

### Patients adherence to treatment and knowledge about chronic obstructive pulmonary disease

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Chronic obstructive pulmonary disease (COPD) is a common cause of morbidity and mortality. It has a severe impact on physical and social activities and hence quality of life of the patient. It is crucial that COPD patients understand the nature of their disease, risk factors for progression and that optimal management of COPD involves appropriate prescription of recommended therapy by medical staff and patient's adherence to prescribed medication. Whereas much has been written about COPD as a disease and about its impact on society, the data is lacking about the patient's point of view in terms of general knowledge, impact of disease, adherence to treatment and effects of these factors on the progress of the disease. Knowledge about the disease is important for better adherence to therapy in patients with chronic disease, however, little is known about the extent of adherence to treatment in COPD.<sup>1,2</sup> In this study, it is aimed to investigate a) Patient's perception of COPD b) patient's adherence to prescribed medication and oxygen therapy, and (c) the impact of educational level and the information provided by the medical staff on patient's adherence. Prospective questionnaire includes patient's characteristics, duration of disease, frequency of COPD exacerbation per year, and the educational level knowledge consists of 25-item that measures the knowledge on COPD. The adherence to therapy of the patients was conducted in 140 COPD patients who fulfilled the Global Initiative for Chronic Obstructive Lung Disease (GOLD)<sup>1</sup> criteria with a stable disease at the outpatient chest clinic. The first part of the questionnaire consisted of questions in order to evaluate patient's comprehension about definition and characteristics of COPD and risk factors, such as smoking. The patients were accepted as "informed patient group" if their physicians provide information on their illness and necessary medication. Another part of the questionnaire consisted of questions evaluating their proper medication use. Patients who have knowledge on at least 2 of their bronchodilator medication doses correctly and who used convenient inhalation technique were classified to use medication "correctly" and patients who said

"they took medication everyday" were included in the "regular therapy group". Patients who used their medication both correctly and regularly were categorized as "good medication adherence group". The factors that have impact on "good medication adherence" were analyzed. Daily duration of oxygen therapy was determined and patients who received oxygen at least 15 hours/day were accepted "to use effective oxygen therapy". Patients were divided into 2 groups according to their educational degree as low education [ $\leq 8$  years; illiterate, elementary and secondary school] (90 patients; 64.3%) and high education [ $> 8$  years; high school, university degree] (50 patients; 35.7%) group.

Chi-square test was used to compare the different groups for constant and categorized variables. A  $p$ -value of  $< 0.05$  was considered statistically significant. The risk of factors influence on "good medication adherence" was analyzed by using multivariate logistic regression analysis. Variables with  $p < 0.10$  in logistic regression were considered as potential predictors of "good medication adherence". Thirty-five patients (25%) correctly named their disease as COPD. Highly educated patients had better understanding of COPD in terms of terminology, definition, chronicity of disease and the differences from asthma was statistically significant ( $p = 0.004$ ,  $p = 0.021$ ,  $p = 0.04$ ). Eighty patients (57.1%) declared that they were informed about the characteristics and treatment of their disease, whereas 60 patients (42.9%) were poorly informed about their disease. Highly educated group and patients who were previously informed by their doctors were significantly better at recognizing their medication ( $p = 0.008$ ,  $p = 0.004$ ) and also highly educated patients used their medication more correctly ( $p = 0.007$ ). Fifty-eight (41.4%) patients were on long term oxygen therapy (LTOT), but only 26 of patients (44.8%) used oxygen effectively. We analyzed the factors that were related to adherence by bivariate logistic regression model. Lower education level, unawareness of the chronicity and terminology of the disease and being on uninformed patients were found to be factors for poor adherence as shown on **Table 1**. In addition, multivariate logistic regression analysis revealed that lower education level, female gender, unawareness of the chronicity of the disease and being an uninformed patient increased the risk of poor adherence by 44.43 times.

Chronic obstructive pulmonary disease is one of the major public health problems worldwide. However, the awareness of this disabling disease (with high mortality) was insufficient in general population. In COPD patients, the information regarding perception

**Table 1** - The factors that influence on medication adherence.

Variables	N	Odds ratio (95% Confidence intervals)	P value
<b>Gender</b>			
Female	11	2.78	0.01
Male	129	(0.77-9.93)	
<b>Educational level</b>			
Low level (<8 years)	90	3.17	0.003
High level (>8 years)	50	(1.47-6.84)	
<b>Know chronicity of disease</b>			
No	67	3.27	0.001
Yes	73	(1.62-6.61)	
<b>Know terminology of COPD</b>			
No	105	2.43	0.04
Yes	35	(1.04-5.70)	
<b>Information about disease and treatment provided by physician</b>			
Non-informed	91	3.02	0.005
Informed	49	(1.40-6.51)	
COPD - Chronic obstructive pulmonary disease			

of characteristics and prognosis of disease and requirement for adequate medication and regular follow-up is very limited. This may be due to several factors including social and cultural factors such as social and cultural status, educational level and inadequate information provided by medical staff.<sup>1,3,4</sup> There are no sufficient data for COPD patients in terms of their knowledge about the disease. Rennard et al,<sup>4</sup> investigated frequency of symptoms, severity of disease and compliance to drug use in North America and Europe. They reported that knowledge about the disease and therapy in 40% of patients was very good while it was adequate in 39%. In our study, there were only few patients who have knowledge about the meaning of COPD and the nature and severity of the disease due to poor adherence to treatment. This difference may be explained by social and cultural differences. In previous reports, knowledge about the general disease features was shown to increase adherence to therapy (including oxygen) in COPD patients.<sup>5</sup> In our study, we observed 70% of patients used their medication correctly and 78% who take regular medication. Approximately 10-20% of the patients did not use correct and regular medication and 80% of them even did not know the name of their disease. Good adherence medication group, who used their medication correctly and regularly, were

influenced some factors such as educational level, knowledge about COPD (chronicity and terminology), information about their disease and treatment provided by the physicians. Lower education level, female gender, unawareness of the chronicity of the disease and being an uninformed patient increased the risk of poor adherence by 44.43 times. In our study the ratio of patients, who declared that they were informed adequately by doctors was 57%, while it was higher in Rennard's study.<sup>4</sup> We thought that "informed by doctors" was very low in our study. This may be due to physician-related barrier in our patients population. Information about their disease and treatment provided by the medical staff increased the ratio of good medication adherence by 3 times.

Life is rather difficult with a chronic disease. It is important for health care staff to understand the feelings of patients, to have good relationship with them, to provide patients with sufficient informations which they ask for and can be able to use, in order to increase adherence to therapy. Although our data did not represent the general COPD population, we considered the level of education, awareness of the chronicity and the amount of information about the disease provided by the medical staff are critical for patient's perception about the disease that lead to better adherence to treatment.

The educational level, knowledge about COPD (chronicity and terminology of COPD) and adequate information about the disease process and treatment of physicians are important criteria for perception of the characteristics of disease and better adherence to treatment in COPD patients.

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## Follow-up of hepatitis C virus infected patients

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**H**epatitis C virus (HCV) infection is an underdiagnosed and prevalent blood-borne illness. Nearly 170 million people are estimated to be infected worldwide.<sup>1</sup> It is the leading cause of cirrhosis, hepatocellular carcinoma (HCC), and liver transplantation in developed countries. In addition to

hepatic involvement, it seems to be related with mixed cryoglobulinemia (MC), rheumatoid arthritis, and membranoproliferative glomerulonephritis (MPGN) like immunological disorders, and non-Hodgkin's lymphoma (NHL) like malignancies. Although the presence of various reports regarding these associations, they are not fully understood except for the MC.

Consecutive patients positive of antibody against HCV (anti-HCV) were randomly selected among patients applying to Internal Medicine Polyclinic of the Mersin University, Adana, Turkey with any complaint between January and September 2004. Patients with previous interferon (INF) therapy, at least for a period of 6 months, or moderate amount of alcohol intake regularly ( $\geq 20$  gr/day), were excluded from the study. Anti-HCV was determined using enzyme-linked immunosorbent assay (Abbott AxSYM HCV, version 3.0) and HCV-RNA by polymerase chain reaction (Roche Cobas Amplicor HCV Monitor Test, version 2.0) methods. Additionally, hepatitis B surface antigen (HBsAg), antibody against HBsAg (anti-HBs), routine hematologic and biochemical tests, urinalysis, and an abdominal ultrasonography were performed in all cases. Hepatitis B virus (HBV)-DNA was studied in HBsAg positive cases via molecular hybridization method. Fine needle aspiration biopsies were performed for the diagnosis of cirrhosis, and hepatocellular carcinoma (HCC). Non Hodgkin's lymphoma was diagnosed via excisional lymph node, whereas MPGN via renal biopsies. Idiopathic thrombocytopenic purpura (ITP) was diagnosed by physical and bone marrow examinations. Beside a normal result of physical examination, except for petechia, purpura, and mucosal bleedings, and reduced number of platelets in peripheric blood, a normal or increased number of megakaryocytes in bone marrow were accepted as diagnostic for ITP. Prolymphocytic leukemia (PLL) was diagnosed via bone marrow aspiration, biopsy and flow cytometry. Prolymphocytic leukemia lack expression of clusters of differentiation (CD) 5, as a difference from chronic lymphocytic leukemia. Spirometry or history were used for the diagnosis of asthma. Dermatologic consultation was obtained for lichen planus (LP), and biopsies were taken. Monoclonal gammopathy of undetermined significance (MGUS) was diagnosed by low M-protein levels in serum ( $< 3$  gr/dL) and urine ( $< 300$  mg/day), normal levels of other serum immunoglobulins, and a normal bone marrow examination in the absence of any lytic bone lesion or Bence Jones proteinuria. Results were compared between the HCV-RNA positive and negative groups according to the total numbers of immunological and

malignant disorders, other than cirrhosis and HCC. Statistical analysis was carried out using student t-test, where a *p* value of <0.05 was considered significant.

A total of 96 anti-HCV positive cases were applied, however, 10 of them had previously taken INF therapy, thus they were excluded. Five of these 10 cases were still positive for HCV-RNA and even one of them was cirrhotic, and one had LP. No patient was excluded for alcohol use. Fifty-five of the 86 untreated patients were found positive for HCV-RNA (63.9%). In addition to 18 cases of cirrhosis (31.5%), and 5 cases of HCC (8.7%) (together with cirrhosis in 3), 2 NHL (together with cirrhosis in one), 2 MPGN (together with cirrhosis in both), one ITP, one PLL (together with cirrhosis), one asthma, and one case of LP were detected in the HCV-RNA positive group. As a great difference, only one case of MGUS was detected in the HCV-RNA negative group (**Table 1**). When we compared the HCV-RNA positive and negative groups according to the total numbers of immunological disorders and malignancies, excluding cirrhosis and HCC, the difference between them was significant ( $t=2.35$ , degree of freedom 54, 95% confidence interval 4.83% for lower and 23.17% for upper,  $p<0.05$ ). Additionally, 4 cases of HBsAg positivity in the absence of HBV-DNA positivity were detected in the 86 study cases and all of them were found in the HCV-RNA positive group.

Presently, INF together with ribavirin are widely used for the treatment of HCV infected patients, and the efficacy of the therapy ranges from 40-85%. However, among the side effects of IFN, there are autoimmune ones, which can be globally divided into appearance or increase in titers of autoantibodies or manifestation of overt autoimmune pathologies. Although the former may concern more than 50% of treated subjects, the latter is reported only in 1-2% of them. Thus, we excluded from the study, patients who previously had INF therapy so as not to confuse the results.

During the development of extrahepatic manifestations, virus may cause an immune response resulting with chronic infection, circulating immune complexes, and an autoimmune phenomenon. As another possible mechanism of the process, virus may trigger production of monoclonal rheumatoid factor (mRF), which causes MC type II as the major extrahepatic manifestation of the virus. Prevalence of MC increases by the duration of infection and 60-80% of patients with MC can be shown as anti-HCV or HCV-RNA positive. Although a correlation between the presence of cryoglobulins, duration of disease, severity of liver pathology, and the presence of extrahepatic manifestations of disease has been

**Table 1** - Comparison of hepatitis C virus-RNA positive and negative groups.

Variable	HCV-RNA positives	HCV-RNA negatives
Gender distribution	55 (26 males, 29 female)	31 (13 males, 18 female)
Mean age, Standard deviation, and range	59.3 ± 10.5 years (39-87 years)	49.2 ± 15 years (14-77 years)
Cirrhosis	18	0
HCC	5	0
NHL	2*	0*
MPGN	2*	0*
ITP	1*	0*
PLL	1*	0*
Asthma	1*	0*
Lichen planus	1*	0*
MGUS	0*	1*

\* $p<0.05$ , HCC -hepatocellular carcinoma, NHL -non-Hodgkin's lymphoma, MPGN -membranoproliferative glomerulonephritis, PLL - prolymphocytic leukemia, ITP - idiopathic thrombocytopenic purpura, MGUS - monoclonal gammopathy of undetermined significance

made, it is inexact and may be violated in individual cases. For example, the prevalence of MPGN is approximately 30% in chronic hepatitis C plus type II cryoglobulinemia cases and no association could be detected between MPGN, and HCV in the absence of cryoglobulinemia. However, in an autopsy study, performed on 188 Japanese dominantly cirrhotic patients with chronic HCV infection, prevalence of histological accumulation of immune complexes in glomeruli was found as 54.8% and the prevalence of MPGN, as the most frequently seen type, as 11.2%.<sup>2</sup> But only 12.2% of cases, especially the MPGN having ones, have been symptomatic for glomerulonephritis during the year just before death.<sup>3</sup>

According to a widely discussed hypothesis, the cause of extrahepatic involvement of the virus is extrahepatic tropism, especially lymphotropism. The lymphotropism is thought to be an important factor for the development of B-cell NHL (B-NHL) and production of autoantibodies. But the results are controversial. There was no evidence found regarding the presence of virus in lymphoma cells in 8 studies, performed on patients with chronic hepatitis C and extranodal B-NHL.<sup>4</sup> In a case with salivary gland lymphoma, no virus was detected in lymphoma cells but detected in normal glandular epithelial cells. In

long term follow-up studies, B cell malignancies have been detected in 4-6% of cases with chronic hepatitis C and type II cryoglobulinemia. The prevalence of chronic hepatitis C was found higher in B-NHL cases than the controls in studies performed in Italy and Japan (9-32% versus 0.0-3.1%), whereas no association was found in England and North America.<sup>5</sup> On the other hand, it suggests that there is a strong relationship between HCV infection and salivary gland lesions, lymphocytic capillaritis, and lymphocytic adenitis. Sialadenitis with the same characteristics of humans has been detected in transgenic mice, expressing membrane genes of the virus. Additionally, HCV has been detected in keratinocytes and glandular epithelial cells of palpable purpuric lesions of patients with type II cryoglobulinemia, but not in normal skin. An increased number of LDL receptors has been detected on keratinocytes of the lesions. An inflammation induced increase in the number of LDL receptors may be terminated with the increased uptake of virus, since it has been shown that LDL receptors regulate endocytosis of the virus.<sup>6</sup> Furthermore, the prevalence of HCV infection was found as higher in patients with porphyria cutanea tarda in South Europe, America, and Japan, which supports the idea that HCV is a precipitating factor of porphyria cutanea tarda.<sup>7</sup>

Until now, HCV is not accepted as an oncogenic virus. But it has been reported that HCV core proteins takes role in malign conversion of cells. Additionally, oncogenesis and hypermutation of immunoglobulin in HCV infected cells have been shown.<sup>8</sup> Furthermore, splenic lymphoma associating with chronic hepatitis C has regressed parallel to the regression of viremia, achieved by antiviral therapy.<sup>9</sup> Even our results, which include 2 cases of NHL and one case of PLL out of 5 cases of HCC, may indicate the oncogenic potential of the virus, and probably the oncogenic effect of the virus is more prominent on the lymphocytic lineage cells as in other extrahepatic involvement types of the virus.

In conclusion, although our number of cases were small, the prominent difference between HCV-RNA positive and negative groups according to various immunological and malignant disorders, even excluding the already known cirrhosis and HCC, indicates the role of the virus in these pathologies. As a result, HCV-RNA positive individuals should be followed up, not only for cirrhosis and HCC, but also for various immunological and malignant disorders, even in the absence of any clinical results regarding hepatic involvement.

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## Diagnostic role of pediatric flexible bronchoscopy in Down's syndrome associated with congenital heart disease

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**D**own's syndrome (DS) is the most frequent human chromosomal syndrome with an incidence in the general population of one in 600-800 live

births.<sup>1</sup> Multiple congenital anomalies are closely linked to DS. Between 40% and 50% of babies with DS have congenital heart defects; of these, 30-40% had complete atrioventricular canal.<sup>2</sup> Respiratory problems are the primary cause of morbidity and hospital admission particularly in young children with DS. Cardiac disease is one of the factors that could be contributing to children with DS having an excess of lower respiratory airway problems not only because of respiratory problems secondary to cardiac failure, but also because of effects on the large airways. The purpose of this study was to identify the spectrum of airway anomalies diagnosed by flexible bronchoscopy in pediatric DS patients with significant respiratory illnesses associated with cardiac defects.

After obtaining approval from the Research Committee (IRB) of Hamad Medical Corporation, a retrospective chart review was made of all confirmed DS patients born between January 2000 and December 2003 at the Hamad Medical Corporation, Qatar. The variables of the study were obtained as follows demographic characteristics, pattern of respiratory symptoms associated with cardiac anomalies, indications for bronchoscopic assessment, procedural complications and bronchoscopic findings. The cardiac diagnoses were established by echocardiography with or without angiography. Flexible bronchoscopy through nasal route was performed in the pediatric intensive care unit using 2 bronchoscopes, an Olympus BF XP40 or an Olympus BF3C 40 (Olympus, Tokyo, Japan), with external diameters of 2.8 mm and 3.6 mm. Children were sedated using midazolam (0.1 mg/kg body weight) and ketamine (1-2 mg/kg body weight). Lidocaine (0.5%) was sprayed in the laryngeal area after initial observation of laryngeal

function, which as followed by bronchoscope insertion into the trachea. The hemodynamic status and respiratory status were monitored continuously and supplementary oxygen was given during the procedure. Airways were examined for intrinsic abnormalities, in addition to evidence of extrinsic compression and abnormal airway dynamics. In 97 DS cases, there were more boys (54.6%) than girls (45.4%) with a ratio of 1.2:1. The mean age of these patients was  $2.51 \pm 1.27$  years (range: 0.2 to 5.0 years). Congenital heart diseases (CHD) was detected in 44/97 (45.4%); single cardiac defect in one third of the total cases (33%), and multiple in 12.4% of them. Among these 44 cases of CHD, the most common was complete atrioventricular canal (AVC) in 20 patients (45.45%) and atrial septal defect (ASD) in 10 patients (22.73%). Five DS children with CHD (11.4%) underwent flexible bronchoscopic assessment together with another one with no cardiac defect. The mean age at bronchoscopic assessment was  $9.33 \pm 7.94$  months (range, 3-24 months). The associated CHD lesions were complete atrioventricular canal (AVC) in 3, ventricular septal defect (VSD) with cleft mitral valve in one and Tetralogy of Fallot (TOF) in another. The indications for the procedure are summarized in (Table 1). Repeated bronchoscopy was performed in 2 cases, one of whom was on ventilatory support with complete AVC and persistent left-sided collapse (case number 3 in Table 1). Flexible bronchoscopy at the age of 3 months showed complete external compression of the left main bronchus by a vascular structure. She required early pulmonary banding. Repeated bronchoscopy at 4 months of age after pulmonary banding showed similar findings. Another patient (case number 2) with complete AVC required

**Table 1 -** Associated cardiovascular lesions and endoscopic findings.

Patients No.	Gender	Age (yrs)	Cardiac diagnosis	Indications	Age at procedure (months)	Bronchoscopic findings
1	F	2.6	No	Persistent right upper lobe collapse	11	Tracheal bronchus
2	M	1.3	Complete AVC	Recurrent bilateral segmental collapse with hyperluency	4	Tracheobronchomalacia
3	F	1.5	Complete AVC	Persistent left-sided collapse	3	External compression of left main bronchus
4	M	2.8	VSD and cleft mitral valve	Recurrent wheezy chest	10	Right middle bronchomalacia
5	M	2	TOF	Chronic stridor	4	Laryngomalacia
6	M	4.8	Complete AVC	Chronic upper airway obstruction	24	Adenoid enlargement

AVC - atrioventricular canal, TOF - tetralogy of Fallot, VSD - ventricular septal defect

bronchoscopy twice for bilateral segmental collapse and hyperinflation before and after cardiac surgery and showed similar findings with mild tracheobronchomalacia and right main bronchomalacia. None of them had complication during and/or after the bronchoscopy procedures. In the present study, flexible bronchoscopy considerably contributed by adding essential information on airway anatomy in DS patients, especially when associated with complicating CHD. A high index of suspicion is warranted in children with DS associated with CHD known to predispose to airway abnormalities but we found only a low frequency of such anomalies (11.4%). Nonetheless, routine bronchoscopic examination of all these children, regardless of the presence or absence of symptoms, is probably not indicated in the light of the invasive nature of this procedure. Tracheobronchial anomalies have been easier to diagnose since the development of the pediatric bronchoscope, which is used now to study patients with persistent atelectasis, and localized recurrent pneumonia.<sup>3</sup> Tracheobronchomalacia is an inherent weakness in the structural integrity of the bronchial tree that results in partial or total collapse of the airway and respiratory embarrassment during infancy but it generally resolves as the airway enlarges.<sup>4</sup> In the present study, one patient had tracheo-bronchomalacia but did not require positive pressure ventilation or CPAP or major surgical intervention. A recent study reported that the left main bronchus is the site of predilection due to its intimate anatomical relation to the left pulmonary artery and left atrium.<sup>5</sup> In the presence of a high pulmonary flow, the hypertensive, dilated left pulmonary artery arching over the left main bronchus exerts a compressive force. An aberrant right upper lobe (RUL) bronchus arising from the trachea (tracheal bronchus) can be responsible for persistent collapse and recurrent pneumonia. Tracheal bronchus in patients with DS could be related to poor handling of secretions and/or aspiration.

In summary, there is a potential role for bedside pediatric flexible bronchoscopy in DS patients with significant respiratory and associated cardiac defects presenting with clinical respiratory signs, symptoms and radiological signs that suggest airway anomalies requiring early intervention.

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## Effects of statins on bone mineral density

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Statins have a stimulatory effect on osteoblastic activity. As it was shown by experimental studies, statins enhance synthesis of a growth factor for osteoblastic proliferation - the bone morphogenetic protein 2 (BMP2) - and cause increase in bone mass after both subcutaneous administration and oral dosing in rodents.<sup>1</sup> In a number of epidemiological studies,<sup>2</sup> but not all studies,<sup>3</sup> use of statin was associated with a reduced risk fracture in human. However, no effect of statin treatment on bone mineral density (BMD) was found in a recent prospective study.<sup>4</sup> There is only one study investigated simultaneously on bone turnover markers and BMD in subjects treated with a statin. In this cross-sectional study by Rejnmark et al,<sup>5</sup> showed that bone turnover markers were significantly lower in the subjects treated with statin compared to the age and gender matched controls, while BMD values did not differ between the case subjects and controls.<sup>5</sup> Because of the limited and inconsistent human data, there are no agreement on the effects of statins on bone metabolism. We conducted a prospective study to investigate the effects of statins on BMD, in hyperlipidemic postmenopausal women.

This study was carried out between May 2001 and October 2002 in the Department of Internal Medicine, Division of Endocrinology, University Hospital in Sivas, Turkey. In this study, 24 postmenopausal women were recruited at the Endocrinology Out-Patient clinic. Patients with hyperparathyroidism, diabetes mellitus, malignant disease, increased glucocorticoid or thyroid hormones, hyperprolactinemia, history of treatment for osteoporosis or hyperlipidemia or any drugs that have ability to interfere with bone metabolism (steroids, heparin, thiazides, anticonvulsants) and severe liver and kidney disease were excluded in this study. Daily urinary calcium excretion, serum osteocalcin and BMD of lumbar spine and femur neck measurements were performed before and after 36 weeks of treatment statins. The treatment was started by giving 40 mg/day atorvastatin (Lipitor, Pfizer). Osteocalcin levels were measured by immunoradiometric (IRMA) method by using Active Human Osteocalcin IRMA DSL 7600 kit (USA). Bone mineral density measurements at the site of lumbar spine (L1-L2) and femur neck were performed by Dual energy-x-ray absorptiometry (DEXA) method on Hologic 4500 W device (USA). The data were analyzed by Wilcoxon test. A probability value of less than 0.05 was considered statistically significant. The subjects had similar demographic data as socioeconomic status, educational levels and physical activity patterns. All patients were housewives and none of the subject was alcohol or tobacco user. The mean age was  $54.85 \pm 1.83$ . The results of 24 patients were given as mean  $\pm$  standard error. Post-treatment values of Z scores of lumbar spine increase to 55.2% and femur neck to 31.2% ( $p < 0.05$ ) compared to pretreatment values (Table 1). T scores of lumbar spine increased to 19.4% ( $p < 0.05$ ) while T scores of femur neck increased to 7.5% ( $p > 0.05$ ) after the

treatment. Urinary calcium excretion level decreased to 12% and serum osteocalcin level decreased to 28% ( $p > 0.05$ ).

In this study, we found a significant increase in BMD, particularly at the site of lumbar spine in postmenopausal hyperlipidemic women after atorvastatin treatment. The increase in BMD in our study supports that statins have effects on bone metabolism. This finding do not support that statins exert anabolic properties in bone tissue. In a recently published study by Rejnmark et al,<sup>5</sup> found that bone turnover markers decreased significantly in the statin treated subjects compared to age and gender matched controls, while BMD values at any site did not differ between cases and controls.<sup>5</sup> This previous study<sup>5</sup> could be failed to show BMD changes, because of difficulties in detecting the moderate effect on bone mass in a cross-sectional study design. On the other hand, the reason for insignificance of the changes in the biochemical parameters in our study could be the limited sample size. Bauer et al<sup>2</sup> recorded that use of statin is associated with an increased BMD in hip region and a reduced fracture risk. There was a number of epidemiologic studies recorded a substantial decrease in fracture risk in patients treated with statin.<sup>4</sup> However, these findings were not confirmed by recently published study.<sup>3</sup>

In conclusion, our results suggest that statins have an effect on bone metabolism, resulting in an increased BMD. Supposed that statins may have an anabolic effect on bone metabolism, the findings in this study did not confirmed. It is not yet clear that the effects of statins on bone metabolism have a clinically useful implication in the patient care. Future studies are needed to explain the underlying mechanism in the discrepancies and the conflicting results in these studies.

**Table 1** - The comparison of pre- and post-treatment measurements.

Treatments	Before treatment	After treatment	Evaluation (%)
Urinary calcium excretions (mg/day)	242.45 $\pm$ 21.70	212.90 $\pm$ 21.70	-12.1*
Osteocalcin (ng/ml)	11.65 $\pm$ 2.10	8.33 $\pm$ 2.39	-28.4*
Vertebra Z score	-1.61 $\pm$ 0.36	-0.72 $\pm$ 0.23	+55.2†
Vertebra T score	-1.75 $\pm$ 0.26	-1.41 $\pm$ 0.28	+19.4†
Femur Z score	0.16 $\pm$ 0.22	0.21 $\pm$ 0.21	+31.2†
Femur T score	-1.20 $\pm$ 0.21	-1.11 $\pm$ 0.21	+7.5*
* $p > 0.05$ , † $p < 0.05$			



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## Obstructed labor. A real problem in Yemeni's rural areas

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Obstructed labor is the failure of the presenting part to descend in spite of uterine contraction.<sup>1</sup> It causes significant short term (notably infection) and long-term (notably obstetric fistulas) maternal morbidity. Fetal death from asphyxia is also common. It is the leading cause of the uterine rupture worldwide,<sup>2</sup> and an important cause of maternal deaths. Obstructed labor in Yemen still exists, and represents a major challenge to maternal health. This adds to the challenge of maternal mortality ratio in the country, which is already too high (570/100,000 live births) according to the World Health Organization report.<sup>3</sup> The likely cause is that the issue of safe motherhood is not yet taken seriously by the health care system.

Most women in our rural areas are poor, illiterate, married at early age before their hips being matured

enough, and got pregnancy too early with inadequate maternal care services. Obstructed labor is an important indicator of obstetric care system, and socio-economic factors.<sup>1,2</sup> It indicates bad care during pregnancy, and labor as the serious risks such as inadequate pelvis, malpresentation and malposition, or fetal anomalies that may run without anticipation, early detection and management is needed. Recognition of such problems in the community, maternity health care and government may lead to construction of strategies, and programs that we hope, if implemented properly, will prevent the obstruction in high proportion of women.

The purpose of this study was to determine the incidence of obstructed labor in one of the Yemeni's rural area, and to identify the risk factors related.

This study was carried out in Dhamar General Hospital, which is located in Dhamar City, one of Yemeni governorate, 100 km to the south of Sana'a City. It is a referral, public hospital, which serves all the governorate population (more than 600,000 persons). In this study, we recorded all pregnant women of 37 weeks gestational age or more who were admitted to labor room with the following: 1) true labor pain, 2) symptoms and signs suggestive of prolonged labor or obstruction. In addition to those already admitted with risk factors such as cephalopelvic disproportion, neglected shoulder, rupture of uterus, and others. After admission, all women with symptoms and signs suggestive of obstructed labor were evaluated completely, and resuscitative measures were performed at once. The decision of immediate delivery was carried out mostly by cesarean section.

A summary of the case was recorded including the time of admission, age, parity, diagnosis, risk factor, management, outcome, and any complication developed either during or post operative period. All women included in the study were subjected to follow-up, 2-3 weeks post delivery. Through a year (April 1st 2003 to March 31st 2004), the total cases admitted to the hospital for delivery were 3622 women, of them, the obstructed labor was reported in 330 cases (9.1%), making the incidence approximately 1 in 11 deliveries. The majority of cases were admitted through the emergency room with a history of labor pain longer than 8-6 hours before transportation to the hospital. Nearly all women admitted were at term 37-42 weeks gestational age. One hundred and seventy-three cases (52.4%) were admitted with clear picture of obstruction without history of intervention, 127 women (38.5%) had history of mishandling by traditional birth attendant, 12 cases (3.6%) with vaginal bleeding, and 18 cases (5.5%) with cessation of uterine contraction. The most common cause of

obstructed labor was cephalopelvic disproportion (46%) followed by malpresentation and malposition (38.8%). The majority of patients [291 (88.1%) cases] were delivered by cesarean section, 24 cases (7.3%) were delivered by outlet forceps, 8 cases (2.4%) by ventouse extraction, and 7 cases (2.1%) were delivered vaginally after cephalocentesis for massive hydrocephalus.

Twelve cases (3.6%) had ruptured of uterus diagnosed at the time of cesarean section, of them, 7 cases had previous one cesarean section. Hysterectomies were performed in 8 cases, while rent repair was carried out for the rest of the 4 cases.

Regarding complications, patients were transient and were managed successfully, however, 9 cases (2.7%) were seen later, complicated by vesico-vaginal fistulas. There was no maternal death in our study.

One hundred and sixty-six fetuses (50.3%) were live born, and 164 fetuses (49.7%) were still born, the perinatal mortality were (54.6%).

The obstructed labor mostly occurred in poor patients, unbooked women, primigravidae (41.9%), and age group of 20–28 year (50.9%).

The high incidence of obstructed labor in our results indicates that the risk factors leading to obstruction were not determined during pregnancy as a result of lack antenatal check-up. The absence of obstetric care, delayed referral, lack of transport facilities are the dominant features in the developing countries.<sup>1</sup> A total of 77.6% of women who had obstructed labor in our study, were without antenatal care, and arrived to the hospital for the first time when labor has already complicated. Clearly, the closer to the expected date of delivery that a women is examined, the greater the predictive value of clinical assessment of a likely mechanical problem, furthermore, many causes of obstruction can be detected before the onset of labor.<sup>1</sup> The essential obstetric care, which incorporates the provision of properly trained, and skilled birth attendants able to recognize abnormality in labor, able to deal with unpredictable complications as they arise, and able to arrange transfer to a facility, which can cope with obstetric emergencies<sup>4</sup> should be considered. Of note, many women in our results, identified to have 6-7 children, whereas their ages ranged between 20–28 years, which indicates early marriage, early pregnancy as well as too close pregnancies.

In the obstructed labor, the cesarean operation is a safe option whether the fetus still alive or dead as laparotomy itself is necessary when the state of the uterus is not known.<sup>5</sup> Cephalocentesis was carried out in 7 cases in which the obstructed labor had resulted from hydrocephalus not detected during

pregnancy. These preventable complications reveal the importance of antenatal care. The high incidence of vesicovaginal fistula (2.7%) could be explained by the long-standing obstructed labor as many of women had labor pain 6–8 hours before arriving to the hospital. The high rate of perinatal mortality (49.7%), was also related to prolonged obstructed labor.

In conclusion, this review shows that obstructed labor is common in our rural areas where illiteracy, early marriage, early and close pregnancies without antenatal care are the predominant features. Likewise, the existence antenatal care, and referral system are inadequate and substandard. While it is a sad commentary in the era of safe motherhood that this problem still exists, the education of women and provision of essential antenatal and obstetric care are the urgent tasks to be addressed promptly.

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## Symptomatology of menopause among middle-aged women in 3 impoverished Lebanese communities

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Larger proportions of women are now entering menopausal transition than before, and spending

approximately one third of their lives in post menopausal state. Onset of menopause was shown to be related to a constellation of symptomatology and chronic conditions affecting age-span, and quality of life. Various symptoms appear at this stage as a result of hormonal, biosocial, or cultural factors. These menopausal symptoms are mainly of vasomotor, somatic, genital, or psychological in origin. Highest frequencies of menopausal symptoms were shown in the peri-menopause and early post menopausal phase.<sup>1</sup> In the absence of optimal medical management, menopausal symptoms are becoming more problematic for physicians and women themselves. This paper describes the menopausal symptoms reported by underprivileged urban middle aged women in their peri and early post menopausal years.

The data used are taken from of the Urban Health Study conducted by the Center of Research on Population and Health (CRPH) at the American University of Beirut. This study consisted of a survey of households in 3 poor communities in the suburbs of Beirut: Nabaa (NA), Hay El Selom (HS), and Burj Al Barajneh (BB). These communities had certain

characteristics in common such as overall poverty conditions, lack of infrastructure, and displaced population. On the other hand, they differed in their ethnic and religious composition. For example, while NA and HS house were predominantly Lebanese population, BB consisted of mostly Palestinian refugees. Also, NA was 80% Christian, while nearly all the inhabitants of the HS and BB communities were Muslim.

The sample was selected using a probability proportional to size sampling design. The communities were divided into blocks using area maps. A sample of households was drawn from each of the selected blocks. The survey was conducted in 2 phases. Phase I, which took place between May and July 2002, has covered household information including demographics, education, general health and insurance coverage, migration, labor, income, women and work issues. Phase II consisted of 3 individual questionnaires regarding the health of adolescents, elderly, and women and was completed during spring 2003. The present paper used information from the reproductive health questionnaire that was addressed to 1869 married women from these communities (response rate= 93.1%). The data were collected using face-to-face interviews by interviewers recruited locally from 3 communities, and trained on the questionnaire and interviewing techniques by CRPH staff, and study investigators.

Out of the 1869 married women, 92 (aged 45-55 years) were in peri-menopausal (had their last menstrual cycle between the last 3-12 months) or post menopausal phase (missed their menstrual cycle for the last 12 months) for no longer than 2 years. Those who were taking hormone therapy or had surgical menopause were excluded from the analysis.

The profile of these women indicated that they were generally of low socio-economic status. The majority (76%) had a household income less than 12500 Lebanese Liras (US\$ 8333), where 25% had less than 3600 Lebanese Liras (US\$ 2400); this is similar to the general household income of these communities. Sixty-five percent had less than elementary educational level and 16% were in labor force (The labor force is defined as the currently active population; which comprises all employed and unemployed persons). Health indicators for women were also not satisfactory; 44% were smokers, 46% were not comfortable with their weight, 65% reported a health problem in the last 2 months, and 47% suffered from a chronic disease.

Out of all women, 95% reported having any menopausal symptom, where 93% reported having somatic symptoms, 91% psychological symptoms, 77% vasomotor symptoms, and 35% genital symptoms. **Table 1** shows prevalence of symptoms by

**Table 1** - Frequency of reported symptoms among middle-aged women in their peri and early post menopause.

Symptoms	(%)	Upper CI	Lower CI
<i>Somatic symptoms</i>			
Joint pain	(63)	73	53
Sleeping problems	(62)	72	52
Palpitations	(56)	66	45
Shortness of breath	(52)	62	41
<i>Psychological symptoms</i>			
Impatience	(77)	86	68
Nervousness	(70)	80	61
Mood swings	(69)	78	59
Anxiety	(64)	74	54
Feeling down	(64)	74	53
Concentration problems	(58)	68	48
Memory loss	(52)	63	42
<i>Vasomotor symptoms</i>			
Hot flashes	(73)	82	64
Night sweating	(68)	77	58
<i>Genital symptoms</i>			
Inability to control urination	(31)	41	22
Vaginal dryness	(14)	21	2
Fatigue, weakness	(77)	86	68
CI - confidence interval			

type. All symptoms were reported by more than 50% of women except for genital symptoms: inability to control urination (31%) and vaginal dryness (14%). Highest frequencies for reported symptoms were fatigue/weakness and impatience 77% each; followed by hot flashes (73%) and nervousness (70%). The frequencies of symptoms are high when compared to women residing in the capital city Beirut<sup>2</sup> and women in other Arab countries like United Arab Emirates<sup>3</sup> and Morocco.<sup>4</sup> This high prevalence supports the evidence that there is no universal symptomatology pattern in developing countries.<sup>5</sup> The large variation of women's backgrounds and cultures and the limited and uneven distribution of studies in the developing region lead to a discrepancy in the menopausal literature as a whole.

Low prevalence of genital symptoms is most probably due to under reporting rather than a real low existence. Certain cultural reservations might mask the reality of such problems; especially that vaginal dryness (22%) and inability to control urination (15%) ranked the first 2 symptoms among all annoying ones.

None of the socio demographic characteristics was significantly related to the frequency of reported symptoms, which sheds the light on the importance of these symptoms in this specific population regardless of any internal differences.

Studies on menopause should encompass women from different communities, and not focus merely on those residing in capital cities. Similar methodologies should be followed when describing the prevalence of menopausal symptoms, allowing for better comparisons across different settings, and a clearer understanding of culture specificities shaping

menopausal life. More research should be carried out to find optimal ways to control, and manage such symptoms especially among poor women to ensure better wellness.

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