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**Obstacles facing primary health  
care physicians in diagnosing and  
managing depressed patients in the  
Tabuk area of Saudi Arabia**

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## From the Editor

This is the first issue of the World Family Medicine journal for 2013. We are grateful for our authors, reviewers, editorial board and the publishing house for all the achievement of the journal during last year where the readership statistics have improved drastically. We look forward this year for more positive steps to put the journal as one of the leaders in the field.

A cross sectional survey from Saudi Arabia looked at the knowledge attitude and practice regarding diabetes and diabetic retinopathy among final year medical students. Diabetes Mellitus is a global public health problem. The morbidity caused by its ocular complication has placed this disease as the fourth leading cause of world blindness. The study concluded in Al Hasa region of Saudi Arabia and various studies conducted in different places have unfortunately shown inadequate knowledge, attitude and practice among the general practitioners and the medical students about diabetes and diabetic retinopathy. This study was conducted to assess the knowledge, attitude and practice of final year students and the interns of King Faisal University Medical College, Al Hasa regarding diabetes and diabetic retinopathy. As future primary care physicians, they are at the frontline of diabetes and diabetic retinopathy management. Their present curriculum does not emphasize these topics. Understanding their baseline Knowledge, Attitude and Practice will allow the medical education department to re-examine their curriculum and design one that is more appropriately targeted to the needs of the diabetic community.

A paper from Sultanat Oman looked at Multidimensional approaches to reduce the rising caesarean section rate in Nizwa hospital. Rising caesarean section rate is a concerning trend for the future of Oman. A retrospective analysis of the rising rates of caesarean section was done from year 2006 up to 2011 and the main indications and complications for caesarean section in year 2011 were analysed. A rising trend of caesarean section has been observed in the last six years as the rate has increased from 15.1% in 2006 to 18.9% in 2011. The authors concluded that a multilevel, multidisciplinary approach and strategies are needed to change the system that would help the midwives, obstetricians and various working groups together to achieve a common goal of developing care to reduce caesarean sections in Oman.

A paper from Nigeria aimed at assessing the knowledge of Nigerian Ophthalmologists about computer vision syndrome. This study was conducted during the annual congress and scientific conference of Ophthalmological Society of Nigeria in 2010. One hundred and forty respondents selected by simple random sampling were asked to participate in this study by filling in a structured questionnaire. A total of 102 filled questionnaires were retrieved out of 140 administered, giving a response rate of 73%. The respondents comprised of 64(62.7%) males and 38(37.3%) females. The majority of the respondents were aware of computer vision syndrome and had fair knowledge of its symptoms and treatment.

A paper from Abia State looked the benefit of supervision in Primary Health Centres. This is often not achieved in developing countries including Nigeria. Traditionally, supervision emphasizes inspection of facilities without regard to facilitation. Supervisors blame individuals rather than look for root causes in deficient processes. For this reason, traditional supervision has tended not to 'empower' staff to engage in problem solving and/or in taking initiatives in improving service quality and access. There is need to change focus of supervision from inspecting facilities and gathering service statistics to concentrating on performance of clinical tasks and resolution of problems

Dr Khashashneh reports on congenital chyloous ascites. Diagnosis was confirmed by abdominal puncture and ascetic fluids were taken. The etiology of most cases of chyloous ascites remains unknown, but it may be congenital or acquired. Congenital chyloous ascites is primarily related to inadequate lymph drainage as a result of maldevelopment and may occur from different causes including genitourinary, gastrointestinal, infections, and metabolic and malignancy. Here we describe an infant with congenital chyloous ascites who improved after total parenteral nutrition (TPN) and somatostatin administration, who was managed in the Neonatal intensive care unit at Prince Rashid Hospital, Irbid, Jordan. The baby needed treatment by octerotide after other forms of conservative therapy proved ineffective.

A paper from Jordan aimed to determine the effect of cholesterol and Chol:HDL ratio in ischemic heart disease patients presented to the emergency department at Queen Alia

Hospital (Jordan) with chief complaint of chest pain. This study was done in Queen Alia Military Hospital. Blood specimens were collected from 509 patients who were also smokers and hypertensive. Results were compared with the control group who had no past history of any illness and normal vital signs. The mean value of Cholesterol:HDL ratio in males and females in CHD: IHD group was greater than that of the healthy individuals. The authors concluded that the total triglyceride and LDL\_cholesterol may be of value to identify people at risk. Lipid levels may be affected by diet, exercise, smoking and certain medications.

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# Obstacles facing primary health care physicians in diagnosing and managing depressed patients in the Tabuk area of Saudi Arabia

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## Abstract

**Background:** Depression is one of the most common morbidities worldwide, including in Saudi Arabia. It is vital to diagnose and manage the disease at the primary health care level. All barriers interfering with this task should be identified and corrective measures implemented.

**Objective:** To assess the barriers facing primary health care physicians in diagnosing and managing depressed patients in primary health care centers

**Design:** Cross sectional study.

**Setting:** All primary health care centers which serve Military personnel and their dependents at the North West Armed Forces Hospital, Tabuk City, Saudi Arabia.

**Subjects:** All primary health care physicians (n=75) working at the time of the study in primary health care centers that belong to North West Armed Forces Hospital.

**Methods:** Subjects completed a self-administered questionnaire consisting of personal and socio-demographic data, organizational and patient's barriers to diagnose and treat depression in primary care settings.

**Results:** All 75 physicians responded and returned the questionnaires. About 78% agreed that the diagnosis of depression is their responsibility and only 4% disagreed. More than two-thirds (69.3%) agreed and 9.3% disagreed that treatment of depression is their responsibility. More than half (57.3%) agreed that lack of knowledge of diagnostic criteria of depression was a limiting factor while 73.3% agreed that lack of knowledge of treatment of depression was another limiting factor. About 90% or more

physicians agreed that the appointment time was too short for taking adequate history, to provide counselling/education; that mental health professionals were not available within the PHC setting; that patients or their families were reluctant to accept the diagnosis of depression and that patients were reluctant to take antidepressants.

**Conclusion:** Continuous medical education is required for the health care providers on depression and needs to be instituted and adequate resources for counseling services and antidepressant medications at primary care level need be made available. There is also a need to improve the quality and to integrate services with the mental health referral services. Efforts to destigmatize depression may result in increased rate of diagnosis and treatment of depression in the primary care setting, improving outcomes in the study population.

## Introduction

The high prevalence of depression and its impact on social well-being and consequential morbidity, is well-recognized [1-4]. Many people suffering from depression receive treatment in primary care settings [1,5-7]. Treatment for depression is increasing rapidly in many countries including the developing world. Major depression is expected to be the second leading cause of disability worldwide [1]. Studies have shown the lifetime prevalence to be as high as 20% in women and 10% in men [8]. Psychological disorders in the Saudi Community in consecutive patients attending Primary Health Care Centers (PHCCs) were estimated to be 30 - 46%. This resulted in a call for a national campaign to combat the growing problem [9].

A survey of 185 countries conducted by the World Health Organization (WHO) found that 41% do not have a mental health policy and 28% have no specific budget for mental health. Of those countries that do report mental health expenditures in the developing world, 36% spend less than 1% of their total health budget on mental health compared to 5 - 10% in developed countries [10]. In addition to these financial constraints, many other barriers were identified concerning diagnosis and treatment of mental morbidity, including depression. Studies have demonstrated that specific factors interfere with recognition of this disorder in the primary care setting and decrease the likelihood of an accurate diagnosis. Variables that relate to the patient include lack of awareness and understanding of the nature of the disease and its symptoms so that they can be accurately reported to the physician. Variability in clinical presentation and the presence of comorbid medical disorders also make detection difficult. Complaints of physical symptoms confuse the clinical picture. In addition, patients are ashamed to admit to psychological symptoms of depression and fear the stigma attached to it. Interfering factors that relate to the physician include a lack of knowledge about

the disease and lack of training in its management that reduces the physician's ability to render a diagnosis and undermines confidence in the capacity to treat the illness successfully. Reluctance on the part of the physician to inquire frankly about depression also plays a role. Other barriers include stigmatization of sufferers, poor coordination between the mental health and primary health segments of the health care delivery system, and a lack of education of primary health workers in providing mental health services [11]. Previous studies in Saudi Arabia showed that there were barriers confronting primary health care physicians (PHCPs) in diagnosing and treating psychiatric morbidity such as depression [12-13].

The WHO is currently developing strategies to address shortfalls in these systems, including information collection, research and policy development, as well as advocacy and the promotion of mental health services in developing countries [10].

Psychiatric illnesses have become a major challenge to PHCPs all over the world but the disease is still mostly under diagnosed and under treated [4,14,]. PHCPs are the providers most likely to see patients when they first become ill but unfortunately only one third to one half of persons with depression are diagnosed by their primary health care (PHC) doctors; however in the end the majority of depressed patients will be handled by their family doctors [15]. Studies showed that 30 - 80% of patients with depressive symptoms are actually missed by their family doctor [16]. In a local study 52.6% of PHCPs admitted their lack of training in psychosocial medicine [7]. This explains the higher referral rate of psychiatric patients to the hospital. Studies found that most of PHCPs are not adequately trained to treat mentally ill patients and that the knowledge and the skills of PHCP in detecting, diagnosing and treating psychiatric diseases are limited [17,18].

The objective of this study is to identify the barriers facing PHCPs in the diagnosis and treatment of depression, and the obstacles encountered by them to treat depression in PHCCs in North West Armed Forces Hospital (NWAFFH) in Tabuk City, Saudi Arabia.

## Methodology

This is a cross-sectional study conducted in all the PHCCs that belong to the NWAFFH in Tabuk City, Saudi Arabia.

The study population was all the 75 PHCPs working at the time of the study in the PHCCs which belong to the NWAFFH, during the period 1/10/2007 through 30/12/2007.

The data was collected using an adopted, locally validated, pilot tested revised self-administered version of the questionnaire used in a previous international study [15]. It contains questions about physician demographics and professional attributes. There are specific questions asked concerning the barriers related to the physicians, patients and the organization affecting diagnosis and treatment of depression in PHC settings.

The collected data was checked for completeness and accuracy, then entered and analysed using the Statistical Package of the Social Sciences (SPSS) version 11.5.

The research project was approved by the Research Committee at NWAFFH and the permission of PHCCs Director was obtained before the commencement of the study. All information was kept confidential, and used for research purposes only. The data was presented in grouped-format without any individual identification

## Results

All physicians working in the PHCCs in NWAFFH in Tabuk City during the study period that constituted the study population, completed and returned the questionnaires. The median age of more than three quarters of the physicians was 39 years ranging from 28 - 55 years with

Response of physicians*	Strongly Agree N (%)	Agree N (%)	Neutral N (%)	Disagree N (%)	Total N (%)
Diagnose	38 (50.7)	21 (28.0)	13 (17.3)	3 (4.0)	75 (100)
Treat	17 (22.7)	35 (46.7)	16 (21.3)	7 (9.3)	75 (100)
Combined %	(36.6)	(37.3)	(19.3)	(6.7)	(100)

\*Statement to which response was sought from physicians was as follows: "It is the primary health care physician's responsibility to diagnose and treat depression"

Table 1: Proportion of physicians who agreed or disagreed that it is their responsibility to diagnose and treat depression in primary health care settings

Level of confidence	Not confident N (%)	Somewhat confident N (%)	Mostly confident N (%)	Very confident N (%)	Total N (%)
Diagnosis	1 (1.3)	25 (33.3)	36 (48.0)	13 (17.3)	75 (100)
Treatment	7 (7.3)	34 (45.3)	26 (34.7)	8 (10.7)	75 (100)
Combined %	(5.3)	(39.3)	(41.3)	(14.0)	(100)

Table 2: Level of confidence of physicians in diagnosing and treating depression in primary health care settings

Degree of limitations	Great deal N (%)	Somewhat N (%)	None N (%)	Total N (%)
Incomplete knowledge of diagnostic criteria	13 (17.3)	30 (40.0)	32 (42.7)	75 (100)
Incomplete knowledge for treating depression	15 (20.0)	40 (53.3)	20 (26.7)	75 (100)
Lack of effective treatment	15 (20.0)	41 (54.7)	19 (25.3)	75 (100)

Table 3: The perception of physicians of the degree of limitations preventing them from diagnosing and treating depression

13.1 median years of experience ranging from 1 to 30 years. About 54% have a degree in family medicine, 29.2% were graduates of the MBBS degree and 16.6% had qualifications in another speciality. Only 64% of respondents received courses in psychiatric illness.

Table 1 shows the level of agreement of the PHCPs with the statement that diagnosis and treatment of depression is their responsibility. More than half and less than a quarter strongly agreed that diagnosis and treatment of depression are their responsibilities. In general about 70% of the PHCPs agreed that both diagnosis and treatment of depression is their responsibility. PHCPs who strongly disagreed with their responsibility for treatment were more than twice those that disagreed with their responsibility for diagnosis (9.3% compared to 4.0%).

Table 2 shows the levels of confidence of the physicians in their ability to diagnose and treat depression. Nearly two-thirds of the PHCPs appear to be confident in their abilities to diagnose, but less than half had the confidence to treat depression (65.3% compared |

to 45.4%). Only 17 and 11% of the PHCPs were very confident in diagnosing and treating depression respectively. The proportion of PHCPs not confident at all in treating depression was about 6 times more than those not confident in diagnosing the condition (7.3% compared to 1.3%).

Table 3 pertains to the degree of limitations faced by PHCPs in diagnosing and treating depression. About a fifth of the physicians think that they are greatly limited by their incomplete knowledge for diagnosing and treating or by the lack of effective treatment. Only 19-32% of the PHCPs are not limited at all in these areas.

Less than 8% of physicians claimed they are not affected by organizational inadequacies to provide care for depression (Table 4). The rest of the PHCPs are somewhat or greatly affected by the inadequate or less than optimal organizational facilities or arrangements. A sizeable proportion of PHCPs appear severely limited by the short consultation time available to treat their patients and the unavailability of mental health professionals in primary care settings.

One of the most important limitations concerns the reluctance of the patient or the patient's family to accept the diagnosis of depression or the patient's reluctance to take the medications and consult mental health specialists (Table 5 - top of ext page). Only less than a fifth of the PHCPs think that the patients' or their family's dispositions or attitudes pose no obstacle or any limitation in the performance of the physicians' duties.

## Discussion

The findings of this study revealed the many barriers faced by PHCPs with regard to the diagnosis and treatment of depression and highlighted the need to ameliorate the deficiencies in the primary health care system. Although this situation is prevalent in the Tabuk region of Saudi Arabia, it may not be inaccurate to assume the situation may be alike in PHCCs in other parts of the country. The exception to this assumption may be the health services available in metropolitan areas of Riyadh, Jeddah and AlKhubar where advanced facilities and expertise are available to diagnose and treat depression.

Degree of limitation	Great deal N (%)	Somewhat N (%)	Non N (%)	Total N (%)
Appointed time is too short for an adequate history taking	33(44.0)	35(46.7)	7(9.3)	75(100)
Inadequate time for me to provide counselling/education	40(53.3)	32(42.7)	3(4.0)	75(100)
Mental health professionals are not within PHC setting	27 (36.0)	42 (56.0)	6 (8.0)	75 (100)

Table 4: The degree of organizational limitations affecting the ability of physicians to diagnose and treat depression

Degree of limitation	Great deal N (%)	Somewhat N (%)	Non N (%)	Total N (%)
Patient's or their family's reluctance to accept diagnosis	34 (45.3)	34 (45.4)	7 (8.0)	75 (100)
Medical problems were more pressing	12 (16.2)	48 (64.9)	14 (18.9)	75 (100)
Patient's reluctance to take antidepressants	33 (44.0)	33 (44.0)	9 (12.0)	75 (100)
Patient's concern for side effects of antidepressants	19 (25.7)	46 (62.2)	9 (12.2)	75 (100)
Patient's reluctance to be seen by mental health professionals	27 (36.0)	38 (50.7)	10 (13.3)	75 (100)
Symptoms may be explained by other medical illness	12 (16.0)	51 (68.0)	12 (16.0)	75 (100)

Table 5: The degree of physicians' limitations concerning patient aspects

Although a vast majority of the PHCPs are in agreement that it is their responsibility to provide services for depression, their desire to provide such services is affected by a lack of confidence in diagnosing and treating depression in primary health care settings which is probably related to lack of training intervention and exposure to continuous medical education. It is also related to a lack of effective treatment in such settings. Other contributory factors include deficiencies in organizational arrangement such as short consultation time and unavailability of mental health professionals in primary care settings. Another factor is the reluctance of the family to accept the diagnosis and or the reluctance of the patient to take the medications or consult mental health specialists.

It appears that that most PHCPs are not adequately trained to treat

mentally ill patients and that their knowledge and the skills in detecting, diagnosing and treating psychiatric diseases are poor. The findings of the present study are, in general, consistent with the findings of other studies which showed that 30 - 80% of patient with depressive symptoms are actually missed by their family doctor [17,18]. This may be explained by the admission of more than half of PHCPs that they lacked training in psychosocial medicine. This may also explain the higher referral rate of psychiatric patients to the hospitals. Lack of availability of appropriate therapies and suboptimal treatment were additional barriers in primary health care settings, similar to previous findings[2, 19,20].

Depression can be treated effectively in PHCCs with proper quality control and appropriate speciality consultations. Indeed studies have demonstrated that antidepressant

medication prescribed for acute continuing treatment of depressed primary care patients was associated with a 50 - 60% decrease in depressive symptoms, similar to that found for psychiatric patients [21].

Another obstacle includes the inability to recognize symptoms of depression in patients by the PHCPs. Physicians attributed this to a lack of structured psychiatric training programs and /or post graduate courses similar to previous reports [17,18]. Training the primary health care team to treat depression using set protocols, guidelines, brochures, videotapes, and quality assurance meetings were found to be very effective corrective measures [13, 21].

Quality improvement is the cornerstone of any system especially in a vital discipline like medicine. By improving the quality of primary

health care programs patients suffering from depression can have a better opportunity for being treated and consequently a higher treatment rate, better health outcome and an increased chance for remaining employed for at least a year if the patient remains treated in primary health care centers [15,18]. Stepwise guidelines prepared for use by the PHCPs for the detection, diagnosis and treatment of major depression are very important to ensure better quality of mental health care. Family doctors should evaluate risk factors and maintain a high index of suspicion on mental morbidity.

There is accumulating evidence that more intensive, organized treatment that integrates mental health practices into primary health care improve outcomes for the depressed patient [22]. We should encourage the PHCP to actively participate in continuous medical educational activities and provide them with continuous quality care programs to correct the depressing image of depression treatment in primary care.

#### Study limitations:

The study did not include Primary Care physicians in the Ministry of Health and the Private sector which affects the generalizability of the findings.

#### Conclusion

Continuous medical education is required for the health care providers on depression, and needs to be instituted and adequate resources for counseling services and antidepressant medications at primary care level need be made available. There is also a need to improve the quality and to integrate services with the mental health referral services. Efforts to destigmatize depression may result in an increased rate of diagnosis and treatment of depression in the primary care setting, improving outcome in the study population.

#### List of abbreviations

**PHCCs:** Primary health care centers  
**WHO:** World Health Organization  
**PHCPs:** Primary health care physicians

**PHC:** Primary health care  
**NWAFH:** North West Armed Forces Hospital

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# Health Related Quality of Life of Patients with Chronic Liver Disease Attending Family Practice Clinic, Suez Canal University Hospital, Ismailia, Egypt

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## Abstract

**Objectives:** A chronic liver disease has a terrible impact on the quality of life of the patients. Such impact could be attributed to annoying symptoms and signs or complications that could affect QOL.

This study was aimed at assessing Health Related Quality of Life (HRQOL) among patients with chronic liver disease (CLD) and identifying factors that might affect their Quality of Life.

**Methods:** A cross-sectional study design was conducted on 172 adult patients (>18 years) of both genders, with chronic liver disease attending Family Practice Clinic of Suez Canal University Hospital, Ismailia, Egypt between 2008-2009. A designed questionnaire was used to identify the socio-demographic data, clinical manifestations of

CLD, severity of the disease and other co-morbidities. Another questionnaire was used to assess the HRQOL in patients with CLD. The questionnaire included 33 questions divided into five domains (physical, social, psychological, impairment and health perception). Answers to these questions had a scale from 1 (best) to 7 (worst). Impaired QOL was considered at the cut off point of 50%.

**Results:** The present study showed that QOL of the majority of the studied population (83%) was affected (QOL score >50% of maximum score). Health perception and physical domain were the most affected. Patients with DM as co-morbid disease were more affected in their QOL than others.

Stepwise regression analysis showed that total score of quality of life was linked to some independent parameters such as illiteracy, having a severe form of

CLD and having ascites or abnormal portal vein ( $P<0.05$ ).

**Conclusion:** Quality of life was affected in patients with CLD. It is evident that co-morbid DM, smoking, presence of cirrhosis and severity of the disease might increase the impairment of the QOL. Such impairment might be explained partially because other variables (which were not addressed in the current study) may play a role in alteration of QOL rather than CLD. Health education regarding the negative impact of smoking on liver disease and control of diabetes mellitus are of high priority during the daily care of patients with CLD. Training of Family physicians about QOL and its related issues in daily practice is crucial for patients with chronic illnesses particularly those with CLD.

**Key Words:** Chronic Liver Disease, Quality of Life

## Introduction

The World Health Organization (WHO) has declared chronic liver disease as a global health problem. The available data suggests that the prevalence of HCV infection is approximately at 2.2-3.0% worldwide (130-170 million people). While individual estimations from different regions and countries have undergone some change since the first estimation made by WHO in 1997, the overall picture is still similar, with the highest prevalence of HCV infection found in the African and the Eastern Mediterranean region.(1,2) After the initial acute phase of infection, the majority (50-85%) of patients infected with the hepatitis C virus (HCV) develop the chronic form of the disease, which, in 20-30% of cases, will evolve to cirrhosis, liver failure or hepatocellular carcinoma, after several decades. (3)

Unfortunately, in Egypt the situation is quite worse; reports indicated an unusually high prevalence of anti-HCV antibodies in different groups in the community. The Egyptian Ministry of Health and Population (MOHP) reported the prevalence rate of 12% in a community-based study with an estimated 7.2 million people affected. Chronic liver disease is one of the important health problems in Egypt due to co-morbidity of schistosomiasis and viral hepatitis.(4)

In a recent community-based study, the estimated overall prevalence of anti-HCV antibody was 14.7% and positive HCV DNA in sera was 9.8% among the studied population (11,126 Egyptian citizens).(5) The high prevalence of active infection with HCV in Egypt is noticed clearly with almost 7.5 million individuals chronically infected with HCV and of these 1.5 million (25%) are cirrhotic. According to the expected prognosis in the later group (cirrhotic patients), about 75,000 (5%) will be decompensated, 30,000 (2%) will have hepatocellular carcinoma (HCC) and 60,000 (4%) will die each year. (6)

Measurement of health-related quality of life (HRQOL) becomes increasingly important in clinical patient management.(7) Chronic liver diseases have a terrible impact on the quality of life of the patients. Such impact could be due to annoying symptoms and signs or complications. Patients with chronic liver disease suffer from fatigue, pruritus and loss of self esteem, depression and other complications of cirrhosis such as hepatic encephalopathy, ascites, spontaneous bacterial peritonitis and recurrent variceal hemorrhages that have effect on QOL.(8)

Health-related quality of life is important in measuring the impact or burden of a chronic disease. The World Health Organization recognized such importance and included mental and social well being as integral part in the definition of health.(9) This study was conducted for the purpose of assessing Health Related Quality of Life (HRQOL) among patients with chronic liver disease (CLD) and identifying factors that might influence their Quality of Life (eg. Severity of CLD, Co-morbidity, residence, illiteracy,...)

## Subjects and Methods

A cross-sectional study design was used to assess HRQOL of patients with CLD. It was conducted on 172 adult patients (>18yrs) of both genders with chronic liver disease attending Family Practice Clinic of Suez Canal University Hospital affiliated to the Faculty of Medicine-Suez Canal University (FOM/SCU). The clinic is different from other clinics in Suez Canal Hospital. This clinic is run by trained Family physicians. The care provided to the attending patients in the clinic is considered to be primary health care.

The sample size was 172 patients. It was increased by 10% to become 185 participants due to the anticipated non-participating and drop-out rate. The calculated sample size was obtained from patients attending Family Practice Clinic and satisfying the inclusion criteria over the period of four

months (July-October 2008). Patients having hepatic encephalopathy, psychiatric disorders, Hepato-Cellular Carcinoma (HCC) and those with severe co-morbid diseases affecting QOL as evident from clinical presentations and investigations in medical records (uncontrolled DM, hypertension, renal failure, heart failure, ischemic heart disease, tuberculosis and chronic obstructive pulmonary disease) were excluded.

A designed questionnaire was used to identify the socio-demographic data, clinical manifestations of CLD, severity of the disease and other co-morbidities. The patients were subjected to history taking, clinical examination, biochemical testing for Liver function evaluation (ALT, AST, serum albumen, total serum bilirubin and prothrombin time), HBsAg and HCV antibody using enzyme-linked immuno-sorbent assay (ELISA). Also, abdominal ultrasonography was conducted for all patients. The spleen was considered as enlarged if it was > 13 cm in length along its axis. Portal hypertension was diagnosed if the diameter of the portal vein was > 13 mm and/or the diameter of the splenic vein > 8 mm.

According to the available data, the severity of liver disease was assessed by Child-Pugh classification that is, based on two clinical data that included ascites and encephalopathy and three laboratory findings (Bilirubin mg/dl, Albumin g/dl and Prothrombin time/INR). The child score is ranged between (5 -15). It is classified as Child A score (5-6), Child B score (7-9) and Child C score (10-15).

Another questionnaire was used as a tool to assess the HRQOL in patients with CLD. This questionnaire has 33 questions divided into five domains: social domain (5 items), psychological (9 items), and physical (10 items), impairment (6 items) and health perception (3 items). Each item had a scale from 1 (best) to 7 (worst). (10) Impaired QOL was considered at the cut-off point of 50%.

### Statistical analysis

The obtained data were coded, entered and processed on a personal computer using Statistical Package of Social Science (SPSS) version 10. The appropriate statistical tests were used to identify significant difference. Chi square test was used for categorical data and Fischer Exact test was used if at least one expected value was less than 5 (in 2 x 2 tables). Un-paired t-test was used for comparing urban and rural subjects according to each QOL domain. One-way ANOVA was used to find the worst QOL domains. A stepwise logistic regression analysis was used to test association of QOL with the studied variables. Statistical significance was considered at p-value  $\leq 0.05$ .

### Results

Out of one hundred eighty five participants who were included in the study, 172 completed the study to the end. Of these 51.2 % were females and 62.2% were in the age group of >45 years. About two-thirds of the studied patients (63.4%) were resident in the rural community. More than two-thirds (68.2%) of the studied patients were illiterate. About eighty two percent (81.4%) of the studied patients were married and 44.2% were unemployed, including housewives. About one third

(28.48%) of the studied patients were smokers and 59.3% have perceived their income as inadequate.

The majority of studied patients (59%) have had CLD for a period of less than five years. Regarding the etiology of CLD among the studied patients, it was found that, HCV infection was identified as a cause of CLD in 78.5%, either alone (44.8%) or combined with others (33.7%) [either with schistosomiasis (31.4%) or with HBV in 2.3%]. On the other hand, HBV and schistosomiasis were responsible for 15.1% and 6.4% respectively. Diabetes mellitus was present in 15% as co-morbid disease.

Fatigue, abdominal pain, bleeding per orifices and dyspepsia were the most frequent symptoms (51%, 50%, 42.4%, and 39% respectively). The main clinical findings detected by clinical examination of the studied patients, were Splenomegaly (74.4%), hepatomegaly (57%) and palmer erythema (26.7%). Concerning the liver cirrhosis among the studied patients, it was detected among 102 patients (59.3%) using ultrasound as the diagnostic tool. According to Child Pugh classification, 66 % of the studied patients were classified as Child A, 25% as Child B and 9% as Child C.

Quality of life of the majority of the studied patients (83%) was affected (QOL score > 50% of maximum score) as shown in Figure 1. About seventy percent (70.3%) of the studied patients were affected in the health perception domain (>50% of maximum score in each domain) followed by physical domain (69.2%), psychological domain (45%); while effect on health (impairment) was the least affected domain (33.1%) as shown in Figure 2.

About one-fifth (18%) of studied patients had only one affected domain of life (>50% of maximum score in each domain), 16% had two affected domains, 17% had 3 affected domains, 26% had 4 domains and 23% showed affection in all domains as shown in Figure 3. The most affected domain of QOL was health perception ( $57.17 \pm 15.58$ ), followed by physical ( $54.33 \pm 15.62$ ), psychological ( $50.26 \pm 12.92$ ) and social ( $45.81 \pm 17.14$ ). The least affected was impairment domain ( $39.96 \pm 14.74$ ) as shown in Table 1 (see page 14).

Concerning factors that might affect the quality of life of patients with CLD, there are some independent predictors such as residence in rural community. The mean score of HRQOL in all domains as well as

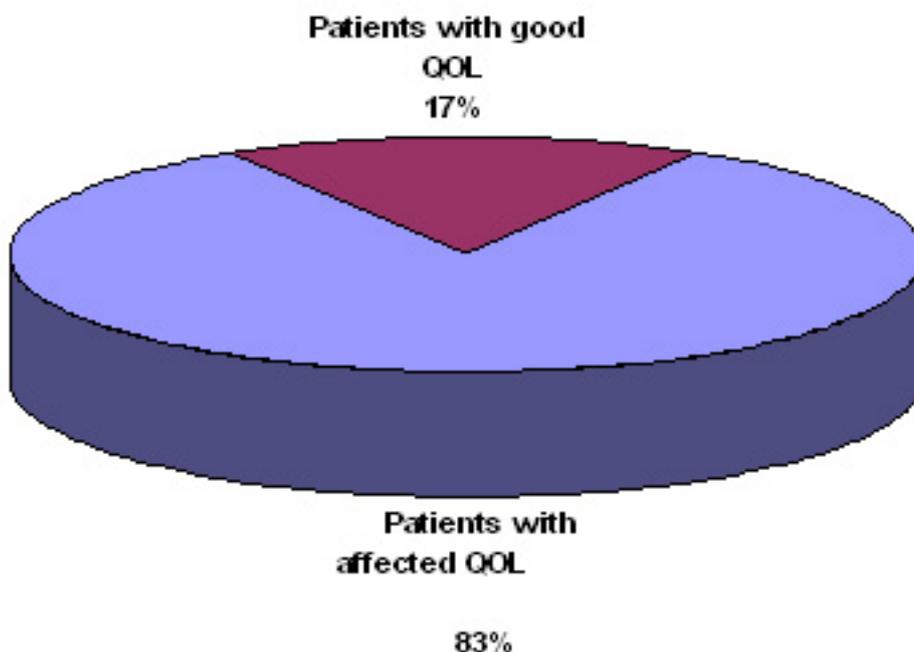


Figure 1: Distribution of studied patients according to their Quality of Life (QOL)

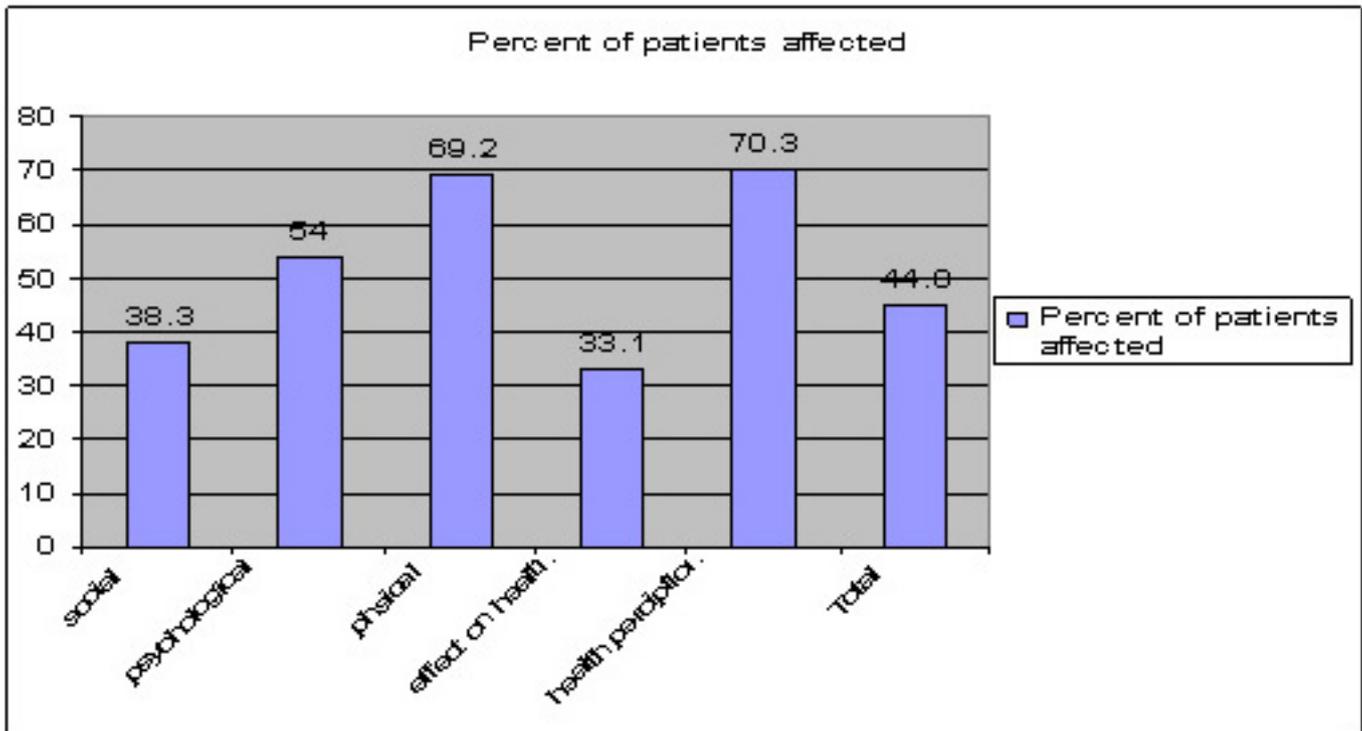


Figure 2: Distribution of studied patients according to their QOL in different domains and in total

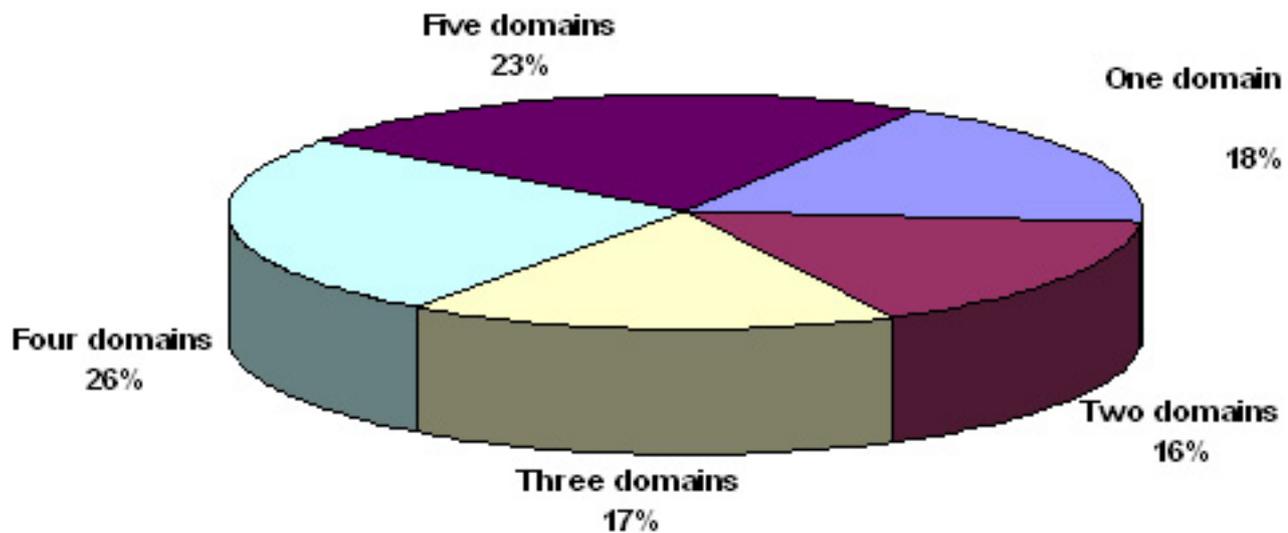


Figure 3: Distribution of the studied patients according to number of affected domains

in the total one are higher among patients from a rural community comparable to an urban area. However, only health perception (impairment) domain was significantly affected among patients from a rural community comparable to those from urban communities ( $P<0.05$ ). As regards to the other factors, it is evident that illiteracy, ascites, abnormal portal veins, as evident by ultrasound or severity of CLD, are leading to a worsening total score of QOL. Using stepwise logistic regression analysis, the

expected probability of being affected in the total score of QOL increased by (12.4) if illiterate ( $P<0.05$ ). Also, it increased by (17.8), (14.5) and (14.5) if having ascites, abnormal portal vein or severe CLD respectively ( $P<0.05$ ) as shown in Table 2 (next page).

There are independent predictors for worsening of HRQOL in different domains. Using stepwise logistic regression analysis, it is evident that illiteracy is a strong predictor for worsening of QOL in all domains

( $P<0.05$ ) except for social and impairment domains. Smoking is a predictor for worsening QOL in psychological and impairment domain ( $P<0.05$ ). Diabetes Mellitus is an independent predictor for worsening of QOL only in social domain ( $P<0.05$ ). On the other hand abnormal portal vein is an independent predictor for worsening of QOL in all domains ( $P<0.05$ ) except in the social one. Also, bleeding per orifices is a predictor in all domains ( $P<0.05$ ) except for physical one. Having a severe form

Score of QOL of the studied population in different domains	Max. score	Mean $\pm$ SD	Obtained score % of Maximum Score (Mean $\pm$ SD)	Range
Social domain	35	16.03 $\pm$ 6.00	45.81 $\pm$ 17.14	5 – 29
Psychological domain	63	31.66 $\pm$ 8.13	50.26 $\pm$ 12.92	10 – 54
Physical domain	70	38.03 $\pm$ 10.93	*54.33 $\pm$ 15.62	10 – 60
Impairment (effect on health)	42	16.78 $\pm$ 6.19	39.96 $\pm$ 14.74	6 – 30
Health perception	21	12.01 $\pm$ 3.27	*57.17 $\pm$ 15.58	3 – 21
Total scores	231	114.52 $\pm$ 29.17	34.60 $\pm$ 8.81	42 – 173

\* Statistically significant difference among mean percentage of quality of life by using one way ANOVA test.

Table 1: Score of Quality of life in different domains

Total Quality of Life of Patients with CLD	Coef.	SE	t-value	P-value
▪ Education (literacy)	12.4	3.900	3.169	0.002*
▪ Ascites	17.8	4.684	3.804	0.000*
▪ Abnormal portal vein	14.5	4.025	3.602	0.000*
▪ Severity of CLD	14.5	3.995	3.624	0.000*
▪ Constant	91.8	3.162	29.039	0.000*

Coef. : factors coefficient in the stepwise logistic regression model

\*Statistically significant

Table 2: Stepwise logistic regression analysis for the total QOL among patients with CLD and studied variables

of CLD (Child C) is a predictor in all domains ( $P < 0.05$ ) except for impairment domain. Ascites is an independent predictor in all domains ( $P < 0.05$ ) except physical and social domains. Fatigue is a predictor for worsening in all domains ( $P < 0.05$ ) except for physical and psychological domains as shown in Tables 3-7.

### Discussion

The current study was conducted on 172 adult patients attending Family Practice Clinic of Suez Canal University Hospital, Ismailia, Egypt. It was aimed at assessing the quality of life among patients with chronic liver diseases and to identify factors that might affect it. In the current study, 83.1% of the studied patients were affected in their quality of life ( $> 50\%$  of the total score). These results reflect the impact of CLD on

HRQOL as emphasized by Poupon et al, who found that the impact of chronic liver disease on HRQOL is multifaceted.(11)

All domains of HRQOL were impaired, with health perception domain the most affected (70.3%) followed by physical (69.2%) and psychological domains (54%). However, the social (38.3%) and impairment (33.1%) domains were less affected. Also, 23% of the

Independent factors related to health perception domain	Coef.	SE	t-value	P-value
▪ Education (Illiteracy)	1.4	0.454	3.175	0.002*
▪ Fatigue	0.8	0.421	2.077	0.039*
▪ Ascites	1.5	0.538	2.853	0.005*
▪ Bleeding per orifices	0.9	0.434	2.214	0.028*
▪ Abnormal portal vein	1.0	0.460	2.240	0.026*
▪ Severity of CLD	1.6	0.454	3.581	0.000*
▪ Constant	9.8	0.461	21.348	0.000*

Coef. : factors coefficient in the stepwise logistic regression model

\*Statistically significant

**Table 3: Stepwise regression analysis between health perception score (dependent variable) and all significant independent parameters**

Independent factors related to physical domain	Coef.	SE	t-value	P-value
▪ Illiterate education	4.3	1.517	2.825	0.005*
▪ Albumin < 3.5	6.3	1.855	3.408	0.001*
▪ Abnormal portal vein	3.9	1.640	2.424	0.016*
▪ Severity of CLD	5.5	1.552	3.530	0.001*
▪ Constant	30.2	1.229	24.563	0.000*

Coef. : factors coefficient in the stepwise logistic regression model

\*Statistically significant

**Table 4: Stepwise regression analysis between physical score (dependent variable) and all significant independent parameters**

studied patients showed affection of all domains of HRQOL. These results were in partial agreement with the reported results from an Egyptian study conducted by El-Seoud et al, where quality of life was impaired among patients with chronic liver disease and the most affected domain of quality of life was the physical domain.(12)

The obtained results of the study were consistent with those reported by Kondo et al, who conducted a study in Japan and found that, HRQOL was impaired among patients with CLD.(13) Such consistency between the obtained results and the above mentioned studies reflect that, existence of CLD among patients seems to affect HRQOL negatively due to the

consequences of such illness on the different domains of life.

Socio-demographic variables might be predictors of quality of life. In the current study, rural residence showed significant association with the worsening of HRQOL in the impairment domain using univariate analysis (P<0.05). These findings were in agreement with the reported

Independent factors related to impairment domain	Coef.	SE	t-value	P-value
Rural residence	1.7	.820	2.098	0.037*
Smoking	2.3	.868	2.659	0.009*
Combined infection	2.4	.853	2.855	0.005*
Bleeding per orifices	2.1	.805	2.566	0.011*
Fatigue	1.8	.787	2.288	0.023*
Ascites	3.5	1.006	3.484	0.001*
Abnormal portal vein	3.6	.826	4.302	0.000*
Constant	13.4	.905	14.815	0.000*

Coef. : factors coefficient in the stepwise logistic regression model

\*Statistically significant

**Table 5: Stepwise regression analysis between effect on health (impairment) score (dependent variable) and all significant independent parameters**

Independent factors related to social domain	Coef.	SE	t-value	P-value
DM	2.4	1.200	2.006	0.046*
Fatigue	2.1	.854	2.487	0.014*
Bleeding per orifices	2.1	.859	2.421	0.017*
Severity of CLD	2.9	.878	3.289	0.001*
Constant	14.2	.902	15.717	0.000*

Coef. : factors coefficient in the stepwise logistic regression model

\*Statistically significant

**Table 6: Stepwise regression analysis between social score (dependent variable) and all significant independent parameters**

results by other investigators, who mentioned that inhabitants of a rural area in Egypt had a very low quality of life compared with inhabitants of other areas.(14,15) Such findings could be explained in the view of CLD among patients from rural areas

could be more severe because the agricultural work required entails more physical performance which makes patients exhausted. People who fall ill often face a choice: either to suffer and perhaps die without treatment, or to seek treatment

and push their family into poverty, particularly for those without health insurance.

Illiteracy among the studied patients showed significant association with health-related quality of life (HRQOL)

Independent factors related to psychological domain	Coef.	SE	t-value	P-value
Illiterate education	2.6	1.156	2.249	0.026*
Smoking	3.6	1.180	3.009	0.003*
Abnormal portal vein	3.1	1.165	2.645	0.009*
Ascites	4.8	1.353	3.573	0.000*
Bleeding per orifices	2.4	1.115	2.113	0.036*
Severity of CLD	3.1	1.152	2.702	0.008*
Constant	26.6	1.023	26.042	0.000*

Coef. : factors coefficient in the stepwise logistic regression model

\*Statistically significant

**Table 7: Stepwise regression analysis between psychological score (dependent variable) and all significant independent parameters**

using stepwise regression analysis ( $P < 0.05$ ). The mean scores of all domains and total scores of HRQOL were higher in illiterate patients comparable to other levels of education except in social and impairment domains. The affection of HRQOL by educational level has been reported by García-Mendizába et al. (16)

However, the results of the current study were not consistent with El-Seoud et al. (12) who reported that QOL of highly educated patients was more impaired in physical functioning and emotional problems. Such discrepancy could be explained in the view of difference in the characteristics of the studied population and site of the study, in the current study and those of El Seoud's study that was hospital-based.

As regards smoking in the present study, current smoking was reported by 28.48% of patients with no great difference among those from rural (30.2%) and urban areas (25.4%). These results were even higher than the reported results from another

Egyptian study in the Nile Delta that showed prevalence of smoking was 18.4%. (17) This situation reflects lack of health education about the negative impact of smoking on the course of chronic liver disease as emphasized by other authors. They found a significant relationship between smoking and degree of liver fibrosis. Smoking increases the risk of fibrosis in patients with chronic hepatitis C via oxidative damage, increased micro-inflammatory activity and immune suppression. (18)

It was evident that HRQOL among patients who were current smokers was significantly affected in the social and impairment domains ( $P < 0.05$ ). These findings, which were in agreement with reported results from other studies, concluded that the health and well-being of smokers are significantly worse when compared to the never-smoker regarding the overall physical functioning, energy/vitality levels, social functioning, and two different measures of mental health and emotional health well-being. (19) Such worsening of QOL of patients who are smokers could be explained by the injurious effect

of smoking. These hazardous effects of smoking encompass three major adverse effects on the liver: direct or indirect toxic effects, immunological effects and oncogenic effects. (20)

Concerning the co-morbidity of diabetes mellitus, it was found that 15% of the studied patients have diabetes mellitus. These results were in agreement with those reported by Papatheodoridis et al. (21) Co-morbidity of diabetes mellitus among patients with chronic liver diseases could be explained on the scientific background of inability of liver cells to handle hyperglycemia properly, which leads eventually to overt diabetes mellitus. In the current study, Patients with DM had worse HRQOL than non diabetic patients. The social domain was significantly affected ( $P < 0.05$ ). These findings were in agreement with those reported by Wee et al. (22)

The impact of DM on quality of life could be explained due to a multi-factorial background; co-morbidity of DM may not only increase health care cost and mortality but also increase physical and psychosocial burden of DM. Chronically elevated blood

glucose levels may lead to increased fatigue, sleep problems, more frequent infections and it increases the demands on diabetes care regimens and side effects of medications. Such consequences add more suffering on the patients with CLD.

Fatigue as a presenting symptom in patients with CLD in the current study was found in 57% among the studied patients. These results were lower than those reported by other authors(23,24) from Egyptian studies. The studies showed that 76.8% and 64% of the studied patients with CLD due to HCV have suffered from fatigue. On the other hand, a lower figure was obtained from another Egyptian study and concluded that 47.2% of patients with chronic HBV have fatigue.(25) The situation in European countries is not an exception. In a study conducted in France, fatigue existed in 53% of the studied patients.(26)

In the current study, fatigue showed a significant association with the worsening of HRQOL in all domains ( $P < 0.05$ ) except physical and psychological domain. The burden of such symptoms on the performance of the patients is of great importance particularly in the rural community where patients need to conduct manual work in the agricultural field in addition to other daily life activities that required good performance. Such view was addressed and emphasized by some authors.(27,28)

Concerning the severity of liver disease, based on Child Pugh classification it was evident in the current study that 66% of the studied patients were classified as Child A, 25% as Child B and 9% as Child C. These results were in agreement with the obtained results from an Egyptian study where compensated cirrhosis (Child A) was found in 65.7% and decompensated cirrhosis (Child B and C) in 34.3% of the studied patients.(23) These finding were not consistent with those of Sumskiene,(8) who found that Child A and Child C were 25% and 75% respectively. The variation of severity of CLD could be explained by the difference in socioeconomic variables

such as residence in rural community where the patients have high prevalence of schistosomiasis along with low socioeconomic levels. Also, smoking and other substance abuse might add a more injurious effect on CLD patients and the net result is worsening of QOL.

Using stepwise regression analysis ( $P < 0.05$ ), it showed that the severity of CLD was significantly associated with the worsening of the total scores as well as all domains of HRQOL except for health perception (impairment) domain. These results were in partial agreement with other studies (29,30) which concluded that physical domain was more affected than the other domains in patients with Child's C compared to those with Child's A and B. In another study, poor health perception was increased significantly with the severity of liver diseases.(31) On the other hand, the results of the current study were contradictory to those obtained by Häuser et al,(32) who reported that there was no significant association of QOL with severity of liver disease.

Such agreement or disagreement between the obtained results from the current study and the above mentioned studies could be explained by correlation of HRQOL and the clinical picture of CLD. Compensated cirrhotic patients may be asymptomatic for years or decades. Ascites and neurological abnormalities are often absent and in general, these patients have a good nutritional state. So, the quality of life in such patients is less affected compared to decompensated patients who have more severe symptoms related to the performance of manual work. The net result is more suffering in all domains of life. On the other hand, medical and mental co-morbidities might be an important determinant in altering HRQOL in patients with chronic liver diseases.

### Conclusion

There was a considerable alteration of HRQOL among patients with CLD. The most affected domain was health perception. It is evident that co-morbid DM, smoking, presence of cirrhosis and severity of the disease

might increase the impairment of the QOL. Such impairment might be explained partially in relation to the other variables (which were not addressed in the current study) that may play a role in alteration of QOL rather than CLD. Health education to these patients regarding the negative impact of smoking on liver disease and control of diabetes mellitus are of high priority for Family physicians or any caring physician. Training of Family physicians about QOL and its related issues in daily practice is crucial for patients with chronic illnesses particularly those with CLD.

### Study Limitation and Generalizability

The obtained results could not be extrapolated or generalized on the Egyptian community because the current study did not include other variables (namely other chronic diseases) that might affect QOL. This study was also conducted only in Family practice clinics affiliated to Suez Canal University Hospital. Further case control studies representing rural, urban and Bedouin communities. are needed to give an overall view of HRQOL among patients with CLD in Egypt.

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# Metabolic deterioration just after infancy

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## Introduction

An association between certain metabolic parameters and hypertension (HT), type 2 diabetes mellitus (DM), coronary heart disease (CHD), stroke, and eventually an increased all-cause mortality has been known for many years, and is defined as the metabolic syndrome.(1,2) It has become increasingly common in developed countries, for example, it is estimated that 50 million Americans have it.(3) The metabolic syndrome is characterized by a group of metabolic risk factors, including overweight, impaired glucose tolerance (IGT), impaired fasting glucose (IFG), hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, white coat hypertension (WCH), and a prothrombotic and proinflammatory state(4,5) instead of being a certain disease. Because it can be reversed completely with appropriate nonpharmaceutical approaches, including lifestyle changes, diet, and exercise,(6) the syndrome actually contains the risk factors for the development of irreversible terminal diseases which decrease duration or quality of life, such as HT, DM, CHD, peripheric artery disease, renal failure, and stroke. Although the life threatening role and high prevalence of the syndrome is well known in adults, its significance is not so clear in children. We tried to understand whether or not there are some relationships between body mass, as the major component of the syndrome, and systolic and diastolic blood pressures (BP) and other metabolic parameters even in children, but we preferred to use body weight alone instead of the body mass index (BMI) as an indicator of excess body fat in the study.

## Abstract

**Background:** We tried to understand whether or not there are some relationships between body weight alone and systolic and diastolic blood pressures (BP) and other metabolic parameters even in childhood.

**Methods:** Consecutive children and adolescents between the ages of 2 and 15 years were studied. Patients with devastating illnesses were excluded to avoid their possible effects on weight. Cases were divided into the four groups according to their percentile for weight alone, including cases below the 3rd percentile in the first, below the 50th percentile in the second, at and above the 50th percentile in the third, and above the 97th percentile in the fourth group.

**Results:** The study included 299 cases. Although mean values of the systolic and diastolic BPs, plasma glucose, total cholesterol, low density lipoprotein

cholesterol, triglyceride, and alanine aminotransferase increased, mean value of the high density lipoprotein cholesterol decreased significantly from the first towards the fourth groups in a gradual manner nearly in all steps.

**Conclusion:** Metabolic syndrome is a reversible progression step between complete physical health and irreversible terminal diseases with a very high prevalence in adults. But these findings suggest that pathophysiological mechanisms of the syndrome are already going on even in childhood, and bases of the syndrome are starting to be built up just after the period of infancy, probably due to the eating habits of the families. Therefore, because of the irreversible natures of the terminal diseases of the syndrome, the care to prevent should be started even in childhood.

**Key words:** Body weight, blood pressure, metabolic syndrome, infancy

## Material and Methods

The study was performed in the Polyclinic for the Pediatrics of the Mustafa Kemal University between May 2009 and February 2010, prospectively. We studied consecutive children and adolescents applying for any complaint between the ages of 2 and 15 years. Infants were excluded due probably to the some protective effects of breastfeeding. A detailed medical and family history was obtained from all patients, and a physical examination was performed. Body weight was measured with a digital scale to the nearest 0.1 kg, and percentile for weight alone of each case was calculated by the measurements of the physician instead of verbal expressions. A routine check up procedure including plasma glucose, total cholesterol, low density lipoprotein cholesterol (LDL-C), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), and alanine aminotransferase (ALT) values was performed on the spot without a fasting state because of the difficulty of fasting in children, initially. A fasting plasma glucose (FPG) was obtained at the second procedure just in case with a plasma glucose level of 126 mg/dL or higher on the random sample, not to overlook diabetic cases. Eventually, patients with devastating illnesses including type 1 DM, malignancies, acute or chronic renal failure, chronic liver diseases, celiac disease, and hyper- or hypothyroidism were excluded to avoid their possible effects on weight. BP was checked after a 5-minute silent state of the children with a mercury sphygmomanometer (ERKA, Germany). All readings were taken from the right arm. Appropriate size cuffs were used with cuff-width 40% of mid-arm circumference, and cuff bladders covering 80-100% of the arm circumference and approximately two thirds of the length of the upper arm without overlapping. The first measured BP was not used alone, and a second was obtained just after. The average of the two measurements was recorded and included in the analysis. Eventually, all cases were divided into the four groups according to their percentile for weight alone, including cases

below the 3rd percentile for his or her age in the first, cases below the 50th percentile in the second, cases at and above the 50th percentile in the third, and cases above the 97th percentile in the fourth groups. Finally, the mean age, female ratio, and mean values of the systolic and diastolic BPs, plasma glucose, total cholesterol, LDL-C, HDL-C, TG, and ALT were detected in each group and compared. Mann-Whitney U Test, Independent-Samples T Test, and comparison of proportions were used as the methods of statistical analyses.

## Results

The study included 299 children and adolescents (173 females and 126 males), totally. Anthropometric and metabolic data are shown in Table 1. Mean ages of the groups were  $8.6 \pm 4.3$ ,  $8.0 \pm 3.6$ ,  $8.0 \pm 3.8$ , and  $8.0 \pm 3.5$  years from the first towards the fourth groups, respectively, without any statistical significance in between. Similarly, female ratios of the groups were similar, too (59.5%, 58.3%, 58.5%, and 55.9%, respectively,  $p > 0.05$  in all steps). When we compared the four groups according to the mean values of the systolic and diastolic BPs, plasma glucose, total cholesterol, LDL-C, HDL-C, TG, and ALT, except one, all of the parameters increased significantly from the first towards the fourth groups in a gradual manner ( $p < 0.05$  nearly in all steps). The only parameter not showing a significant increase was the HDL-C, and as an opposite feature, its mean value decreased significantly in the same direction in a gradual manner again ( $p < 0.05$  nearly in all steps).

(See Table 1: Characteristics of the study cases, next page)

## Discussion

The metabolic syndrome is a collection of metabolic risk factors for many terminal diseases. Although there is not any universally accepted definition for the syndrome, it basically includes five features: obesity (high body weight, BMI, or waist circumference), high glucose and insulin levels, low HDL-C, high TG, and high BP.(7) But the

already used definitions as a BP of 135/85 or 140/90 mmHg or above and a FPG of 100 or 110 mg/dL or above, also include patients with DM and HT. But actually the syndrome is a collection of risk factors instead of the final diseases, and it is a reversible condition with appropriate nonpharmaceutical approaches, whereas the diseases, obesity, HT, DM, and symptomatic atherosclerosis, are irreversible and final states which almost always require drug therapy to delay complications. For example, in a previous study by us(5), prevalences of hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, IGT, and WCH showed a parallel fashion to excess weight by increasing until the seventh decade of life and decreasing afterwards, significantly ( $p < 0.05$  nearly in all steps). On the other hand, prevalences of HT, DM, and CHD always continued to increase with aging without any decrease ( $p < 0.05$  nearly in all steps), indicating their irreversible properties.(5) So metabolic syndrome alone is a disadvantageous but reversible status but not a final disease, and after the development of one of the final metabolic diseases, the term of metabolic syndrome probably loses most of its significance, since from now on, the nonpharmaceutical approaches will provide little benefit to prevent development of the others, probably due to cumulative effects of the risk factors on systems for a long period of time. So the definition of metabolic syndrome should include reversible metabolic risk factors such as overweight, hyperbetalipoproteinemia, hypertriglyceridemia, dyslipidemia, IGT, IFG, and WCH but not obesity, HT, DM, CHD, and stroke like terminal diseases. HT has been recognized as a cardiovascular risk factor for several decades, and it is a prevalent pathology in adults. For example, it has been reported that more than 85% of cases with the metabolic syndrome have elevated BP levels.(6) Because BP tends to tract along the same percentile throughout life, children with higher BPs are more likely to become adults with HT in the near future. So it is

Variables	Cases below the 3rd percentile for weight	p-value	Cases below the 50th percentile for weight	p-value	Cases at and above the 50th percentile for weight	p-value	Cases above the 97th percentile for weight
Prevalence	15.7% (47)	ns*	16.0% (48)	< <u>0.001</u>	37.1% (111)	ns	31.1% (93)
Mean age (years)	8.6 ± 4.3 (2-15)	ns	8.0 ± 3.6 (2-15)	ns	8.0 ± 3.8 (2-15)	ns	8.0 ± 3.5 (2-15)
Female ratio	59.5% (28)	ns	58.3% (28)	ns	58.5% (65)	ns	55.9% (52)
Mean value of systolic BP† (mmHg)	102.0 ± 13.3 (79-136)	ns	104.4 ± 10.9 (78-124)	<u>0.000</u>	112.1 ± 12.5 (84-145)	<u>0.009</u>	116.4 ± 10.2 (83-136)
Mean value of diastolic BP (mmHg)	59.2 ± 11.7 (34-86)	ns	62.2 ± 11.0 (39-81)	<u>0.000</u>	69.9 ± 11.9 (41-92)	<u>0.001</u>	75.0 ± 10.4 (40-93)
Mean value of blood glucose (mg/dL)	85.2 ± 20.9 (45-131)	<u>0.014</u>	94.5 ± 14.6 (65-128)	ns	98.4 ± 17.0 (71-146)	<u>0.000</u>	132.5 ± 30.3 (71-225)
Mean value of total cholesterol (mg/dL)	122.5 ± 46.0 (40-245)	ns	137.2 ± 46.3 (68-266)	ns	141.6 ± 51.6 (52-274)	<u>0.000</u>	218.1 ± 71.3 (74-352)
Mean value of LDL-C‡ (mg/dL)	75.0 ± 33.0 (32-162)	ns	84.8 ± 33.6 (33-152)	ns	91.0 ± 41.8 (25-205)	<u>0.000</u>	141.7 ± 52.0 (32-257)
Mean value of HDL-C§ (mg/dL)	76.2 ± 26.8 (27-142)	ns	69.2 ± 22.3 (22-118)	<u>0.000</u>	52.8 ± 18.0 (15-96)	<u>0.000</u>	41.2 ± 19.0 (8-81)
Mean value of TG    (mg/dL)	72.8 ± 45.4 (20-184)	<u>0.000</u>	106.6 ± 38.0 (26-186)	ns	116.1 ± 44.7 (33-225)	<u>0.000</u>	233.0 ± 50.3 (42-312)
Mean value of ALT¶ (U/L)	29.8 ± 16.9 (10-66)	ns	34.1 ± 16.9 (8-66)	ns	36.5 ± 14.1 (12-74)	<u>0.000</u>	50.7 ± 20.9 (10-91)

\*Nonsignificant (p>0.05) †Blood pressure ‡Low density lipoprotein cholesterol §High density lipoprotein cholesterol || Triglyceride ¶Alanine aminotransferase

Table 1: Characteristics of the study cases

now widely accepted that cardiovascular health originates in childhood. Similarly, we observed very high prevalences of WCH even in early decades in a previous study(8), 23.2% in the third and 24.2% in the fourth decades of life. The high prevalences of WCH in society were shown in some other studies, too.(9-11) When we compared the sustained normotension (NT), WCH, and HT groups in another study in adults(12), prevalences of nearly all of the health problems including obesity, IGT,

DM, and CHD showed significant progressions from the sustained NT towards the WCH and HT groups, and the WCH group was found as a progression step in between. So the detected high prevalences of WCH even in early decades, despite the low prevalences of excess weight in these age groups, may show a trend of getting weight and several terminal diseases. As an interesting finding of the present study, although the increased systolic BP values alone parallel to the increased BMI

in some previous studies(13), the mean diastolic BP values were also increased parallel to the increased body weight alone, significantly.

It is already known that excess weight leads to both structural and functional abnormalities in many systems of the body, and risk of death from all causes, including cardiovascular diseases and cancers, increases parallel to the range of moderate to severe weight excess in all age groups.(14,15) The effects of body

mass on BP were also shown previously by us(16) that the prevalence of sustained NT was significantly higher in the underweight (80.3%) than the normal weight (64.0%) and overweight cases (31.5%) ( $p < 0.05$  for both), and 55.1% of cases with HT had obesity against 26.6% of cases with NT ( $p < 0.001$ ) in another study.(17) So the dominant underlying risk factor of the metabolic syndrome appears as an already existing excess weight(6), or a trend towards excess weight, which is probably the main cause of insulin resistance, dyslipidemia, IGT, IFG, and WCH. Even prevention of the accelerating trend of body weight with diet or exercise, even in the absence of a prominent weight loss, will probably result with resolution of many parameters of the metabolic syndrome.(18-20) Since obesity tends to tract along the same percentile throughout life, children with higher body weights are more likely to become adults with obesity in the future. So it is now widely accepted again that obesity originates in childhood. But according to our opinion, limitation of excess weight as an excessive fat tissue in and around the abdomen under the heading of abdominal obesity is meaningless; instead it should be defined as excess weight including overweight and obesity via body weight alone or BMI, since adipocytes function as an endocrine organ that produces a variety of cytokines and hormones anywhere in the body.(6) The resulting hyperactivity of sympathetic nervous system and renin-angiotensin-aldosterone system is probably associated with insulin resistance, endothelial dysfunction, and elevated systolic and diastolic BPs.

Body weight alone may also be a sensitive method to detect excess fat in the body.(21) The Adult Treatment Panel III reported(22) that although some people with a large muscular mass are classified as overweight according to the BMI, most of them also have excess fat tissue, so they are actually obese according to body weight alone. So BMI should not be accepted as the final progression step for the detection of excess

body fat, and research should be continued to find some more appropriate methods. For example, the detected significant positive correlations of body weight with systolic and diastolic BPs, plasma glucose, total cholesterol, LDL-C, and TG and the negative correlation with HDL-C in the present study may also support the sensitivity of body weight alone for detection of the metabolic syndrome. As a similar result to ours, increasing weight showed significant increases in prevalence of HT in a linear relationship in some other studies in adults.(21,23)

Nonalcoholic fatty liver disease (NAFLD) is another consequence of excess weight, and probably it is the hepatic component of the metabolic syndrome. NAFLD is a term used to define a spectrum of disorders characterized by macrovesicular steatosis which occurs in the absence of consumption of alcohol in amounts considered to be harmful to the liver. Since the possibility of having NAFLD is directly proportional to body weight, and there is an increasing prevalence of excess weight in society, NAFLD is becoming an important health problem, nowadays. According to the literature, sustained liver injury will lead to progressive fibrosis and cirrhosis in 10% to 25% of affected individuals.(24) There are two histologic patterns of NAFLD, including fatty liver alone and nonalcoholic steatohepatitis (NASH). NASH represents a shift from simple steatosis to an inflammatory component. Obesity and insulin resistance are main factors in exacerbating hepatic inflammation and fibrogenesis in NASH. NAFLD markers such as ALT may independently predict the metabolic syndrome in adults. But as a similar result to ours, a strong association of the metabolic syndrome with elevated ALT levels was detected even in children and adolescents, and this association existed in a graded fashion across the number of metabolic components.(25) Additionally, a correlation between degree of obesity and severity of the hepatic steatosis has also been reported, ultrasonographically.(26,27)

As a conclusion, the metabolic syndrome is a reversible progression step between physical health and irreversible terminal diseases with a very high prevalence in adults. But these findings suggest that pathophysiological mechanisms related to the syndrome are already going on even in childhood, and the bases of the syndrome are started to be build up just after the period of infancy, probably due to the eating habits of the families. Therefore, because of the irreversible natures of the terminal points of the syndrome, the care to prevent should be started even in childhood.

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# H. pylori infection among children with cancer in Nanakaly hospital for blood diseases in Erbil

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## Introduction

The pattern of infection is an early childhood acquisition of H. pylori. This has been attributed to poor socioeconomic status and overcrowded conditions.[1,2] H. pylori infection and extra gastrointestinal diseases have been increasing, especially in immunocompromised subjects. [3] There are two types of diagnostic tests used to detect H. pylori infection; non-invasive and invasive. Non-invasive tests include the urea breath test, stool test and serological tests antibodies (IgG, IgM and IgA) in serum. Tests of serum IgA or IgM antibodies are unreliable in detecting gastric colonization and therefore, only IgG antibodies against H. pylori denote active infection which continues throughout life unless a course of eradication therapy is instituted. [4] Infection is more frequent and acquired at an earlier age in developing countries.[5] Factors such as density of housing, overcrowding, number of siblings, sharing a bed, and lack of running water have all been linked to a higher acquisition of H. pylori infection.[6-7] Person-to-person transmission of H. pylori through either fecal/oral or oral/oral exposure seems most likely.[8] Many investigators from different parts of the world have observed an association between H. pylori and recurrent abdominal pain. [9-10]

The aim of the study was to identify the frequency of H. pylori among patients with cancer with a correlation between H.pylori and age, sex, blood group, crowding index and socioeconomic status in both groups.

## Abstract

**Background:** Helicobacter pylori (H. pylori) are spiral-shaped gram negative bacteria associated closely with a gastric and duodenal ulcer in adults and children.

**Objective:** Evaluate the prevalence of H. pylori infection in children with different types of cancer, admitted to Nanakaly hospital for blood disease and malignancy, during a period of 3 months.

**Study design:** A case-control study of 50 children (31 male, 19 female) with different types of cancer (30ALL, 2AML, 1CML, 9HL, 4NHL, 2NB, 1WT, 1RMS). The age ranged from 3-14 years; all enrolled in the study received corticosteroids, cytotoxic drugs or. In addition 50 age-and-sex matched children served as the control group. All children were subjected to history taking, clinical examination and serum ELISA for the detection of IgG antibodies specific for H.pylori antigens.

**Results:** The prevalence of H. pylori seropositivity accounted for 20% in the patient group versus 44% in control children. No associations were found between prevalence of H. pylori infection and any factor tested including sex, age, blood group and crowding index, but a significant association between socioeconomic status and H. pylori seropositivity was present.

**Conclusion:** There was no significant association between H. pylori positive patients and childhood cancer.

**Key words:** H pylori bacteria, children, cancer

## Patients and Method

A case-control study of 50 children (31 male and 19 female) with different types of cancers (acute and chronic leukemia, ALL, AML, CML, and Solid tumours) who were admitted for treatment from 1st of March 2011 to 29th of May 2011 in the Nanakaly hospital for malignancy and blood diseases in Erbil city Iraq, to receive chemotherapy or steroids or both (just two patients were newly diagnosed; blood sample tested before using chemotherapy or steroid). Their age ranged from 3-14 years, with another 50 children matched for age-and-sex (26 male and 24 female) as control group. Information regarding age, sex, residence, Clinical symptoms and signs (abdominal pain, dysphagia, vomiting, hematemesis, melena... etc) was taken.

For types of cancer (ALL, AML, CML and solid tumors) and Family history of peptic ulcer, crowding index was calculated as the total persons in the household divided by the number of rooms: Low, <1; medium, 1-2; high, >2. [11-12] A special scoring system of socio-economic status was developed which is modified from Darwish et al.[13] Toukan et al. [14] and Shabu.[15]. The socio-economic status of the family was divided arbitrarily into three main categories: low status (< 9 points), medium status (10-18 points) and high status (>18 points). The socio-economic status of the family was determined according to educational level of parents, occupation of parents, crowding index, type of housing (owned or rented), possessing of car (no car or > one car) and number of electrical appliances like TV, refrigerator, air conditioner...etc. Enzyme immunoassay serology was used to detect anti-H. pylori immunoglobulin-G (IgG) antibodies using the Accubind™ H. pylori IgG kit (Monobind, Inc., United States). According to the manufacturer, this kit provides 98.7% sensitivity and 97.0% specificity.

Cut-off was defined with positive and negative control sera that were included in each assay, according to the manufacturer's instructions.

Samples were considered positive if the value was > 20 u/ml and the value <12.5 u/ml was considered negative and the values between (12.5-20u/ml) considered equivocal, and were excluded from the study. A statistical analysis program (SPSS version 18; SPSS, Inc), and Graph PadInStat (version 3) were used to analyze the data. The data were expressed and comparisons were performed using chi square and t-test; p-value of less than 0.05 was considered as statistically significant.

## Results

The majority of subjects were male with male:female ratio equal to 1.6:1, while in the control group male:female ratio was equal to 1.08:1, with a p value >0.05.

The mean of age (in years) in the patient group was ( $X=8.58\pm3.21$ ) and in the control group was ( $X=8.75\pm2.78$ ).

Table 1 (opposite page) shows that there is no significant association between age (in both patient and control groups) and H.pylori, as p-value >0.05.

Table 2 shows that the seroprevalence of anti-H. pylori antibodies was 20% in patients with cancers versus 44% in control children.

ALL acute lymphocytic leukemia  
AML acute myeloid leukemia  
HL Hodgkin lymphoma  
NHL non Hodgkin lymphoma  
CML chronic myeloid leukemia  
RMS rhabdomyosarcoma  
NB neuroblastoma  
WT Wilm's tumor.

There is a statistically significant higher percentage of patients with negative anti H.pylori IgG compared to control group as p value < 0.05.

There is no significant association between crowding index and H.pylori as p-value is more than 0.05 in both patients and controls.

Table 5 shows that there is a significant association between symptoms and H.pylori, as p-value is less than 0.05.

Table 6 (page 28) shows that the majority of children in the control group have low socioeconomic status (74%) and 40% have anti-H. pylori antibody so there is a statistically significant association between seroprevalence of H. pylori and socioeconomic status. In the patient group there is no statistically significant relationship between socioeconomic status and prevalence of H.pylori infection.

## Discussion

In this study, the seroprevalence of anti-H.pylori antibodies was significantly higher in control subjects (44%) than in patients with cancer (20%) (p value < 0.05). This means there is no statistically significant association between H. pylori and the type of cancer. A study was done in adults by Matsukawa Y, Itoh T., Nishinarita S, et al. which showed low seroprevalence of H. pylori in patients with leukemia.[16] Seroprevalence of H.pylori is low in patients receiving organ transplants, possibly due to the use of antibiotics[17-18], suggesting that systemic administration of antibiotics eradicates H.pylori, and most of the patients in Nanakaly Hospital had received antibiotics in their course of treatment; also the false negatives occur in immunocompromised patients.[19] Nonetheless, the sensitivity of serological assays is poor in children. The strains in Asia are different from those that are circulating in the rest of the world. [20]The mean antibody levels in young children are significantly lower than in older children and adults and these age-related standard values have not been established for children. [21]

The seroprevalence of anti-H.pylori antibodies done by Amal M Abd El-Latif, Adel SA Ali, et al. [22], was 60% (36/60) in patients with secondary immunodeficiency; the remaining cases with malignancies account for 72.2%; (26/45) have anti-H. pylori antibodies, so this study reported a significant association between H.pylori seroprevalence and types of cancer.

There is no significant relationship of age with H. pylori seroprevalence,

		Age		P value
		≤ 6 yr	>6 yr	
Patient	IgG -ve	15(30%)	25(50%)	0.29
	IgG +ve	2(4%)	8(16%)	
Control	IgG-ve	10(20%)	18(36%)	0.32
	IgG+ve	5(10%)	17(34%)	

Table 1: Distribution of age in patient and control groups according to H.pylori-IgG.

	Patient (n=50)	Control (n=50)	p value
H. Pylori-IgG +ve	10(20%)	22(44%)	0.017
H. Pylori-IgG -ve	40(80%)	28(56%)	

Table 2: Results of H. pylori antibody testing among patient and control

Cancer Type	Number	H. Pylori-IgG -ve	H. Pylori-IgG +ve
ALL	30(60%)	24(48%)	6(12%)
HL	9(18%)	8(16%)	1(2%)
NHL	4(8%)	2(4%)	2(4%)
CML	1(2%)	1(2%)	0(0%)
AML	2(4%)	1(2%)	1(2%)
RMS	1(2%)	1(2%)	0(0%)
NB	2(4%)	2(4%)	0(0%)
WT	1(2%)	1(2%)	0(0%)

Table 3: Anti- H. pylori IgG status with different types of malignancies in patient group

	Crowding index	H.pylori-IgG +ve	H.pylori-IgG -ve	p-value
Patient	low	0(0%)	2(4%)	0.7
	moderate	3(6%)	14(28%)	
	high	7(14%)	24(48%)	
control	low	0(0%)	3(6%)	0.64
	moderate	6(12%)	13(26%)	
	high	16(32%)	12(24%)	

Table 4: Relation between crowding index and H. pylori-IgG in patients and controls

	symptomatic	asymptomatic	Total	p-value
H. pylori-IgG +ve	7(70%)	3(30%)	10(100%)	0.04
H. pylori-IgG -ve	9(18%)	31(82%)	40(100%)	

Table 5: Symptoms and H. pylori among patient group

	Socioeconomic status	Anti-H. pylori IgG +ve	Anti-H. pylori-IgG -ve	p-value
Control	low	20(40%)	17(34%)	0.04
	medium	1(2%)	8(16%)	
	high	1(2%)	3(6%)	
Patient	low	8(16%)	36(72%)	0.52
	medium	1(2%)	3(6%)	
	high	1(2%)	1(2%)	

**Table 6: Relation of H. pylori according to socioeconomic status in control and patient groups**

similar to that obtained by Amal SM Sayed et al. in Egypt, Mansour - Ghanaei, et al. in Iran, and Amal M abd El-Latif et al. in Egypt 2010. [,23-24] Nguyen BV, et al. in Vietnam and Vitor Camilo Cavalcante Dattoli et al study showed that age more than 8 years was positively associated with prevalence of anti-H. pylori antibody.[25-26]

This supports the hypothesis that in developing countries the acquisition of H. pylori infection can occur in early childhood. [27] H. pylori infection was also not found to be related to gender, in agreement with Nguyen et al. in Vietnam 2006, and a similar study was done by Mohammed A Mohammed et al. in Egypt, .[-25,28] Taiwan, Korea, and Mexico,[29-31] while Mehmet Kanbay et al. in Turkey[32] reported a significant relation between H. pylori and female gender, while another study done by Marilyn L. et al. in California reported a significant association between H. pylori and male gender.[33]

Regarding the symptoms in our study most patients with H. pylori were symptomatic, similar to a study done by Luigi satacroce[34]; there was no significant association between rate of H. pylori infection and crowding index. Similar results were obtained by Hoda M. Malaty et al. in South Korea[35], Milman N et al.[36] and also by A.H.M. Alizadeh, et al.[37]. McCallion WA et al showed positive associations between H. pylori infection and the following household variables; number of children in the household, household density, sharing a bedroom, and sharing a bed with a parent.[38]

Low socioeconomic status in the control group is a risk factor for the acquisition of H. pylori bacterium during childhood. This result is similar to that obtained by Hoda M. Malaty et al. and also by Stephen C. Fiedorek, MD et al.[39] Regarding the patient group our study showed that there is no statistically significant association between H. pylori seroprevalence and socioeconomic status, and this result may be influenced by low seroprevalence of H. pylori in children with malignancies in spite of the majority of cases being of low socioeconomic status.

### Conclusion

A significant association between H. pylori positive patients and symptomatic patients was present, as well as between socioeconomic status and H. pylori seropositivity in the control group, in contrast to the patient group, but there was no significant association between H. pylori positive patients and childhood cancer, and age, sex, blood group, and crowding index in both groups.

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# Basal cell carcinoma with perineural invasion: a case report

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## Background

Perineural invasion of skin cancers was first mentioned by Cruveillier in 1835(1) involving the facial nerve, followed in 1862 when Neumann reported a lower lip carcinoma with mental nerve invasion. (2)

Basal cell carcinoma (B.C.C), the most common skin cancer in white races is generally a benign form of skin cancer; but certain types like morpheaform, infiltrative and sclerosing tend to be aggressive, more likely to recur, or to have positive margins at excision.(3-6)

Incidence of Perineural invasion for (B.C.C) was found by mohs (7) to be 1% and 0.178% by Niazi and Lamberti. (8)

“Skin cancer with neurotropism is an uncommon phenomenon that occurs when cancer cells surround a nerve sheath and spread down the length of the nerve whether superficial or intracranial (9). This is sometimes associated with skip lesions along the involved nerve and this explains why despite negative margins being obtained there is a risk of recurrence of the tumor after resection”. Symptoms of early perineural spreading usually needs a high index of suspicion along with leading questions and neurological examination which is frequently formication (a skin sensation of ants or worms crawling underneath the skin) which will progress to pain, numbness and motor deficit if untreated (10).

## Case Report

The patient is a 67 year old female with a history of prior skin cancer removed by excision in 2005. She recalls developing a scab along the left ala of her nose approximately 5 months ago. There was no history of numbness or parasthesia in the area, no history of weight loss or loss of appetite and no previous radiation therapy.

## Abstract

Perineural invasion of skin tumor was first mentioned by Cruveillier in 1835.

Perineural invasion is an important mode of tumor spread and is associated with increased aggressiveness and a tendency for recurrence among cutaneous malignancies. Skin cancer with neurotropism is an uncommon phenomenon that occurs when cancer cells surround a nerve sheath and spread down the length of the nerve whether superficial or intracranial. This is sometimes associated with skip lesions along the involved nerve.

Neurotropism involvement is most often asymptomatic necessitating a keen search, particularly for tumors overlying major nerve trunks.

A leading question of history of skin cancer in suspicious cases

along with neurological examination is important in detecting some cases of skin cancer with perineural invasion. Magnetic resonance is the preferred imaging method of the evaluation of head and neck perineural tumor spread because of its superior tissue contrast and multi-planar capabilities and it worsens the prognosis if it is positive for perineural invasion.

A combined therapy (MOHS micrographic surgery and post operative radiation therapy) is preferable for better cure in cutaneous cancer with perineural invasion.

We present here the first reported case of skin cancers with perineural invasion in Jordan, in addition to highlight this phenomenon since its incidence is much more common than previously recognized.

**Key words:** perineural invasion, basal cell carcinoma, mohs micrographic surgery

**Past history:** hypertension, hepatitis, diabetes, previous skin cancers and mitral valve prolapsed.

**Family history:** her mother had a colon cancer

On examination: a well appearing lady, body weight 71 kg. With stable vital signs.

**Head and neck:** a small scab 0.7 \*1.1 cm in left ala of her nose (Figure 1)



Figure 1. Preoperative physical examination

**Examination:**

No adenopathy or parotidopathy.

2-3mm blanching erythematous area in the region of excision of skin carcinoma on the right side of her nose, two hypo pigmented areas of the left temple where previous moles had been removed. Cranial nerve examination was normal with no neurological deficit.

**Back:** A few small surgical scars consistent with excision of basal cell carcinoma. Biopsy was done in Dec-17-05 showing sclerosing basal cell carcinoma, so she was scheduled for mohs micrographic surgery in King Hussein medical center in Jan-14-06.

During procedure she was found to have an infiltrating basal cell carcinoma with squamous differentiation and in the second stage perineural invasion was prominent (Figure 2) so the case was reviewed by a dermatopathologist and he felt additional examination of all blocks should be made so all mohs specimens were bottled and sent for routine H&E examination to ensure that the margins were negative and the patient was cleared after five mohs stages.

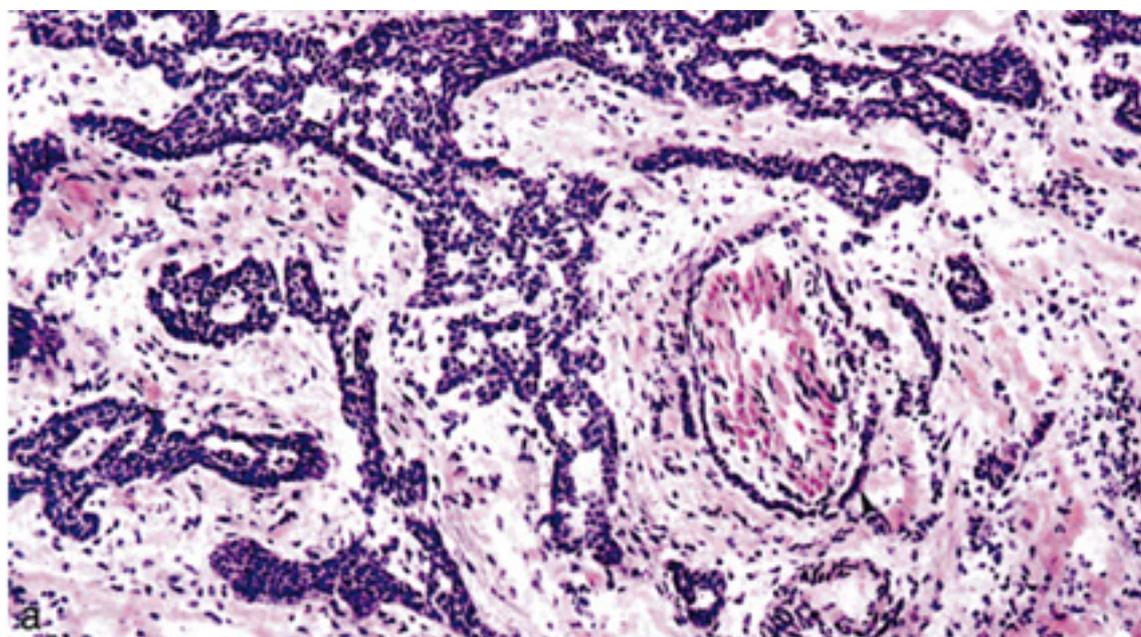


Figure 2: Basal cell carcinoma with perineural invasion in a low power magnification

MRI brain scan done for her post mohs margin clears (Figure 3) with and without contrast and there was no evidence of metastatic disease.



**Figure 3: The defect post mohs margin clearance**

The case was presented to a multidisciplinary tumor board with review of pathologic slides and discussion with dermatologist, medical oncologist, pathologist and radiation oncologist whose recommendation was to give her radiotherapy prior to proceeding with reconstruction based upon the aggressive nature of her tumor area and the likelihood of recurrence.

Radiotherapy was done for her on 02-18-06 for the nose area with 36 elapsed days (no. of treatments 25) with a total dose of 50 Gy and repeated on 03-27-06 for 4 elapsed days (no. of treatments 5) with a total dose of 10Gy, so the final total dose was 60 Gy.

Follow up was done at 3 weeks, 2 months and 7 months post radiotherapy. There was no evidence of local recurrence and no adenopathy.

She was scheduled for reconstruction plastic surgery in December 06.

## Discussion

Incidence of neurotropism in basal cell carcinoma is much more common than previously recognized. This was documented by a study done by Desiree, Lori, Timothy and Darrell (11), which showed 8 of 78 (10%) of examined specimens exhibiting perineural invasion and 21 of 78 (27%) revealing perineural inflammation and that tumors with perineural inflammation and or tumor invasion extend further beyond clinically detectable margins than those without perineural involvement.

Several factors that play a role in perineural spread include tumor location on the face, male sex, tumor size more than 2 cm and previous treatment of the lesion. (12, 13, 14)

Basal cell carcinoma with perineural invasion is reported in the literature by Ballantyne (9) Dodd (15) Mark (16) Gormley (17) Hanke (18) Eng (19) Carlson (20) and had the following results: the most common location was the head, with no primary lesion but there was a history of previous radiation therapy.

That was nearly consistent with our case since the tumor was located on the nose and there was a previous history of treating skin cancer on the face but the gender was female and there was no history of previous radiation therapy.

In our case the tumor was basal cell carcinoma with squamous differentiation and perineural invasion so the decision was to treat her by a combination therapy of mohs micrographic surgery and post operative radiation therapy for better result.

Magnetic resonance (MR) is the preferred imaging method of the evaluation of head and neck perineural tumor spread because of its high tissue contrast and multiplanar capabilities and it plays a prognostic factor if it is positive for perineural invasion. (27)

Recommendations for MR include BCC with neurological symptoms, histopathological evidence of neurotropism and locally advanced or deeply infiltrating recurrent squamous or BCC. (10)

It was obvious in our case it was infiltrative type basal cell carcinoma with perineural invasion with a history of previous skin cancers so MR imaging was done and it was negative.

## Conclusion

Skin cancer with perineural invasion is seemed to be increasing in incidence. A leading question of history of skin cancer in suspicious cases along with neurological examination is important in detecting some cases of skin cancer with perineural invasion.

Also, a combined treatment plan is recommended for better outcome in the appropriate cases. MR imaging is a useful tool in evaluation of skin cancer with perineural invasion, together with team planning (Dermatologist, Pathologist, Oncologist and Radio Oncologist) is recommended in evaluation of skin cancer with perineural invasion.

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# Musculoskeletal pain in children is different

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## Aim

This study was to highlight the musculoskeletal manifestations of AL as initial clinical presentation of acute leukemias (ALs) of children who had misdiagnosis of leukemia at presentation, in Nanakaly hospital for blood disease, Erbil.

## Patients and Methods

This is a retrospective descriptive study that assessed the medical records of 125 patients with AL from June 2007-June 2012 in Nanakly hospital, Erbil, Iraq, reviewing age, sex, type of leukemia, clinical presentation, and lab findings. Bone pain as evidenced by inability to walk was reported, number of joints affected, back pain, and duration of illness is considered, and any abnormal findings on X-ray or MRI reported.

## Result

From those 125 diagnosed with AL there were 12 cases who were misdiagnosed or referred to our center late with advanced disease and morbidity complaining of joint pain, arthritis or backache or bone pain, and constituting 9.6% of total admissions because of musculoskeletal complaint. Patients were ALL in 76% of the cases; of those 12 were all ALL except one AML; initial diagnosis was with pallor and anemia (94.6%), fever(52.9%), Initial WBC > 50.000 in (24%), splenomegaly in 7% , hepatosplenomegaly in 27% , organomegaly and lymphadenopathy in 18%; male to female ratio was 61:38(1.6); 1-9 years constituted 60% of total admissions. Four of 12 presented with late onset backache, four with early presentation backache, five with mono or poly arthritis and/or migratory arthritis.

Those 12 cases of anemia are clear, WBC high in 4, blast cells not present in peripheral blood in 5 with low blast count in the rest; level of platelets mild to moderate depression; while 3 of normal range; although ESR is

## Abstract

**Introduction:** Musculoskeletal manifestations are the presenting complaint in up to 20% of patients with pediatric leukemia; 17% of all new cases of leukaemia initially presented via the orthopaedic department, (1,2). Leukaemic arthritis may occur at any time during the course of leukaemia and may be the presenting manifestation (3,4). In children, acute leukemia (AL) at presentation can mimic several orthopaedic pathologies, so that a variable delay of the correct diagnosis is often reported (4-6). The musculoskeletal manifestations of leukemia include symmetric or migratory polyarthritis or arthralgias, bone pain and tenderness, and back pain mimicking a radiculopathy. Approximately 4% of adults and 14% of children have articular symptoms as presenting features of leukemia (7).

Vertebral body collapse and back pain are an unusual presentation for childhood leukemia that can cause significant back pain in children without other systemic symptoms. The back pain was relieved after chemotherapy (4,8-9).

In childhood, AL the history and clinical examination can be misleading and haematological and radiological investigations are not pathognomonic. (9)

Arthritis, is much more common in children compared to adults and may result from leukemic infiltration of the synovium and subperiosteal tissue(4).

Leukemia, therefore, presents nonspecific signs and symptoms which may simulate the clinical presentation of much other pathology, including juvenile rheumatoid arthritis (JRA), rheumatic fever (RF), systemic lupus erythematosus (SLE), idiopathic thrombocytopenic purpura (ITP), bone marrow aplasia and infectious mononucleosis (10). The arthritis in leukemia can be chronic or recurrent and generally presents in an asymmetrical pauciarticular form, normally additive but sometimes migratory too, and its onset may be either insidious or sudden(10). The importance of bone marrow examination for correct diagnosis before emergence of blasts in the peripheral blood is very crucial.(4,9)

**Key words:** acute leukemia, bone pain, arthritis, backache

NO	Hb	WBC	N	L	Blast	platelets	ESR	LDH	Ur.ac.
1	11	126	2	12	96	36	130	899	5.5
2	7	13	20	85	0	40	112		3.9
3	7.6	4,5	22	68	10	34	116	560	3.4
4	12	118	10	40	50	301	123	1080	7
5	9.5	14.6	18	82	0	113	140	825	5.2
6	9.7	8.7	8	58	30	33	34		3.8
7	10.7	5.2	11	83	0	383	107		4.4
8	10.9	9.1	14	40	44	106	37		3.7
9	8	2.5			0	108	142		3.3
10	6.6	128	3	65	32	24	100	2583	4.3
11	7	82	2	87	65	82	120	1820	6.7
12	7.7	11.5	75		0	400	150		

Table 1: Initial hemogram of the 12 children on presentation

Chief complaint	Reference patients	%
Pallor	1,2,3,10,11,12	4.8
Bleeding	1,10	1.6
Lymph node enlargement	11	8.3
Bone pain	1,2,3,4,5,12	4.8
Joint swelling (arthritis)	1,2,4,5,12	4
Limbing	1,3,4,5,6,9	4.8
Lower limbs weakness	1,3,6,7,	3.2
Back pain	1*,3,4,6,7,8*,9,10*,11*	4
Musculoskeletal pain	All cases	9.6
*Backache Late in induction 2-3 wk. #overlapping between symptoms		

Table 2 : Clinical symptoms on presentation of the 12 children

non specific reactant it is high in 10 cases; LDH is elevated always, while the uric acid is within normal range.

Those 12 cases present mainly with pallor, bone pain, limbing, joint swelling even though there are overlapping in between signs and symptoms of all patients.

We have 7 male and 5 females, age range 4-14 average, duration of chief complaint 8 wk, knee joint, elbow, ankle j migratory, single or multiple joints with backache and bone pain.

### Discussion

Although we know that the majority of cases of limb pain are of benign origin, organic causes should

nevertheless be investigated. A worrying possibility which should always be taken into consideration is that of neoplastic disease, especially leukemia (10). In children, acute leukemia (AL) at presentation can mimic several orthopaedic pathologies, so that a variable delay of the correct diagnosis is often reported( 4,5,6,9).

The presentation of leukaemia can mimic septic arthritis, osteomyelitis, transient synovitis, Lyme disease or juvenile rheumatoid arthritis and hence can cause difficulty in its diagnosis(2,9). According to extant literature, arthritis occurs with a frequency of 13.5%, being more common with ALL (9-11) in our cases

arthritis less, with 9.6% (Table 2). This is because of the small number of patients studied.

Approximately 4% of adults and 14% of children have articular symptoms as presenting features of leukemia( 7). Not surprisingly, 11% to 17% of patients with ALL are initially referred to orthopedists for workup of presumed juvenile rheumatoid arthritis, septic arthritis, or osteomyelitis (1-2). 5.8 % of the patients were found to present with rheumatic manifestations(4) musculoskeletal diffuse tenderness (15.0%)(11) , while in our patients' study 9.6% had musculoskeletal manifestations.

No	Sex	Age y	Duration in wk	Type of leukemia	No & type of joints affected
1	f	12	3	ALL	Neck & small *joint, fighting arthritis back pain late
2	F	13	5	ALL	>3 large & small migratory
3	F	4	3	ALL	Back pain, multiple vertebrae
4	M	12	6	ALL	Cervical vert. sacral , small hand joints
5	M	8	16	ALL	Rt knee swelling and arthritis
6	M	13	9	ALL	Multiple vertebral compression
7	M	10	18	ALL	Compression of dorsal vertebral bodies
8	m	10	6	ALL	migratory*arthritis Back pain late
9	f	8	16	AML	Back pain
10	M	14	5	ALL	Backache*
11	M	11	4	ALL	Backache*
12	f	10	4	ALL	elbow, ankle swelling, pain

Table 3 : Characters of the 12 children

Joint pain was the presenting feature in (9.26%) in ALL cases though it was observed in 6% of cases in a similar study (Karimi et al., 2008). Bone pain was observed in 11.11% of ALL, compared to reported incidence of 25% (Lanzkowsky, 2005) (12). In table (2) joint pain was 4% and bone pain 4.8% of cases. We have 7 patients with joint involvement, mainly elbow, knee and ankle are involved with objective swelling apart from migratory arthritis or bone pain in the rest. Our result is lower than other studies which may be because of under-estimation of musculoskeletal symptoms and

because the study group size was small.

Patients with this manifestation frequently have normal initial hemograms, which can contribute to late diagnosis (5); in one study (4.9%) had normal blood count. (10).

In Table 1 the anemia was obvious; the WBC high (>50000) in 4 cases; the platelet mild to moderately low and in a few cases normal count. The LDH is high in all cases, more than 400, while uric ac is normal in all cases. ESR was high in all cases although it's a non specific test, the

initial blood tests were not done with complete blood film or weren't read by a hematologist until referral to our hospital which was attributed to this misdiagnosis.

Though some of these presentations are well known, their occurrence is so infrequent that one may miss the malignancy (10).

The use of corticosteroids in children with arthritis and with a suspicion of collagenosis, even without a definitive diagnosis, can delay the identification of leukemia, because it relieves the symptoms and can

Pt . ref.	Disease diagnosis	Therapy and management
1	Rheumatic disease	Aspirin, brufen
2	Rheumatic, rheumatoid, connective tissue	Aspirin then steroid
3	Tonsillitis	AB* & antipyrol
4	Brucellosis, septicemia	Antibrucellosis, heavy AB
5	Rheumatic disease	Aspirin, benzathin penicillin, salazopyrin
6	Sciatica	Analgesia
7	Rheumatoid arthritis, brucellosis, sciatica, SLE	Aspirin, steroid
8	Rheumatic arthritis in adult department	different analgesia
9	Puo, Sciatica, brucellosis, TB	AB. antTB
10	Anemia of poor nutrient,	Tonic, blood
11	Tonsilitis, cervical adenitis	AB
12	Iron deficiency anemia	Tonic, vitamins

AB\*:ANTIBIOTIC

Those 12 cases were treated wrongly as rheumatoid , rheumatic. Brucellosis and TB

**Table 4: Initial diagnosis and type of therapy in the 12 children**

change the cytology and histology of the bone marrow. (6,10) Two of our patients had received steroid and chemotherapy, and Cases number two and seven for treatment of rheumatoid arthritis or rheumatic fever. Rheumatoid factor and anti nuclear antibodies (ANA) are not useful diagnostic tests for evaluating those patients, being falsely positive and not discriminating patients with and without rheumatic manifestations(6,13), while case number nine was treated as TB for fifty days after therapy as brucellosis (Table 4).

About two-thirds of children with ALL have signs and symptoms in bones and joints of less than 4 weeks duration at the time of diagnosis (14), and duration of rheumatological prodrome was 3 months (4) and period of delay, ranging from 2 weeks to 44 months (15) .

In our patients, 12 cases were referred to our center after a prolonged period of mismanagement, range 3-18 weeks on average 8 weeks. This is due to different

improper consultation, range age (3-14) mean 10 years. We have cases (3,4,6,7,9 ) who presented initially with backache. Most of the cases are ALL except number 9 who was female and was treated as TB spine in Erbil while diagnosed in Jordan as (AML).

Children tend to present with joint symptoms rather than bone pain, which may be mono or polyarticular. Joint and bone symptoms are more common in the extremities in children, although back symptoms can occur. Vertebral body collapse and back pain are an unusual presentation for childhood leukemia that can cause significant back pain in children without other systemic symptoms (4,8-9,11 ,16 ).

This is usually secondary to vertebral body involvement (9).

Compression fracture of vertebra and femoral neck is occasionally found in patients with childhood ALL (2,5,12,14), we have 5 (4%)cases (4 ALL and 1 AML) who presented with backache compared to 3.3% in one

study(3) and with 4 (3.2%) cases presenting late with backache (Table 3) compared to (5.7%),in the same study, but this symptom has also been reported as an adverse effect associated with chronic systemic use of glucocorticoids(4).

Osteopenia and associated vertebral fractures have been noted in newly diagnosed ALL patients, with an incidence as high as 1.6% vs 9% and are likely related to the bone-resorbing effects of lymphoblasts,( 5, 14,17-18) while 25% to 60% of patients do not show any abnormalities on initial X-rays(1).

Glucocorticoid sensitivity is known to vary between individuals (17). We have 4 (3.2%) cases (1, 8,10,11) with such clinical presentation in the 2-3 weeks of induction with dexamethasone. Osteonecrosis of ALL constituted approximately 3.2% of our 1 to 9 year old cases.

The indicates the importance of having a high index of suspicion when a seemingly common disease does not respond to adequate therapy(1).

Rheumatic syndromes can be seen in the course of neoplasia either predating the diagnosis, accompanying it or postdating. They can occur in the context of paraneoplastic syndromes, by the local inflammatory reaction as a result of invasion of musculoskeletal structures by tumor cells or secondary to bony, peri-osteal or capsular infiltration rather than any direct synovial involvement, or secondary to hemorrhage into the joints or peri-articular structures and by hyperuricemia as a result of massive cell turnover either spontaneously or in response to treatment.

Paraneoplastic syndromes are induced by the tumor via mediators (4,14); our result of uric acid was almost within accepted level and the WBC count within low value except 4 children (Table 1).

Arthritis occurs with a frequency of 13.5% (10,8), while in our study arthritis happened in 4% being more common with ALL maybe because of under evaluation of the skeletal involvement in our study.

To differentiate between leukemia and other childhood rheumatic disease like juvenile rheumatoid arthritis (JRA), a study stated that children with leukemic arthritis at onset of disease had less leukocytosis and a relative lymphocytosis, or they had leucopenia. The identification of blasts in peripheral blood is possible in one third of the patients; 46% of leukemia patients with musculoskeletal manifestations present normal initial counts. These children can have leukemic expansion in the peripheral organs without blastic changes in the blood smear for several months.(6)

In Olcay Y. Jones et al, study (6) only 25% of children with leukemia had blast cells in the initial blood smear and the remaining 75% did not.

Due to nonspecific clinical findings and to the delay in the appearance of hematologic alterations diagnosis can be late by periods of between two weeks and 13 months(10).

In our study, uric acid was not found to be useful as predictive factors for ALL, while LDH were high in all cases, which is important to differentiate from rheumatic diseases. Children with symptoms consistent with JRA exhibiting high LDH levels should undergo investigation for neoplasia.(10,16).

What happened in most of our twelve cases is they had received different treatment and management such as aspirin, non steroidal anti inflammatory drugs, different AB treating, PUO, TB, sepsis even methotrexate was given for rheumatoid arthritis.

The arthritis in leukemia can be chronic or recurrent and generally presents in an asymmetrical pauciarticular form, normally additive but sometimes migratory too, and its onset may be either insidious or sudden (10). This is applied to three of our cases misdiagnosed as rheumatic fever and given prophylactic penicillin because of knee joint manifestation which took 4 month's duration, cases number five 2, 5 and 7.

Glucocorticoid sensitivity is known to vary between individuals. (17) We have 4 cases (1, 8, 10, and 11,) with such a clinical presentation in the 2-3 weeks of induction with dexamethasone. Osteonecrosis of ALL constituted approximately 3.2% of those 1 to 9 year olds of our cases, comparable to 3.3% in another study (5).

Hence it is important to have a high index of suspicion of malignancy in any children who present with suspicion, in spite of absence of blasts in peripheral blood. A bone marrow aspiration should be performed for early diagnosis of ALL, in children presenting like JRA especially when steroids or methotrexate are indicated. (3,6,10,13,18)

### Conclusion

Accurate history, general physical examination, with awareness of rheumatic manifestations is of great importance as some of these may

be helpful in early detection of the malignant disease. The hemogram should be repeated in order to detect early alterations which are suggestive of leukemia; avoid using steroid or chemotherapy nonspecifically before being confirmed by a peripheral and/or iliac crest bone marrow biopsy.

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# Knowledge and Practice of Primary Care Physicians in Management of Gastroesophageal Reflux Disease

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## Abstract

### Background:

Gastroesophageal reflux disease is a high prevalence disease ranging from 21-56% in different countries. Although the economic costs of treating this disorder are enormous, the knowledge and practice of physicians who treat patients with GERD are not well known. This study was undertaken to determine how physicians manage patients with GERD.

**Methods:** A questionnaire was distributed to 150 primary care physicians working in King Abdul Aziz Medical City in Riyadh including consultants, staff physicians, and residents.

**Results:** A total of 108 completed questionnaires were returned with a response rate of almost 72%. A total of 57.4% of the respondents were males; 26.9% of the respondents had practiced for more than 15 years, and 35.2% had practiced 5 years or less. Almost half of the physicians were unaware of generally accepted guidelines for the evaluation and treatment of GERD. Staff physicians and younger physicians prescribed proton pump inhibitors more often than consultants, for mild or intermittent GERD symptoms. Male physicians were more likely to use step-down therapy in patients with well controlled GERD symptoms than female physicians.

**Conclusions:** Age, gender and the position of physician significantly influenced how physicians evaluated and treated patients with GERD.

## Introduction

Gastroesophageal reflux disease affects millions worldwide. It is a highly prevalent disease with rates ranging from 21 to 56% in various countries (1,2). More than 40% of adult Americans suffer from GERD each month, while nearly 7% suffer from acid reflux on a daily basis(3). The National Ambulatory Medical Care Survey (NAMCS) reported that in 4.6 million office visits, GERD was the sole reason for the office visit (4). )The quality of life of patients with acid reflux disease is rated worse than that of patients with hypertension, angina, mild congestive heart failure, or diabetes (Types I and II combined) (5, 6) . In North America, up to 10% of GERD patients have to be absent from work( 7,8).

The treatment of acid reflux disease in the outpatient setting often follows an algorithm that uses a stepwise approach, progressing from simple lifestyle changes to the use of increasingly potent and frequent medications (referred to as "step-up" approach). Using this algorithm, patients are initially treated with a PPI to more rapidly suppress the symptoms of acid reflux and to heal erosive esophagitis (if present) more quickly.

For many patients, acid reflux disease is a chronic problem and when medications are stopped or tapered to lower doses, symptoms typically recur. Nearly 80% of patients will have a relapse of their symptoms within 6 months of stopping medical therapy (11). The persistence of reflux symptoms in an important minority of patients receiving proton pump inhibitors is a major problem in clinical practice. Most patients require chronic medications when followed over 3-10 years (12, 13).

There is variation among physicians in the way they manage GERD (14). Many recommendations, guidelines and consensus-conference documents are available to help primary care physicians (PCPs) achieve optimal and cost-effective management of GERD (15,16,17,18,19) and to spread best-practice throughout primary care.

However, it is unknown whether such recommendations are followed in real life, and the few studies published on this topic have been based on data from interviews only(20,21,22,23). Despite the chronic nature of GERD, little is known about why physicians choose different treatment regimens(14).

The aim of this study was to determine the prescribing patterns and how physicians evaluate and treat patients with GERD.

## Methodology

This is a cross-sectional study, to assess the knowledge and practice of Primary Care (PHC) physicians in management of Gastroesophageal Reflux Disease (GERD) and to assess how often published guidelines on management of (GERD) are followed.

The participants in this study were primary health care physicians, including consultants, residents, and staff physicians working at National Guard in Riyadh, Kingdom of Saudi Arabia in 2008.

A two-page questionnaire was developed to assess the knowledge, diagnostic plans, and treatment patterns of physicians who evaluate and treat patients with GERD. This questionnaire was taken from J clin Gastroenterology in 2005 after permission was granted from the author, with some modifications (14). The first section of the questionnaire asked about the demographic information; age, gender, medical qualifications, position (consultant, resident and staff physician), and years in practice were included. Number of patients seen weekly was also included. In addition, basic questions concerning preferred diagnostic evaluation of uncomplicated GERD, medications commonly used to treat GERD, and awareness of published guidelines for the treatment of GERD were also asked.

The second section of the questionnaire consisted of a series of 8 case scenarios, each of which involved a patient with GERD.

These cases were designed to assess treatment patterns and strategies of physicians when faced with patients with varying degrees of GERD. These cases described patients with different levels of severity of symptoms and different levels of complexity, in an attempt to determine when physicians would initiate, maintain, or change GERD-related therapy. Cases were also presented to determine whether and how, physicians initiate a diagnostic workup for acid reflux disease. Questions regarding clinical practice were based on recently published guidelines for the diagnosis and treatment of GERD in the American College of Gastroenterology(15).

A total of 150 questionnaires were distributed with a cover page explaining the purpose of the survey, to physicians in four large Primary care Centers: Iskan Al Yarmouk, Umalhamam, Dirab and Khashmala'an. No reimbursement was made in any form to any of the participating physicians. Respondents' identities were not requested and confidentiality was maintained throughout the distribution and collection of the forms. Questionnaires were forwarded to the data entry clerk. Data were entered in SPSS version 15 and cleaned for analysis. Descriptive analysis was primarily carried out including counts and percentages. Cross tabulation was also carried out using Chi-square test with p-value (<0.05) on demographic data and treatment strategies.

## Results

Of 150 questionnaires distributed, 108 were completed and returned with a response rate of 72%. Response rates were similar for the three groups, and no significant differences in demographics were noted among the groups (Table 1). More than half of the respondents were males (57.4%), 26.9% of the respondents had practiced more than 15 years, and 35.2% had practiced 5 years or less. 52.8% of the respondents were staff physicians and 57.4% were with MBBS certificate.

<b>Table 1. Characteristics of Primary Healthcare Physicians</b>		
Demographic	Frequency	Percentage
<b>Age group</b>		
25-35	51	47.2
36-45	38	35.2
46-55	15	13.9
>55	4	3.7
<b>Total</b>	<b>108</b>	<b>100</b>
<b>Sex</b>		
Male	62	57.4
Female	46	42.6
<b>Total</b>	<b>108</b>	<b>100</b>
<b>Certificate</b>		
MBBS	62	57.4
Diploma	19	17.6
Board	19	17.6
Master	8	7.4
<b>Total</b>	<b>108</b>	<b>100</b>
<b>Post</b>		
Consultant	24	22.2
Staff	57	52.8
Resident	27	25
<b>Total</b>	<b>108</b>	<b>100</b>
<b>Years in Practice</b>		
1-5	38	35.2
6-10	26	24
11-15	15	13.9
>15	24	26.9
<b>Total</b>	<b>108</b>	<b>100</b>

All of the respondents saw patients with acid reflux disease. More than 35% and 37% of physicians routinely prescribed H2 blocker and PPIs in their practices, respectively. Almost fifty five percent of the respondents stated that they were aware of published guidelines regarding

acid reflux disease; no significant differences were noted among the groups.

When physicians were asked which test they would recommend in the evaluation of uncomplicated reflux disease, 65.7% recommended

that no testing be performed, while 14.8% recommended a barium swallow, 13.9% recommended esophagogastroduodenoscopy (EGD), and 5.6% thought that other testing should be performed, primarily a pH probe. When we analyze it by post, we found that 53.5% of staff

Table 2. Description of important clinical data	Frequency	Percentage
<b>Patients seen weekly with GERD</b>		
1-5	73	67.6
6-10	23	21.3
11-15	5	4.6
>15	7	6.5
Total	108	100
<b>Preferred test of patients with uncomplicated GERD</b>		
No test requested	71	65.7
PH probe	6	5.6
Barium Swallow	16	14.8
Upper GI endoscopy	15	13.9
Total	108	100
<b>Medications commonly used</b>		
Anti-acid	20	18.9
H2 inhibitor	38	35.8
Promotility agent	8	7.5
PPI	40	37.7
Total	106	100
<b>Awareness of guidelines</b>		
Aware	59	54.6
Not aware	49	45.4
Total	108	100

physicians recommended that no testing be performed compared with residents 22.5% or consultants 23.9% with no significant difference between the groups. Barium swallow was more likely to be ordered by residents and staff physicians 37.5% in the evaluation of uncomplicated reflux disease compared with consultant 25%.

In the evaluation of a young patient (37 years old) with new intermittent

symptoms of GERD, without warning signs, and no previous treatment (Case 1), most respondents (58.9%) recommended an initial treatment with lifestyle modifications while 23.4% recommended lifestyle modifications and over the counter treatment. No significant differences were found among the groups.

In the evaluation of a young patient (28 years old) with new GERD symptoms who had failed lifestyle

modifications (Case 2), most respondents recommended step-up therapy using an H2 blocker inhibitors (37%) as initial therapy. Twenty-four percent of physicians recommended step-in therapy with a PPI, while 29.6% stated they would continue lifestyle modifications and use an over the counter medication and 4.4% recommend promotility agent. When we analyze it by post, we found that 53.8% of staff physicians recommended PPI

compared with 26.9% of residents or 19.2% of consultants with significant difference ( $P=0.032$ ).

In a middle-aged patient with GERD symptoms completely relieved with the use of a twice daily over the counter H2 blocker (Case 3); the majority of the respondents (44.4%) recommended continuation of the current treatment. However, 5.6% stated they would change therapy to H2 blocker twice daily; 9.3% recommended the use of a PPI and 9.3% recommended that the H2 blocker be changed to night time use only. Twenty-eight percent recommended esophagogastroduodenoscopy (EGD). No significant differences were noted among the three physician groups.

In a patient with persistent symptoms of GERD despite the use of a twice daily over the counter H2 blocker (Case 4), most physicians (79.6%) recommended the initiation of PPI therapy. Six percent recommended H2 blocker, while 2.8% stated they would use H2 blocker QHS and 8.3% recommended the use of a prokinetic agent. When we analyze it by age group, we found that 51.2% of young physicians (from 25-35 years) will prescribe PPI compared with 10% of old physicians (< 45years) with significant differences ( $P=0.001$ ).

In the evaluation of an older patient with complicated acid reflux disease (Case 5, dysphagia present), 45.4% of all physicians recommended a barium swallow while 42.6% of them recommended esophagogastroduodenoscopy (EGD) and 7.4% stated no change in treatment. There is no significant difference between groups.

In the evaluation of a middle-aged man (48 year old) with long-standing GERD symptoms (5 years) without warning signs and no previous treatment (Case 6), 45.8% of all physicians recommended esophagogastroduodenoscopy (EGD). Twenty-five percent of all physicians recommended a step-up approach using lifestyle modifications and the use of over the counter

medications, while 2.8% stated they would use an H2 blocker and 8.4% of physicians responded that they would use a step-in approach and initiate therapy with a PPI. Sixteen percent of physicians recommended a barium swallow with no significant difference between groups.

For the treatment of a young woman with GERD, asymptomatic on a twice daily H2 blocker after three months of therapy (Case 7), 16% of all physicians recommended step-down therapy to a nightly H2 blocker. Twenty-four percent recommended that the current therapy be continued, while 28% stated they would change therapy to lifestyle modifications. Eight percent of physicians stated they would change therapy to either a once- or ever other- day PPI and 23.4% stated they would like to prescribe H2 blocker as necessary. When analyzed by sex, 64% of males physicians recommended H2 blocker as necessary, compared with 36% of female physicians. There is significant difference noted among the groups ( $P=.048$ ).

In the evaluation of step-down therapy for a young woman free of GER symptoms for three months on daily PPI therapy (Case 8), 24.3% of physicians surveyed recommended a decrease in therapy to an every other day PPI. Nearly the same number (25.2%) stated they would not change therapy, while 5.6% recommended a change in therapy to H2 blocker QHS. Eight percent of respondents recommended a change to a twice daily H2 blocker, while 32.7% recommended lifestyle modifications only. When analyzed by sex, we found that 89% of male recommend a step down therapy to an H2 blocker twice daily compared with 11% of females with significant differences found among the two groups ( $P=0.005$ ).

## Discussion

We used a case scenario approach to examine how physicians evaluate and treat patients with GERD. Case scenarios were designed to assess knowledge and practice, of primary care physicians, of published guidelines for the treatment of

GERD. Almost all primary care physician respondents stated that they routinely evaluate patients with acid reflux disease.

Despite the availability of numerous publications that provide algorithms and guidelines for the treatment of GERD, only 55% of them were aware of guidelines of acid reflux disease. The result is almost similar to a previous study, which showed that 60% of physicians were aware of GERD guidelines, (15) which reflects lack of awareness of guideline availability in the literature.

Sixty six percent of all respondents correctly replied that no diagnostic testing is required for mild uncomplicated GERD. However, 37.5% of staff physicians and residents responded that they would order a barium swallow, with no significant difference. Although a barium swallow can diagnose complications of acid reflux disease, it is less effective than EGD at diagnosing Barrett's esophagus and mild esophagitis. Overuse of barium swallows by staff physicians, and residents may reflect less training or a lack of adequate knowledge concerning the use, and efficacy of barium swallows. This finding is inconsistent with a previous study which showed that almost all physicians agree that the most common strategy used for patients with mild symptoms of GERD is treating before testing (24).

The concept of step-up, step-down, and step-in therapy for the treatment of GERD is becoming more widely recognized (14). In the evaluation of a young patient (37 years old) with new intermittent symptoms of GERD, without warning signs, and no previous treatment (Case 1), although Over-the-counter medications are effective in treating symptomatic GERD disease (25), 23.4% of physicians recommended lifestyle modifications and over the counter (OTC) treatment with no significant difference.

For a young patient without warning signs who had failed lifestyle modifications (Case 2), a significant

number of staff physicians correctly recommended step-down therapy (54%) with a PPI, compared with 29% of residents and 20% of consultants who recommended step-up therapy with an H2 blocker ( $P=0.032$ ). A recent study showed that the majority of patients tolerate step-down therapy for GERD quite well without the recurrence of symptoms (24, 29). This may reflect the proven efficacy of PPIs with regard to symptom relief and healing of esophagitis as compared with H2 blocker (15, 26).

The age of physician significantly affected physician-prescribing behavior. In a patient with persistent symptoms of GERD despite the use of a twice daily over the counter H2 blocker (Case 4), more than half of Young physicians (25-35 years) were more likely to prescribe PPIs compared with 10% of older physicians (<35years) who prescribe H2 blocker. This may reflect better reading of the literature, or better satisfaction with these medications in the treatment of their patients. Alternatively, older physicians may have greater exposure to educational efforts directed at practicing medicine in a cost-conscious manner.

In the evaluation of an older patient with symptoms of dysphagia, 48% of staff physicians recommended EGD, which is in accordance with guidelines developed by the American College of Gastroenterologists (10, 15), however, only 25% of consultants and 28% of residents recommended an upper endoscopy in this case where a cardinal warning sign (dysphagia) was present, with no significant difference.

In patients with heartburn symptoms of greater than 5 years' duration, many clinicians now recommend that upper endoscopy be performed to rule out Barrett's esophagus. Fifty seven percent of staff physicians recommended EGD for a patient with long-standing reflux symptoms without warning signs (Case 6). This practice was less common in consultants (25%) and residents

(18%). This variation in response may represent differences in knowledge and training.

Physicians practiced step-down therapy in two cases of patients symptom free after three months of continuous therapy. In the first case (Case 7), about half of the physicians with MBBS degree only recommended correctly H2 blocker as necessary compared to 20% of physicians with board degree and 12% with master degree ( $P=0.016$ ).

In the second case (Case 8), sex was also found to play a role in prescribing behavior. Male physicians were more likely to use step-down therapy in the management of patients with well-controlled GERD symptoms, than females. About 90% of males recommended a step down therapy to an H2 blocker bid compared with 11% of females with significant differences found among the two groups ( $P= 0.005$ ).

There are some limitations to this study:

1. Although the questionnaires were distributed to four PHC centers, the overall response rate was not reasonable. It is possible that the attitudes and practices of non-responders are significantly different than those of responders.
2. This study was performed at a specific community in Riyadh, thus may not reflect national practice patterns.

## Conclusion

Our findings suggest that large numbers of practitioners are unaware of, or do not follow, generally accepted guidelines for the evaluation and treatment of GERD.

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