1996; 18:681-3.
16. Ansari MR, Laghari MS. Acute renal failure in pregnancy: one year observational study at University Hospital, Hyderabad. J Pak Med Assoc 2008; 58: 61-4.
17. Randeree IG, Czarnocki A, Moodley J, Seedat YK, Naiker IP. Acute renal failure in pregnancy in South Africa. Ren Fail. 1995; 17:147-53.
18. Chugh KS, Sakhusja V, Malhotra HS, Pereira BJ. Changing trends in acute renal failure in third-world countries-Chundigarh study. Q J Med. 1989; 73: 1117-23.
19. Selcuk NY, Tonbul HZ, San A, Odabas AR. Changes in frequency and etiology of renal failure in pregnancy (1980-1997). Ren Fail. 1998; 20:513-7.

Malaria as a Cause of Acute Renal Failure and/or Hepatic Dysfunction in Aden Haemodialysis HD Center, Al-Gamhouria Teaching Hospital, Yemen

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Abstract

Introduction: Malaria, a common health problem in certain parts of the world, has a considerable morbidity and mortality. This study reports its occurrence with serious complications, acute renal failure (ARF) and hepatic dysfunction HD, at a third tertiary care center. The clinical presentations of severe and complicated malaria vary. The prognosis is poor when associated with cerebral malaria, hepatic damage and acute renal failure.

Material and Methods: Clinical profile, biochemical parameters and outcome were studied in 64 adult malarial patients complicated with ARF, HD, or both and requiring hospital admission in Al-Gamhouria Teaching Hospital, Aden, Yemen, between May 2006 to May 2008. The data were retrieved from the patient medical records.

Result: The age of the patients ranged from 15 to 78 years. The majority (n=40) of the patients were in the age group of 15 to 34 years. 67% of the patients were from Aden. Mean duration of febrile illness was 6 days at the time of presentation. 42% (n=27) patients had hepatic dysfunction and 37.5 % (n=24) had acute renal failure (ARF) and 13 patients (20.5%) had both complications according to WHO criteria. 100% of patients with ARF were oligo-anuric and required dialysis support. Eleven patients (17%) died, of which 8% had pure ARF and 3% pure hepatic failure and 6% died of mixed ARF and liver damage 5, 2, 4 patients respectively.

Conclusion: Although malaria remains a major health problem, malarial hepatic-renal disease has not been reported previously from Yemen. Early initiation of anti-malarial effective therapy, close observation for organ failure and early initiation of dialysis in ARF are instruments in the recovery of the patient.

Key words: Malaria, Acute renal failure, hepatic dysfunction, Yemen

Introduction

Malaria, a protean disease, is widely prevalent throughout South West Asia, Middle East, Africa and Latin America. Malaria is endemic in Yemen and at present >70% of the total population of Yemen are at risk of disease (1,2) and the disease is prevalent up to 4,000 ft. Malaria is a major public health problem in the tropical developing world. Almost the entire population of India (95.9%) is now deemed to be under malaria risk. Almost parallel to this, an upsurge in the incidence of ARF in malaria has been reported in India and varies from 13% to 17.8% (1). ARF lasts from a few days to several weeks and is occasionally non-oliguric type. Several factors; intravascular coagulation, intravascular haemolysis, hyperbilirubinaemia and severe hyperpyrexia have been implicated in the pathogenesis of ARF in Malaria. The clinical presentations and prognosis of malaria gets worse and varied when anemia, hepatosplenomegaly, and cerebral, liver and renal involvement takes place. Renal involvement in malaria is usually caused by Plasmodium falciparum and Plasmodium vivax(2). In general, falciparum is associated with acute renal failure (ARF). The hepatic involvement with malaria can be due to intravascular hemolysis, disseminated intravascular coagulation and rarely due to malaria hepatitis (3).

Objective

To study the clinical profile, biochemical parameters and outcomes in malarial patients complicated with ARF and hepatic damage.

Methods

It is a retrospective analysis and patients included were consecutive. 1306 cases of fever were evaluated for malaria during May 2006 - May 2008. Sixty-four patients with ARF, hepatic dysfunction or both complications with positive peripheral smear(PS) for malarial parasite (MP) were detected and included in the study. The case sheets of these 64 patients requiring admission in tertiary care hospital, (Al-Gamhouria teaching Hospital (mainly at ICU and haemodialysis unit- Aden governorate, the tertiary care hospital in Aden-Yemen) in between May 2006 to May 2008 were retrieved from the Medical Record Section under the ICD 10 and a detailed study of clinical features, biochemical parameters and outcomes was done. It was then analyzed using Microsoft XL 2000. Patients having malarial parasite positive on peripheral blood smear were considered as malarial patients. Acute renal failure was considered according to the recently revised WHO criteria of serum creatinine >3mg/dl (265 mmol/L) with/without urine output less than 400 ml per 24 hours despite rehydration(2). The study includes patients diagnosed and treated primarily at different clinics as well as patients already diagnosed before presentation who had received partial or complete treatment with antimalarials before referral to us for the management of ARF, and other malarial complications. Serum creatinine >2 mg/dl was taken to be indicative of renal failure. Cerebral involvement in malaria commonly manifests as drowsiness progressing into coma. These features may also be present in advanced uraemic and hepatic encephalopathy (HE). Due to difficulty in segregating the relative contribution of these three factors to central nervous system (CNS) symptoms in malarial ARF, HE, the CNS depression alone was selected as a marker of poor prognosis in the context of the present study. Peripheral blood smears stained with Giemsa were available for all patients. Quantification of parasitaemia, however, was not available for all patients and, therefore, it was not considered during data analysis. Patients who were afebrile on presentation, had received antimalarials elsewhere and had fresh Giemsa stains negative for parasitaemia did not receive additional antimalarials. Some patients were treated with quinine sulphate for 7 days, artesunate, and a drugs combination in other patients, in the early part of the study, and those initially managed outside, received chloroquine or Fansidar (sulphamethoxazole + pyrimethamine). Halofantrine was briefly and rarely used in the later part of the study in four patients. Renal replacement therapy in the form of haemodialysis was performed if clinically indicated. Broadly, those so treated were patients with advanced uraemia, acidosis, hyperkalaemia, fluid overload and rising creatinine with or without oliguria. Double-lumen catheters inserted into the subclavian, internal jugular veins were used as vascular access. Cellulose membranes were used for dialysis and the frequency and duration of dialysis were adjusted according to clinical or biochemical parameters.

Results

In our study of 64 adult malarial patients (M=38, F=26) already complicated with renal or liver dysfunction or both of them, most were in the age group 15-34 years (n=40) as depicted in Table 1.The presenting features were those as depicted in Table 1. The mean duration of febrile illness was 6 days at the time of presentation and in half of the patients, malaria was detected within 2 weeks. (Table 1)

P value (linear by linear association) = 0.665

The patients' presentations included fever (95 %), nausea-vomiting (91%), oligo/anuria (38%), abdominal pain/tenderness (55%), jaundice (24%), dyspnea (30%), altered sensorium (38%), convulsions (11%), diarrhea (27%), splenomegaly (64%) and hepatomegaly (27%) [Table 3]. Both renal and liver symptoms were detected in about one fifth of our cases.

Sixty-one of the patients were anaemic (i.e. hemoglobin below 12gm/dl) and 5% of the patients had severe anemia (i.e. hemoglobin below 5gm/dl) (Table 4 - page 48). More than 50% were jaundiced patients having their bilirubin measured >3mg%, besides ALA increased level.

ARF was presented in 58% of the patients; all of them were in a oligo/anuria state (creatinine >3mg%). Most of the malarial patients received Quinine therapy (n=28) and remaining (n=23) were treated with artemisinin derivatives and other treatments (halofantrine, chloroquine) was given to the remaining cases.

Discussion

Malaria is a major public health problem in Yemen including other countries of South West Asia(4), the Middle East (5) and Africa(6) which is endemic for the disease. Early identification of malaria and related conditions and their management is extremely important to prevent morbidity and mortality related to it. The situation is more alarming with increasing incidence of falciparum malaria in the region(2). Regarding the presenting features of malaria, we note nearly equal incidence in our study with other researchers, mainly in India where the patients' presentations included the following: fever (100 %), nausea-vomiting (89%), oligo/anuria (82%), abdominal pain/tenderness (55%), jaundice (55%), dyspnea (30%), altered sensorium (31%), convulsions (18%), diarrhea (17%), splenomegaly (69%) and hepatomegaly (39%)(1).

ARF is a common complication in falciparum malaria infection and occurs most in adults with an incidence of 1 to 4% (2,3,4,7,8). However, the incidence may reach up to 60% and the condition is more common in males(4). In our study, almost all the cases were adults , mostly males; 37.5% had acute

Age group	Total patients with complicated malaria	
	No.	%
15-24years	21	33
25-34years	19	30
35-44years	9	14
45-54years	6	9
55-78years	9	14
Total	**64**	**100**

Table 1: Complicated Malarial Cases according to Age group

Febrile duration in days	No. of patients according to fever duration					
	Male		Female		Total	
	No.	%	No	%	No	%
<7	19	29.5	15	23.5	34	53
8-14	12	19	4	6	16	25
15-21	5	8	6	9	11	17
>21	2	3.5	1	1.5	3	5
Total	**38**	**59**	**26**	**41**	**64**	**100**

P value (chi-square)=0.433
(so No-significant difference (p value > 0.05) between males and females in the duration of fever before the diagnosis of malaria.

Table 2: Distribution of Febrile duration (in days) before malarial diagnosis according to gender

Symptoms	Patients	
	No.	%
Fever	61	95
Cough	28	44
Altered consciousness	11	17
Oligo-anuria	24	38
Jaundice	27	42
Anuric-jaundice combination	13	20
General symptoms	64	100
Bleeding disorders	2	3
Splenomegaly	38	59
Hepatomegaly	17	27
Convulsion	7	11
Nausea-vomiting	58	91
Diarrhea	17	27
Breathlessness	12	19
Abdominal pain-tenderness	31	48

Table 3: Illustrates The Clinical Symptoms of Complicated Malaria at Presentation

renal failure and the others (20.5%) had both ARF and jaundice, compared with 5-15% in other Asian studies [2],[4],[5]. However, this 58% of patients having acute renal failure should be interpreted cautiously as the facility to diagnose and treat complicated malaria is limited to a few other hospitals. ARF is a serious complication of falciparum malaria, dreaded for its mortality and commonly found in South East Asia[6]. Our study showed 14% mortality in malarial ARF, consistent with 15-45% mortality reported by others[7]. Several factors including various chemical mediators, catecholamine release, cytoadherence of parasitized erythrocytes, dehydration, intravascular hemolysis, intravascular coagulation, sepsis, hyperbilirubinaemia and hyperparasitemia have been implicated in the pathogenesis of

Blood hemoglobin n=64	Patients	
	No.	%
9-12gm%	25	39
5-<9gm%	36	56
<5gm%	3	5
Total	**64**	**100**
Serum creatinine n=37	**In Malarial Patients with Predominantly ARF.**	
	Patients	
	No.	%
<2mg%	1	3
2mg% -3mg%	2	5
>3mg%	34	92
Total	**37**	**100**
Total Bilirubin Level n=40	**In Malarial Patients with Predominantly Hepatic Function Impairment.**	
	Patients with jaundice	
	No.	%
1mg%-3mg%	7	17.5
>3mg%	33	82.5
Total	**40**	**100**

Table 4: Hemoglobin Level In Renal And Hepatic Complicated Malarial Patients

	No	%
Blood hemoglobin n=64		
9-12gm%	25	39
5-<9gm%	36	56
<5gm%	3	5
Total	**64**	**100**
Serum creatinine (n=37*)		
<2mg%	1	3
2mg% -3mg%	2	5
>3mg%	34	92
Total	**37**	**100**
Total Bilirubin Level (n=40)**		
1mg%-3mg%	7	17.5
>3mg%	33	82.5
Total	**40**	**100**

* Serum creatinine in malarial patients with predominantly Acute Renal Failure.)
** Total Bilirubin Level in malarial predominantly hepatic function impairment (patients with jaundice)

Table 5: Some laboratory investigations for patients with Renal And Hepatic Complicated Malaria

Final outcome	Malarial patients with renal and hepatic impairment n=64							
	With ARF		Hepatic damage		Both		Total	
	No.	%	No.	%	No.	%	No.	%
Improved	17	26.5	21	33	8	12.5	46	72
DAMA	2	3	4	6	1	2	7	11
Died	5	8	2	3	4	6	11	17
Total	24	37.5	27	42	13	20.5	64	100

P value = 0.398
(no-significant differences (p value >0.05) in the outcome of patients with renal and hepatic complicated malaria)

Table 6: Final Outcome With Malarial Patients Complicated With Renal And Hepatic Impairment (the outcomes of patients with renal and hepatic complicated malaria)

ARF in malaria[8]. More than 70% of the complicated cases improved after antimalarial therapy, haemodialysis and supportive measures. Eleven patients (i.e. 17%) died during therapy of which five (i.e. 8%) had ARF (Table 4).

Men were more affected in our study, compared with women, similar to observations of other groups[2],[4],[5]. This could be explained by the fact that men are more mobile and moving about, including in the swampy areas, compared with women in Asian countries, since women are more confined to their homes and near cooking fires, which offers them protection from biting mosquitoes. P. falciparum was observed in 100% of our cases[9]. ARF in P. falciparum can occur in three ways: acute tubular necrosis (ATN), the commonest presentation, acute tubulo-interstitial nephritis or less commonly acute glomerulonephritis (GN). ATN may be monitored in 1-4% of P. falciparum malarial ARF, but may reach up to 60% in severe malaria[7],[10]. Patients with ARF are usually oliguric (<400ml/dl) or anuric (<50-100ml/dl)2,5, and hyper-catabolic; the oliguric phase lasts for a few days to several weeks, which was also found in our study, where all patients were oligo-anuric. Hyperbilirubinaemia in falciparum malaria possibly predisposes to ARF, which may be only revealed by laboratory investigations[11]. Most patients of ARF and jaundice had predominantly conjugated hyperbilirubinaemia with cholestasis. ARF associated with jaundice had high mortality in comparison with non-jaundiced ARF patients[12]. However, it may be normal or increased duration of oliguric phase for a few days to several weeks(10).

Patients with oliguric renal failure were more common in our series, 100% of ARF patients, which is different from other studies (50-70%)(1). Earlier studies in Thailand showed 30% of adult patients with cerebral malaria had serum creatinine levels higher than 2 mg/dl (7,9). Such patients had higher incidence of hypoglycemia, jaundice, more prolonged coma and pulmonary edema (7,9). Similar studies recently done in Vietnam showed that about 50% of patients had serum creatinine levels greater than 2mg/dl (7,10). What is more interesting in our work is, 21% of the patients with ARF were jaundiced, compared with 20% of others (12,19). In our study, more than 42% patients had hepatic dysfunction without ARF, i.e. jaundice, raised T. bilirubin (level> 3 mg/dl). Hyperbilirubinaemia usually results from the complication of hemolysis and intrahepatic cholestasis rather than hepatocellular necrosis(9,20,21,22). The true malarial hepatitis is usually distinguished by more than threefold elevation of ALT, and is rare(11, 22). In our study 62% had hyperbilirubinaemia, and other clinical and paraclinical parameters of hepatic damage according to WHO criteria of severe and complicated malaria(9).

The major factors associated with mortality in our study were increased serum creatinine Scr, low hemoglobin, severe oligo/anuria, CNS involvement, and hyperbilirubinaemia. ARF is a serious complication with a reported mortality of 15 to 33%(16,17,18). In our research mortality was in 8% (n=5) having ARF. Whereas 6% (n=4) were having both ARF and hepatic dysfunction, and only 2 (3%) with hepatic dysfunction alone.

Prognosis of renal and complicated malaria depends upon the severity of the condition, associated extra-renal complications, response to antimalarial drugs and earlier indication of dialysis. 50% to 75% of patients without dialysis rapidly die(10,19,20,21). The selected mode of treatment is hemodialysis and should be initiated early in the course of illness, as peritoneal dialysis would be less effective because of impaired peritoneal microcirculation (2,3,6,7,11,13, 20). In our study the patients had undergone haemodialysis according to the indication mentioned (about 50% were haemodialyzed, due to lack of peritoneal dialysis).

The majority of the patients with jaundice had conjugated hyperbilirubinaemia with cholestasis. This association with malarial ARF is well described and may contribute to the reduction of GFR or development of ATN. In developing countries, limited medical resources at primary health care centers and late referrals compound outcomes(20,21). This is reflected in the need for immediate dialysis at presentation of 50% of patients referred to our center; lower than in other reports, which shows a need of dialysis in only 60% of patients with malarial ARF. Availability of renal replacement therapy for malarial ARF has been shown to improve outcome. In our present study, mortality was 14%, which is in agreement with other studies where renal replacement therapy was available.

Quinine is the drug of choice and is most widely used antimalarial drug in the case of severe and complicated malaria(10, 20). In this study also, most of our patients showed marked improvement, and the rest were treated with artemisinin derivatives.

From the above discussion, it shows that malarial acute renal failure and hepatic dysfunction is fairly common in Yemen. However, till date no such detailed studies have been done and this is the first of this kind. So the true incidence and prevalence of the disease in our country needs to be re-evaluated. We believe that survival can be improved by education and early transfer to a tertiary care center, where prompt dialysis and supportive management can be instituted.
We concluded that malaria is an important clinical entity in Yemen and other developing and undeveloped countries and the physicians should be vigilant about the deteriorating kidney and liver functions as early initiation of antimalarilal drugs and dialysis can be lifesaving.

References

1. Prakash J, Singh AK, Gujrati S, Maheshwari A. Acute renal failure in Malaria: Changing trends. Indian J Nephrol 2002;12:113-7. Annual Report, Department of Health Services 2057/058 HMG Nepal,

MOH: Malaria Control:pp108
2. WHO Malaria Action Program. Severe and Complicated malaria Trans R Soc Trop Med Hyg 1986;80 (suppl) 3-50
3. Sitprija V. Nephrology forum. Nephropathy in falciparum malaria, kidney Int 1988;34;866
4. Trang TT, Phu NH, Vinh H et al, acute renal failure in patients with severe falciparum malaria. Clin Infect Dis 1992;15 (5):874-80
5. Mate-kole MO, Yeboah ED, Affram RK, et al. Blackwater fever and acute renal failure in expatriates in Africa. Renal Fail 1996; 18(3):525-531
6. Eiam-Ong S: Malarial nephropathy : Seminars in Nephrology, 2003 Vol 23, No 1(January),: pp21-33
7. WHO: severe falciparum malaria, Trans R Soc Trop Med Hyg 2000 94:1-90, (Suppl 1)
8. Phillips RE, White NJ, Looareesuwan S, et al : Acute Renal failure in falciparum malaria in Eastern Thailand : Successful use of peritoneal dialysis. Presented at the XI international congress for tropical medicine and malaria, Calgary, Canada, 1989, September 6-11
9. Trang TT, Phc NH, Vinh H, et al: Acute renal failure in patients with severe falciparum malaria. Clin Infect Dis 1992,15:874-880
10. Anand AC, Ramji C, Narula AS, et al: Malarial hepatitis: A heterogeneous syndrome? Natl Med J India 1992;5(2):59-62
11. Barsoum RS: Malarial acute renal failure. J Am Soc Nephrology 2000:11:2147-2154,
12. Boonpucknavig V, Sitprija V: Renal disease in acute plasmodium falciparum infection in man kidney Int 1979:16:44-52,
13. Barsoum RS, Sitprija V: tropical Nephrology in Schier RW(ed): Diseases of the kidney and urinary tract (ed 7) Philadelphia, PA, Lippincott Williams and Wilkins, 2001, pp 2301-2349
14. Eiam-Oug S, Sitprija V: Falciparum malaria and the kidney : A model of inflammation , Am J kidney Dis 2000:36:1-11,
15. Barsoum R: Malarial nephropathies. Nephrol Dial Transplant 1998;13: 1588-1597
16. Lallo DG, Trevett AJ, Paul M et al. Severe and complicated falciparum malaria in Melanesian adults in Papua New Guinea. Am J Trop Med Hyg 1996;55(2):119124
17. Weler MW, Boker K, Horstmann RD, et al. Renal failure in a common complication in non-immune Europeans with P. falciparum malaria. Trop Med Parasitol 1991;42(2):115-118
18. Naqvi R, Ahmed E Akhtar F, et al. Predictors of outcome in malarial renal failure. Renal Fail 1996; 18(4): 685-688.
19. Prakash J, Gupta A, Kumar O et al. Acute renal failure in falciparum malaria: increasing prevalence in some areas of India. Nephrol Dial Transplant 1996; 11: 2414-2416.
20. Kanodia KV, Shah PR, Vanikar AV, Kasat P, Gumber M, Trivedi HL. Malaria induced acute renal failure: A single center experience. Saudi J Kidney Dis Transpl 2010;21:1088-91
21. Uncertainty in Mapping Malaria Epidemiology: Implications for Control Epidemiol Rev 2010 0: mxq013v1-mxq013
22. Pati SS, Mishra SK, Mohanty S, Patnaik JK, Das BS. Influence of renal impairment on plasma concentrations of conjugated bilirubin in cases of plasmodium falciparum malaria. Ann Trop Med Parasitol 2003;97:581-6.

Renal Colic during Pregnancy: Review of 21 cases

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Abstract

Objective: To determine the problems related to renal colic due to urinary stones during pregnancy, and the principles of management of those patients in our hospitals.

Material and Methods: It is a retrospective analysis of a series of 21 cases of renal colic due to urinary stones during pregnancy from March 2008 to April 2010 at Prince Rashid Ben Al-Hassan Military Hospital, Jordan. Presenting symptoms, diagnostic studies and management of renal stone were evaluated.

Results: There were 15,824 deliveries during this period in our study. 21 of them had renal colic due to urinary stones during pregnancy, with an overall incidence in this series of 0.13%. Most of them were in the third trimester of pregnancy followed by the second trimester and the least were in the first trimester. The most common complaints were flank pain (95.2 %), urinary symptoms (hematuria, dysuria and urgency) in 80.9%, nausea and vomiting in 14.3% and fever in 28.6 %. Spontaneous passing of stones was noted in 19 cases (90.5%) with conservative treatment. Two patients were unresponsive or relapsing after medical treatment and were treated surgically in the urological department by double J stents insertion, but no maternal or fetal loss was noted.

Conclusion: The majority of cases of renal colic due to urinary stones during pregnancy can be safely managed conservatively. The commonest presenting symptoms in our study were flank pain, urinary symptoms (hematuria, dysuria and urgency), and early surgical intervention resulted in safe maternal and fetal outcome.

Key words: Renal colic, urinary stones, pregnancy.

Introduction

Pregnancy has been described as a test of renal function. Major anatomical and physiological changes affecting the entire urinary tract occur during pregnancy. Renal function dramatically alters with a 50% increase in renal blood flow and glomerular filtration rate; also increased circulating hormone levels and the pressure effects of the gravid uterus on the collecting system result in dilatation of the ureter, renal pelvis and calyx. All these alternations in urinary tract physiology and anatomic changes during pregnancy may affect the interpretation of renal function tests during pregnancy and make diagnosis and treatment a more challenging issue(1).

Generally though, renal colic due to urinary stones during pregnancy is a relatively uncommon occurrence during pregnancy. The prevalence of renal stone in pregnancy has been estimated at approximately 1 per 1,500 women similar to the nongravid woman, with the vast majority being asymptomatic and a chance finding(2). Urinary stones complicates 0.026-0.531% of pregnancies and presents an interesting challenge to the obstetrician, radiologist and urologist(3).

Renal colic can occur at any time during gestation but is most common in the second and third trimester as seen in this study, because the enlarging gravid uterus increases the symptoms of the calculus, as gestation progresses(4). In a pregnant woman with symptoms suggestive of urinary calculi, it is imperative to confirm the diagnosis as quickly as possible with the minimum of risk to the developing fetus. Renal colic can precipitate premature labor and delayed diagnosis and intervention can result in permanent renal impairment(5).

Recurrent renal colic is a common complication of renal stones and represents the most common non-gynecological condition requiring hospitalization and intervention in pregnant woman(6). However, the differential diagnosis of appendicitis, pyelonephritis and premature labor should be considered with the latter two often associated with stones(7).

The use of ultrasound may confirm the diagnosis in the majority of non-gravid patients, but diagnostic accuracy is reduced during pregnancy, as the imaging diagnosis of urolithiasis in pregnancy is further complicated by the physiologic and hemodynamic alterations in the maternal urinary tract. Ultrasound also has limitations in detecting ureteral calculi. Recent use of trans-vaginal ultrasound has improved the detection rate of calculi at the ureterovesical junction(8).

Over three-quarters of renal calculi presenting during pregnancy will pass spontaneously with conservative management comprising bed rest, hydration, analgesia and antibiotics where indicated. In cases where there is calculus causing obstruction of the urinary tract, relief of the obstruction has required minimally invasive techniques as cystoscopic stent placement and percutaneous stent insertion(9).

Our aims in this study were to determine the problems related to renal colic due to urinary stones during pregnancy, to report our experience in its management and its effect on fetus outcome and to find out the overall morbidity and mortality of the disease in our hospitals.

Materials and Methods

This is a retrospective study at Prince Rashid Ben Al-Hassan Military Hospital from March 2008 to April 2010. All patients with renal colic due to urinary stones during pregnancy who were admitted to the gynecology and obstetrics department were enrolled in treatment protocol.

All diagnoses were made with a combination of medical history and physical examination, laboratory tests (such as WBC, Serum urea, creatinine, also urine analysis and culture was requested) and ultrasonography. All patients were initially managed conservatively. Conservative management varied according to the admission diagnosis. Patients unresponsive or relapsing after medical treatment were considered conservative treatment failures and were referred to the urological department. Also surgical measures are reserved for patients with sepsis, intractable pain, and acute renal failure.

We collect data from their medical records on age, gravidity, parity, trimester of pregnancy, symptoms, signs, laboratory and radiological tests, postoperative complications, duration of hospital stay and fetal and maternal outcome. Operative reports were also reviewed.
The local ethics committee approved the protocol and all patients signed an informed consent prior to their inclusion in the present study.

Results

There were 15,824 deliveries during this period in our study. The age of these patients ranged from 16 to 40 years. Of those, 21 women were admitted following diagnosis of renal colic due to urinary stones during pregnancy. The overall incidence of renal colic during pregnancy in this series was 0.13%. Most of them were in third trimester of pregnancy 57.1% (no=12) followed by the second trimester 28.6% (no=6) and the least were in the first trimester 14.3% (no=3).

The most common complaints were flank pain in 20 patients (95.2 %), urinary symptoms (hematuria, dysuria and urgency) in 17 women (80.9%), nausea and vomiting in 3 women (14.3%) and fever in 6 women (28.6 %) as shown in Table 1. Physical examination of patients revealed that costovertebral angle tenderness was present in 12 patients (57.1%). Only 6 patients were febrile (28.6%) whereas leukocytosis more than 15.000/mm3 was found in 5 patients (23.8%), while abnormal kidney function tests was found in 2 patients (9.5%) and microscopic hematuria in 17 patients (80.9%). Sterile urine culture was seen in 5 patients (23.8%). Also all of these patients underwent renal ultrasound on admission and it confirmed the diagnosis and visualized stones were obtained in 85.7 per cent of the cases (18 patients). Plain KUB film was done in 3 cases and stones could be seen in 2 cases (66.7%). Limited IVP was done in one case and the diagnosis could be done in all of them (100%). These are shown in Table 2.

The treatment of such patients requires a multidisciplinary team approach involving the urologist, obstetrician, and radiologist. The initial management should be conservative, consisting primarily of bed rest, adequate hydration with intravenous fluids, correction of electrolytes, and pain management with analgesia when required. Combining opioids with non-steroidal anti-inflammatory drugs (NSAIDs) is the optimal evidence-based regimen to treat severe symptoms.

Conservative medical management is recommended initially, especially during the first and third trimesters, in which surgical intervention may confer risk of abortion or premature labor, respectively. Conservative management varied according with the admission diagnosis, so patients with urinary tract infection also received broad spectrum antibiotics.

Spontaneous passing of stones was noted in 19 cases (90.5%) with conservative treatment. The remaining two patients (9.5%) unresponsive or relapsing after medical treatment, were considered conservative treatment failures and were treated surgically during pregnancy in the urological department by double J stents insertion. Mean hospitalization time was 4 days. Fetal distress was not evident in any of the patients; also there were no maternal and fetal losses noted.

Discussion

Our incidence of renal colic during pregnancy in this series was 0.13%, which is comparable to other