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Original Article

Case Report

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Original Article

Prevalence of Osteoporosis in Male Patients with Chronic Obstructive Pulmonary Disease

Bari MZJ[1], Patwary MI[2], Hossain MD[3], Hye AQMA[4], Rahman SM[5]

Abstract

Osteoporosis is one of the systemic features of COPD. Aims and objective is to determine the prevalence of osteoporosis in male COPD. In a cross-sectional study, we conducted dual-energy X-ray absorptiometry bone mineral density scans of the femoral neck and lumbar spine and collected data on smoking, duration of COPD, inhaled and oral corticosteroid treatment and staging by pulmonary function tests. We included 60 male patients with COPD, the mean age was 62.4 ± 8.1 years, smoking was 36.8 ± 17.2 smoking-pack year, duration of COPD was 5.4 ± 3.3 years, GOLD stage-III (56.7%) stage-IV (38.3%) and stage-II (5.0%), use of oral steroid (11.7%) inhaled steroid (63.3%) and none (25.0%). Normal bone mineral density was in 6 (10.0%), osteopenia in 24 (40.0%) and osteoporosis in 30 (50%) patients in femoral neck; whereas normal bone mineral density was in 4 (6.7%), osteopenia in 17 (28.3%) and osteoporosis in 39 (65.0%) patients in lumbar spine. Osteoporosis is highly prevalent in male COPD patients in both femoral neck and lumbar spine.

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality in adults and is the fourth leading cause of death in the world[1]. It is characterized by chronic air flow limitation that is usually progressive[2]. COPD is now considered as a multicomponent disorder associated with systemic inflammation and extra pulmonary manifestations[3]. Osteoporosis is a systemic skeletal disease characterized by a low bone mineral density (BMD) and microarchitectural changes in bones leading to an increased bone fragility and, in turn, resulting in an increased fracture risk[4].

The prevalence of osteoporosis in COPD patients is 2-fold to 5-fold higher than in age-matched subjects without air-flow obstruction[5-7]. Osteopenia is present in 35-72% of patients with COPD, and 36-60% of patients with COPD have been reported to be osteoporotic[8,9]. Moreover, COPD patients have a 60 to 70% higher risk of death following hip fracture than people without COPD[10]. It is therefore of high clinical importance to diagnose and treat osteoporosis in COPD according to international guidelines[11].

The gold standard for the diagnosis of osteoporosis is dual-energy absorptiometry (DXA)[11]. Multiple sites can be used to measure BMD by DXA. The sites most frequently used are the hip, the lumbar spine, forearm and/or whole-body. Several studies investigated the best location for DXA-scanning to diagnose osteoporosis[12,13]. Indeed, the International Society for Clinical Densitometry advocates to measure BMD of the lumbar spine and the hip and to diagnose osteoporosis based on the lowest T-score of the measured locations[14].

Now COPD has been identified as a disease associated with osteoporosis and has been included in the fracture risk assessment in a few guidelines on osteoporosis and fracture prevention[15]. However, data is scarce in Bangladesh on the prevalence of osteoporosis in male patients with COPD, hence we aimed to assess the prevalence of osteopenia and osteoporosis in male patients with COPD.

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Materials and Methods

This was a cross sectional study carried out in the Department of Medicine, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet during the period from 1st July 2013 to 30th June 2015. Sixty male smokers at least 10 pack years, aged more than 40 years and diagnosed as cases of COPD fulfilling the inclusion and exclusion criteria were enrolled in this study. Patients with bronchial asthma, chronic heart failure, liver cirrhosis, thyroid dysfunction and rheumatologic disorders, malignancies, chronic renal disease; those using systemic steroid (at least for 3 month during the recent year); bisphosphonate, erygocalciferol, levothyroxin, lithium, calcium and vitamin D preparations were excluded.

Informed written consent was obtained from the patients or attendants after full explanation of the details of the disease process and purpose of the study.

Height and weight was determined barefoot and in lightweight indoor clothing and the body mass index (BMI) calculated.

Diagnosis of COPD based on clinical history and confirmed by pulmonary function testing. All subjects performed spirometry (Forced expiratory volume in 1 second [FEV_1], Forced Vital Capacity [FVC], and FEV_1/FVC ratio) using RMS Helios 702 spirometer (Recorders and Medicare systems private limited, MEDSPIROR, India) in the Department of Medicine Sylhet MAG Osmani Medical College Hospital, Sylhet. Staging of COPD was done as per GOLD Criteria, stage-I: FEV_1/FVC < 0.70, $FEV_1 \geq 80\%$ predicted, stage-II: FEV_1/FVC < 0.70, FEV_1 50-79% predicted, stage-III: FEV_1/FVC <0.70, FEV_1 30-49% predicted and stage-IV: FEV_1/FVC < 0.70, FEV_1 < 30% predicted or FEV_1 < 50% predicted if respiratory failure present[16].

Bone mineral density of the patient was determined using whole body densitometer, DEXA Scan (Dual Energy X-Ray Absorptiometry) (GE Healthcare Lunar prodigy advance, scanner serial no. PA + 302343, software version ± ENCORE 2008 version 12.2, Germany). BMD, bone mineral content (BMC), and area were measured at the lumbar spine (vertebrae L2-L4) and at the femoral neck. All parameters were expressed in standard globally accepted terms: BMD (g/cm^2), BMC (g), and area (cm^2). A patient's BMD was given a T-score, which was derived by comparing it to an average score for a healthy 30-year-old male. The difference between the "normal young" score and the patient's score were referred to as a standard deviation (SD). T-score values below -2.5 SD was delineable for osteoporosis; between -1.0 and -2.5 SD was definable for osteopenia and -1 SD are definable for normal bone density[17].

All the collected data were compiled and analyzed using the SPSS (Statistical package for social science) 21 for windows.

Results

The age of the patients of COPD ranged from 43 to 80 years with the mean age of 62.4 ± 8.1 years. The most of the COPD patients (75.3%) were aged between 51 to 70 years (Table-I).

The mean smoking-pack year was 36.8 ± 17.2 (range, 10-90) pack-years (Table-I).

The mean duration of COPD was 5.4 ± 3.3 years (range, 1-15 years); the duration of COPD was 1 to 5 years in 38 (63.3%), 6 to 10 years in 18 (30.0%) and 11 to 15 years in 4 (6.7%) patients.

GOLD stage-III was the most frequent severity of COPD constituted 56.7% cases, followed by stage-IV (38.3%) and stage-II (5.0%) (Table-I).

Use of oral steroid in 7 (11.7%) patients, inhaled steroid was in 38 (63.3%) and 15 (25.0%) patients did not use any types of steroid (Table-I).

Table-I: Baseline characteristics of patients.

Variables	Frequency	Percent
Age		
41-50 years	6	10.0
51-60 years	18	30.0
61-70 years	32	53.3
71-80 years	4	6.7
Mean ± SD	62.4 ± 8.1	
Smoking (pack-years)		
<20	10	16.7
31-40	34	56.7
41-60	11	18.3
≥61	5	8.3
Mean ± SD	36.8 ± 17.2	
Severity of COPD		
Stage-II	3	5.0
Stage-III	34	56.7
Stage-IV	23	38.3

T-score in femoral neck was -2.31 ± 0.96 (range -3.80 to -1.1) and BMD in femoral neck was 0.77 ± 0.17 gm/cm^2 (range, 0.58 to 1.03) (Table-II).

When BMD were categorized according to T-score in femoral neck, normal bone mineral density was in 6 (10.0%), osteopenia in 24 (40.0%) and osteoporosis in 30 (50%) patients (Table-II).

T-score in lumbar spine was -2.92 ± 1.33 and BMD in lumbar spine was 0.87 ± 0.16 gm/cm^2 (Table-II).

When BMD were categorized according to T-score in lumbar spine, normal bone mineral density was in 4 (6.7%), osteopenia in 17 (28.3%) and osteoporosis in 39 (65.0%) patients (Table-II).

Table-II: Distribution of the patients by BMD (n=60).

DXA	Femoral neck	Lumbar spine
T-score	-2.31 ± 0.96	-2.92 ± 1.33
BMD (gm/cm^2)	0.77 ± 0.17	0.87 ± 0.16
Normal	6 (10.0%)	4 (6.7%)
Osteopenia	24 (40.0%)	17 (28.3%)
Osteoporosis	30 (50%)	39 (65.0%)

Discussion

Osteoporosis continues to be a major problem in men with chronic illness. In men with COPD, osteoporosis may be particularly disabling because vertebral fractures reduce vital capacity, which further compromises ventilation[18]. Evidence suggests that the prevalence of osteoporosis in patients with COPD is high and potentially important[19,20].

In this study the age of the patients of COPD ranged from 43 to 80 years with the mean age of 62.4 ± 8.1 years. This result was almost similar to the study of Jorgensen et al[18] that the mean age of the male COPD patients was 62.8 ± 5.6 years. This result also correlated with other studies[5,20].

This study revealed that the mean smoking-pack year was 36.8±17.2 (range, 10-90) pack-years. This result was consistent with the study of Graat-Verboom et al[5] that the mean smoking-pack year of the COPD patients was 39.7± 0.8.

In the present study the mean duration of COPD was 5.4 ± 3.3 years (range, 1-15 years); the duration of COPD was 1 to 5 years in 38 (63.3%), 6 to 10 years in 18 (30.0%) and 11 to 15 years in 4 (6.7%) patients. Nuti et al[21] reported that COPD duration was ≤1 year in 13.1%, 1-5 years in 31.2% and above 5 years in 55.8% of patients.

In this study GOLD stage-III was the most frequent severity of COPD constituted 56.7% cases, followed by stage-IV (38.31%) and stage-II (5.0%). Graat-Verboom et al[5] found that GOLD stage-I and II in 22%, GOLD stage-III in 34% and GOLD stage-IV in 44% patients with COPD.

This study showed that use of oral steroid in 7 (11.7%) patients, inhaled steroid was in 38 (63.3%) and 15 (25.0%) patients did not use any types of steroid. Nuti et al[21] reported that oral corticosteroid in 4.5%, inhaled corticosteroid in 54.1% and both oral and inhaled corticosteroid in 10.6% cases of COPD.

In this study T-score in femoral neck was -2.31±0.96 (range -3.80 to-1.1). Jorgensen et al[17] found that the T-score in femoral neck was -1.51±1.08 in male COPD patients. This study also revealed that T-score in lumbar spine was -2.92±1.33. Jorgensen et al[17] found that the T-score in lumber spine was -1.25±2.08 in male COPD patients.

In the present study BMD in femoral neck was 0.77 ± 0.17 gm/cm^2 (range, 0.58 to 1.03). This result was almost similar to the study of Duckers et al[22] that BMD in femoral neck was 0.74 ± 0.11 gm/cm^2 in men with chronic obstructive pulmonary disease. Jorgensen et al[17] found that BMD in femoral neck was 0.888 ± 0.138 gm/cm^2 in men with chronic obstructive pulmonary disease. This study also showed BMD in lumbar spine was 0.87 ± 0.16 gm/cm^2. Duckers et al[22] found that BMD in lumbar spine was 1.03 ± 0.20 gm/cm^2 in men with chronic obstructive pulmonary disease. Jorgensen et al[17] found that BMD in lumbar spine was 1.089 ± 0.152 gm/cm^2 in men with chronic obstructive pulmonary disease. Jorgensen et al[17] found that BMD in lumbar spine was 1.089 ± 0.152 gm/cm^2 in men with chronic obstructive pulmonary disease.

In this study bone mineral density was normal in 6 (10.0%), osteopenia in 24 (40.0%) and osteoporosis in 30 (50%) patients as regards BMD in femoral neck; while normal bone mineral density was in 4 (6.7%), osteopenia in 17 (28.3%) and osteoporosis in 39 (65.0%) patients as regards BMD in lumbar spine. Also it was demonstrated that 90% of patients with COPD varying from moderate to very severe had abnormal BMD in femoral neck and about 93% of patients with COPD varying from moderate to very severe had abnormal BMD in lumbar spine. These results were in agreement with the results of the cross sectional study carried by Jorgensen et al[17] on 62 COPD patients who found that 78% of patients had low BMD either osteopenic or osteoporotic. Also, these results were in agreement with results of the study carried by Dubois et al[23] which carried on 86 patients with COPD and revealed that; 28% of patients were normal as regards BMD, 50% of patients were osteopenic as regards BMD, and 22% of patients were osteoporotic as regards BMD. Naghshin et al[24] reported the frequency of osteopenia was 36% and osteoporosis was 26% COPD patients according to spinal densitometry; while using femoral neck densitometry results the frequency of osteopenia was 24% and osteoporosis was 52% COPD patients.

Conclusion

A low BMD and osteoporosis is highly prevalent in male er in COPD patients both in femoral neck and in lumbar spine. This study suggests a disease related causative component. The mechanism of BMD loss in COPD remains unclear but our results suggest increased bone turnover. These findings highlight the potential value of studying BMD and reinforce the need for earlier identification and targeting of risk factors for osteoporosis as part of the management of COPD. However further study is warranted.

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Original Article

Effectiveness of Carvedilol versus Indapamide in Uncontrolled Diabetic Hypertensive Patients being Treated with Olmesartan and Amlodipine

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Abstract

Hypertension is the commonest preventable cause of death among the diabetic patient. Current guidelines recommend using combination drug therapy in case of uncontrolled hypertension in diabetic patient. Even though, duel combinations are sometimes insufficient to achieve target blood pressure. Objective of this study was to evaluate the efficacy and safety of Indapamide and Carvedilol as third drug in controlling hypertension in diabetic patients. This prospective comparative study was conducted in 32 well controlled diabetic patient with uncontrolled hypertension those who taking Olmesartan (20 mg/day) and Amlodipine (5 mg/day). Addition of both the drugs showed significant reduction of all the blood pressure parameters at the end of six weeks therapy without any major adverse effects. Systolic blood pressure decreased from 169.71±9.26 to 119.41±12.48 in Indapamide group ($p<0.001$) and 167.67±12.94 to 122.67±18.79 in Carvedilol group ($p<0.001$). Diastolic blood pressure decreased from 98.23±7.06 to 76.76±8.65 in Indapamide group ($p<0.001$) and 94.67±11.41 to 79.33±10.83 in Carvedilol group ($p<0.001$). Mean arterial pressure also reduced from 122.06±5.35 to 90.98±8.72 in Indapamide group ($p<0.001$) and 119.00±10.61 to 93.78±12.51 in Carvedilol group ($p<0.001$). Only ten patients suffered from mild adverse effects, such as epigastric discomfort, nausea, light headedness and drowsiness; which did not required stopping the therapy. Both the drugs are found to be equally effective as well as safe as third drug along with Olmesartan and Amlodipine in controlling hypertension in well controlled diabetic patients.

Keywords: *Hypertension, Indapamide, Carvedilol, Efficacy, Safety.*

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Introduction

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels[1]. The prevalence of hypertension is disproportionately high in patients suffering from diabetes,[2] and individuals who have hypertension are nearly 2.5 times more likely to develop diabetes within 6 years than those without hypertension[3,4]. Hypertension is the most common preventable

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cause of death, accounting for 7.5 million deaths in 2004[5]. The relationship between increasing Blood Pressure (BP) and cardiovascular risk is well established[6] with even modest changes in BP substantially increasing cardiovascular risk[7]. Individuals who have hypertension, diabetes, and other related co morbidities are likely to need multiple antihypertensive agents to achieve the target BP goals recommended to these high-risk populations[8,9]. Blocking two or more regulatory systems provides a more effective and more physiologic reduction in BP. Current guidelines also have recommended the use of combination therapy as first-line treatment, or early in the management of hypertension[8,10,11].

Fixed combination therapy is an efficacious, relatively safe, and may be cost-effective method to decrease BP in most patients with essential hypertension. Similar to other combinations, fixed-dose combination containing the dihydropyridine calcium channel blocker (CCB), Amlodipine, and the angiotensin II receptor blocker (ARB), Olmesartan, bring together two distinct and complementary mechanisms of action[10]. This combination produced greater mean reduction in BP than either drug alone. Moreover addition of Olmesartan to Amlodipine decreased the Amlodipine-related adverse effects (peripheral edema)[10]. Even though, dual combinations are sometimes insufficient to achieve target BP those need a third drug.

However, recently the third generation β-blocker, Carvedilol, has been reported to possess characteristics different from the previously available non-selective and β1 selective-blockers that have adverse effects on glucose and lipid metabolism[12,13]. Nevertheless, little is known about the effects of co-administration of Carvedilol as the third agent with a combination of Renin-Angiotensin System (RAS) inhibitors and CCB on BP regulation and glucose metabolism[13]. Hence this study was aimed to examine the safety and efficacy of adding either Carvedilol or Indapamide as a third drug on elevated blood pressure in well controlled type-II diabetic patient being treated with Olmesartan and Indapamide combination.

Materials and Methods

This study was a prospective comparative study among the well controlled diabetic patient with uncontrolled hypertension. This study was conducted at the Department of Pharmacology and Therapeutics, Sylhet MAG Osmani Medical College, and Diabetic Hospital, Sylhet between the period of July 2013 and June 2014. All Diabetic hypertensive patients aged 40 years and above, who failed to achieve target blood pressure with Olmesartan 20 mg/day and Amlodipine 5 mg/day for 8 weeks was included in this study. Patients with diabetic complications, secondary hypertension, and other co-morbidities (such as malignant hypertension, arrhythmias, asthma, renal insufficiency etc.) were excluded.

The clinical histories of the patients were noted. Each patient was examined thoroughly. All the findings, previous history and reports and investigations were analyzed. Patients were screened for the exclusion criteria. BP was measured on same arm by the investigator using an appropriate cuff with a standard aneroid sphygmomanometer after at least 5 minutes of rest with the patient in the lying as per NICE/BHS guideline[14] between 10.00 am to 1:00 pm in each working day. A mean of three recordings (each one minute apart) was taken. Heart rate was estimated after the third BP measurement. Routine haematological, bio-chemical, radiological and urine examination were done. A 12-channel ECG was performed to exclude cardiac abnormalities. Those who met the inclusion criteria were selected and met the exclusion criteria were excluded from the study. In this way 40 poorly control diabetic hypertensive patients were enrolled in this study.

Recruited patients were then divided randomly in group-A and group-B. The patients of group-A were treated with Indapamide 1.5 mg daily in single dose in the morning for 6 weeks and of group-B were treated with Carvedilol was given in dose of 12.5 mg twice daily as add-on treatment of ongoing Olmesartan 20 mg/day and Amlodipine 5 mg/day for 6 weeks. Follow up BP was measured and treatment related adverse effects were recorded at 2 weeks, 4 weeks and 6 weeks. All relevant data were recorded in preformed data collection sheet.

Quantitative data were expressed as mean and standard deviation and comparison was performed paired t test or repeated measure ANOVA and between groups by unpaired t test. Qualitative data were expressed as frequency and percentages and comparison was performed between two groups by Chi-Square (X^2) test. Statistical analysis was performed by using SPSS (Statistical package for social science) for windows version 16.0. A probability value (p) of <0.05 was considered as significant.

Informed written consent was obtained from the patients after detailed explanation of the disease process and purpose of the study. Prior to the commencement of the study, the research protocol was approved by the Ethical Committee of Sylhet MAG Osmani Medical College, Sylhet.

Results

There were a total of 40 patients recruited in this study. In course of follow up period 3 patients from Indapamide group (due consent withdrawn one patient and failed to complete follow up two patients) and 5 patients from Carvedilol group (consent withdrawn one patient and failed to complete follow up four patients) were dropped out. So, per protocol analysis was done in 17 patients of Indapamide group and 15 patients of Carvedilol group. Both the groups are statistically similar in terms of their sex ($\chi^2=0.014$; $p>0.05$) and age ($t=-1.312$; $p>0.05$).

Effect of Indapamide and Carvedilol as add on therapy on systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) showed in the Table I.

Table-I: Comparison of the effect of Indapamide or Carvedilol administered as add-on treatment on lying systolic blood pressure, diastolic blood pressure and mean arterial pressure estimated before and 2nd, 4th and 6th week of treatment.

Study group	Baseline 0 week	At 2nd week	At 4th week	At 6th week	p value
Systolic blood pressure (mean ± SD mm Hg)					
Indapamide group (n=17)	169.71 ± 9.26	127.94 ± 12.25	118.82 ± 16.82	119.41 ± 12.48	p<0.001
Carvedilol group (n=15)	167.67 ± 12.94	132.67 ± 14.74	125.00 ± 24.71	122.67 ± 18.79	p<0.001
Diastolic blood pressure (mean ± SD mm Hg)					
Indapamide group (n=17)	98.23 ± 7.06	81.76 ± 7.89	82.06 ± 8.85	76.76 ± 8.65	p<0.001
Carvedilol group (n=15)	94.67 ± 11.41	87.33 ± 6.78	81.00 ± 12.84	79.33 ± 10.83	p<0.001
Mean arterial pressure (mean ± SD mm Hg)					
Indapamide group (n=17)	122.06 ± 5.35	97.16 ± 8.63	94.31 ± 9.82	90.98 ± 8.72	p<0.001
Carvedilol group (n=15)	119.00 ± 10.61	102.44 ± 6.98	95.67 ± 15.45	93.78 ± 12.51	p<0.001

Data were expressed as mean±SD; n: Number of the subject; SD: Standard deviation; p: probability value

Mean of the baseline SBP in these groups were 169.71(±9.26) and 167.67(±12.94) mm of Hg, which gradually decreased to 119.41(±12.48) and 122.67(±18.79) mm of Hg at the end of 6th week. Mean of the DBP at baseline were 98.23(±7.06) and 94.67(±11.41) mm of Hg that reduced to 76.76(±8.65) and 79.33(±10.83) mm of Hg respectively. Similar reduction also observed in MAP; from 122.06(±5.35) to 90.98(±8.72) mm of Hg and from 119.00(±10.61) to 93.78(±12.51) mm of Hg among the respective group. However, variation of the parameters from baseline to the end of 2nd week, 4th week and 6th week within the respective group were found to be significant statistically; while intergroup variations at baseline, 2nd week, 4th week and 6th week between the study groups were not significant.

Percentage changes in SBP, DBP and MAP of the Indapamide and Carvedilol groups showed in Figure 1 to 3. Overall difference of SBP from baseline to end of the research was found to be significant in Indapamide group (F=3.735, df=2, p<0.05), while insignificant in Carvedilol group (F=2.015, df=2, p>0.05). Similar result also observed in DBP; p-value in Indapamide group was <0.05 (F=2.659, df=2) and in Carvedilol group was >0.05 (F=3.625, df=2). On the other hand, opposite result observed in case of MAP. Overall difference from baseline to end point of treatment was insignificant in Indapamide group (F=3.215, df=2, p>0.05) while significant in Carvedilol group (F=4.510, df=2, p<0.05).

However, percentage changes between the study groups at 2nd, 4th and 6th week were found to be insignificant in all statistics except two occasions. The p-value for SBP of Indapamide group compared to Carvedilol group were >0.05 (t=-1.130, 95% CI,-10.616 to 3.055) at 2nd week, >0.05 (t=-0.966, 95% CI,-14.900 to 5.330) at 4th week and >0.05 (t=-0.735, 95% CI,-10.618 to 5.000) at 6th week. The p-value for DBP of Indapamide group compared to Carvedilol group were <0.05 (t=-2.278, 95% CI -17.982 to -0.982) at 2nd week, >0.05 (t=-0.510, 95% CI,-15.137 to 2.645) at 4th week and >0.05 (t=-1.435, 95% CI,-15.137 to 2.645) at 6th week of treatment. The p-value for MAP in comparison between Indapamide group and Carvedilol group were <0.05 (t=-2.216, 95% CI -12.961 to 0.530) at 2nd week, >0.05 (t=-0.844, 95% CI -11.424 to 4.742) at 4th week and >0.05 (t=-1.361, 95% CI -11.285 to 2.260) at 6th week of treatment.

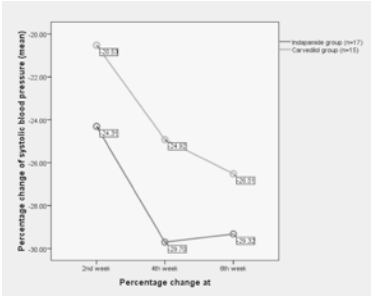

Figure-1: Percentage change in lying systolic blood pressure estimated at 2nd, 4th and 6th week .

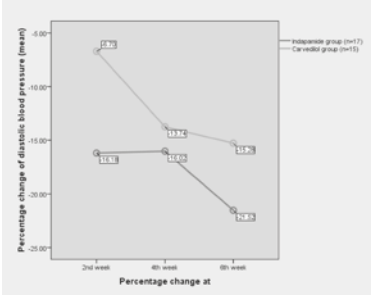

Figure-2: Percentage change in lying diastolic blood pressure estimated at 2nd, 4th and 6th week.

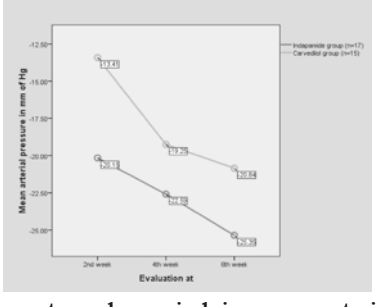

Figure-3: Percentage change in lying mean arterial pressure estimated at 2nd, 4th and 6th week.

There were very few patients experienced drug adverse effects, which were mild in nature and does not require

stopping the therapy. In Indapamide treated group, six (35.3%) patients experienced adverse effect; while in Carvedilol treated group, four (26.4%) patients experienced adverse effect. There was no statistical significant difference between the groups in respect to the adverse effects (p>0.05). The recorded adverse effects were almost similar in both groups such as epigastric discomfortness [1 (5.9%) vs 0 (0.0%); p>0.05], nausea [2 (11.8%) vs 3 (20.0%); p>0.05], light headedness [3 (17.6%) vs 0 (0.0%); p>0.05] and drowsiness [0 (0.0%) vs 1 (6.7%); p>0.05].

Discussion

Hypertension is a serious public health problem, because it is a major risk factor for cardiovascular events, chronic kidney disease (CKD), cognitive decline and premature death. Randomised clinical trials demonstrate that lowering blood pressure in people with hypertension substantially reduces the risk of cardiovascular morbidity and mortality[15].

Some clinical trials recently documented that only 30-50% of patients with hypertension actually achieved a BP goal of <140/90 mm Hg. Patients with multiple organ damages usually have hypertension that is difficult to control. In such cases, the use of a single antihypertensive agent is insufficient to lower BP[13]. Thus, the latest British Hypertension Society[14] and European Society of Hypertension guidelines[16] indicate that renin-angiotensin system (RAS) inhibitors, such as angiotensin II receptor blockers (ARB) and angiotensin-converting enzyme (ACE) inhibitors, are the first-line agents to reduce BP and the rate of decline in renal function[13]. Recent studies demonstrating equivalent clinical outcomes of ACE inhibitors and ARBs[17,18]. As second-line agents, CCB are widely used for the prevention of organ damage. If a combination of the two at the usual doses is ineffective, increasing the dose of either ACE inhibitors or CCB to the maximum dose may be the next option. However, renal insufficiency increases the risk of adverse drug reactions by dose elevation[13]. Dual combinations do not achieve BP control in 15-20% of patients, and it is estimated that three antihypertensive agents are needed to achieve BP control in approximately 25% of patients[16,19]. Therefore, adding thiazide-like diuretics [such as Chlortalidone (12.5-25.0 mg once daily) or Indapamide (1.5 mg modified-release or 2.5 mg once daily)] is suitable as a third-line agent introduced at Step 314. In a study Kereiakes et al[20] compared the efficacy and tolerability of triple-combination treatment with Olmesartan 40 mg, Amlodipine 10 mg and Hydrochlorothiazide 25 mg versus the component dual-combination treatments (Olmesartan 40 mg and Amlodipine 10 mg, Olmesartan 40 mg and Hydrochlorothiazide 25 mg, Amlodipine 10 mg and Hydrochlorothiazide 25) in patients with moderate-to-severe hypertension. The triple combination resulted in a significantly greater percentage of patients achieving BP goal at weeks 6, 8, 10, and 12 (with week 6 representing 2 weeks on triple-combination therapy); $p < 0.001$ for all comparisons).

Adding another class of medication would be an alternative strategy, although the guidelines do not indicate clearly the third choice for uncontrolled hypertension. In these patients, β-blockers seem to be more effective than increasing the dose of either ACE inhibitors or CCB[13]. National Collaborating Centre for Chronic Conditions[21] recommended an alpha blocker or beta blocker should be added to third agent.

In the present study systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were decreased significantly from initiation of treatment to the end point of treatment of 6 weeks in both Indapamide treated group and Carvedilol treated group; but no significant difference was observed between two treatment groups. Yasuda et al[13] found that both SBP and DBP was reduced in combination therapy of Carvedilol, Olmesartan and Amlodipine treated group.

This study also showed that the percentage reduction of lying SBP (-29.32% vs -26.51%; p>0.05); DBP (-21.52% vs -15.28%) and MAP was (-23.35% vs -20.84%; p>0.05) did not differ significantly in Indapamide treated group compared to Carvedilol treated group estimated at 6th week of treatment. Kereiakes et al[20] reported triple combination of Olmesartan, Amlodipine and Hydrochlorothiazide in participants with hypertension and diabetes, chronic kidney disease, or chronic cardiovascular disease lowered BP effectively. Oparil et al[22] found that long-term efficacy of a combination of Amlodipine and Olmesartan Medoxomil ± Hydrochlorothiazide in patients with hypertension stratified by age, race and diabetes status was effectively reduced BP.

In Indapamide treated group, 6 (35.3%) patients experienced adverse effect; while in Carvedilol treated group, 4 (26.4%) patients experienced adverse effect. There was no statistical significant difference between the groups in respect to the adverse effects (p>0.05). Adverse effects reported in our study were mild and well tolerated and no discontinuation was needed. Several previous studies also showed well tolerability of triple drug combination[13,20].

Conclusion

Addition of either Indapamide (1.5 mg/d) or Carvedilol (25 mg/d) as a third drug along with Olmesartan (20 mg/day) and Amlodipine (5mg/day) in uncontrolled hypertension in controlled diabetic patients were found to be equally effective and safe in this study. However, the authors like to recommend conducting clinical trial involving larger number of patients for a longer period of follow up in order to have more reliable result.

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Original Article

Liver Enzymes Correlation among Chronic Hepatitis C Patients with Virus Infection Fibrosis Progression

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Abstract

The main aim of the study is to identify the association between liver enzymes and virus infection fibrosis progression among the patients, suffering from HCV infection. The study has recruited 195 patients, and data has been gathered for a five years' period from January 2010 till March 2015. The laboratory analyses were conducted on the blood samples to evaluate the level of liver enzymes (ALT, AST, GGT). A slight increase in ALT levels was observed among the patients, who received treatment for HCV infection. The ALT level was estimated to be 48.04% for patients with negative PCR. There is no significant correlation between ALT levels and development of HCV, even when the serum levels of ALT are increased. The patients with negative or positive PCR were observed to have increased level of AST. A slight increase was observed in the negative HCV patients for mean GGT levels, as compared to the positive HCV patients. The hepatic enzymes depicted significant correlation with hepatitis infection.

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Introduction

Hepatic diseases play a major role in the development of morbid and mortal complications among male and female individuals. The most serious complication, related with the impaired hepatic functioning, is cirrhosis. Chronic hepatitis C has been identified as a major pathological manifestation for the development of cirrhosis[1]. The prevalence rate of HCV among developed countries along with the Arab region had increased. The common factors for increased prevalence rate of HCV include transfusion of infected blood and blood products, IV drug, and sharing of non-sterilized medical equipment or needles. In order to diagnose chronic hepatitis C infection, noninvasive biochemical markers, serological test and molecular testing are comprehensively used[2].

Liver biopsy has been identified as a major standard for the evaluation of liver damage; however, patients usually refuse for it. Therefore, noninvasive methods are commonly utilized to diagnose the complications accordingly. Iron is considered as a major mineral, which plays a significant role in the metabolic processes. Along with the minerals, a substantial number of hepatic enzymes also play a vital role for the regulation of normal body processes and functioning[3,4].

Elevated liver enzymes that mainly include ALT, AST, and GGT are widely observed among the patients, suffering from hepatitis C infection. A past study has identified that serum iron markers along with liver enzymes were elevated while the patients were chronically infected with HCV[3]. Therefore, it is necessary to establish the correlation between the hepatitis C virus and liver enzymes among patients, with fibrosis progression.

Liver enzymes have a pivotal role in the control of various hepatic complications among patients. It is said that liver enzymes correlation is necessary to be identified among chronic hepatitis C patients, suffering from virus infection fibrosis progression[5]. Therefore, it is necessary to identify the correlation of hepatic enzymes among chronic

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hepatitis C patients. There is a need for adequate follow-up of the patients, infected with HCV to improve the understanding of chronic HCV infection and clinical consequences associated with the infection. The study has aimed to identify the correlation of liver enzymes among chronic hepatitis C patients, with virus infection fibrosis progression.

The process of necro-inflammation is associated with the presence of liver enzyme; including alanine aminotransferase and aspartate. When the liver damage starts, the alanine aminotransferase is released in the bloodstream. However, the deterioration of liver function is evaluated through a series of liver blood tests, which include the test of ALT. This procedure is used extensively by the physicians to diagnose HCV infection, but there is no strong association between the progression of fibrosis and presence of aminotransferases in the bloodstream. Therefore, ALT is considered as a significant sign for liver inflammation; however, it does not reflect the progression of liver fibrosis[6].

A study revealed the increased rate of liver fibrosis among the HCV patients, having elevated levels of serum transaminase. However, no correlation was found between the hepatic fibrosis and viral load among the patients, infected with HCV[7]. Majority of the HCV infected patients do not experience liver related complication in the initial years of developing infection because HCV is considered as a slowly progressive chronic disease. Defining the hepatic decompensation, rate of progression of liver fibrosis and potential mediators for the condition are recognized as the severe risk factors and consequences of chronic HCV develop due to liver disease[8].

The ALT levels are used for the diagnosis of acute condition of hepatitis as ALT levels remain elevated for about 1-2 months after the onset of hepatitis infection. However, ALT levels are not elevated among the patients, suffering from chronic hepatitis, because ALT generally returns to normal level in about 3-6 months. The natural course of HCV infection is comprised of four phases, which include[9].

- Immune-tolerant phase - characterized by HbeAg positive, increased HCV infection, and minimum elevation of alanine transaminase
- Immune-clearance phase - characterized by increased liver inflammation
- Inactive carrier phase
- Reactivation of virus

The immune clearance phase in HCV infection is characterized by elevated ALT levels during the immune clearance phase. A study conducted by Hui et al.[10] revealed that elevated levels of ALT are taken as a marker for immune clearance and used as predictive measure to evaluate the progression of disease. According to the guidelines given by AASLD, the patients with HCV infection need to be monitored by every 3 months during their first year to verify them as inactive carrier of HCV[11].

A study revealed that around 25% of the patients presented serum ALT activity to be persistent with normal range, despite of the association between chronic HCV infection and elevated activity of ALT[12]. Another study reported 26% of persistent normal aminotransferase levels among the co-infected patients with HCV[13]. There is variation in the natural history of chronic hepatitis C; and majority of the patients are not likely to develop liver cirrhosis if proper treatment is administrated. However, the progression of liver disease occurs over several decades; and the rate of progression is increased due to steatosis, alcohol consumption, old age, insulin resistance, and other co-infections[13].

The progression of liver fibrosis after the development of hepatitis C is driven by different environmental, viral, and host related factors. The association between serum ALT and liver damage is unclear; therefore, the degree of liver damage is evaluated through liver biopsy[14]. The patients, who have persistent normal levels of ALT, are considered to be affected with mild degree of histological hepatic damage. A study was conducted to compare the inflammation and different stages of fibrosis among the HCV infected patients with elevated serum ALT levels. The results revealed that normal level of serum ALT is not an indication of healthy liver; therefore, histological evaluation of liver is necessary for the precise assessment of liver damage[15].

A significant number of HCV infected patients with ALT levels are diagnosed with cirrhosis, moderate to severe fibrosis, and they may even develop hepatocellular carcinoma[16]. Normally, the patients suffer from hepatitis C, but have normal functioning of liver enzymes. This is because the rate of response to treatment is better among the patients, who suffer less liver damage. Apart from hepatic enzymes, viral load, and individual contraindications towards any treatment measure; viral genotype and presence of hepatic fibrosis should also be evaluated among the patients suffering HCV infection[17].

Materials and Methods

A retrospective study has been conducted in Qatar University to examine the effects of iron depletion on chronic hepatitis C. The results were obtained over a five years period from January 2010 till March 2015. 195 patients with HCV were recruited in this study. The subjects were diagnosed with HCV through chemiluminescent microparticle immunoassay (CMIA), which has been verified by real-time PCR for RNA of the virus. Multiple results have been gathered for each patient, which reflected several follow-ups during the treatment course. All the incomplete results, which were not complied with the required tests, were excluded from the study.

Several laboratory analysis have been conducted through the blood samples including serum iron, ferritin, transferrin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and g-glutamyltransferase (GGT). The parameters were conducted in Hamad General Hospital's biochemistry laboratory. The ethical approval was taken from Medical Research Centre of Hamad Medical Corporation (HMC). The data has been analyzed using SPSS version 23.0. One-way ANOVA test has been applied to check the normality; whereas, p-value and correlation coefficient have been evaluated through paired t-test.

Results and Discussion

The patients, recruited in the study, were infected with chronic viral disease. The hepatic enzymes represented significant correlation with hepatitis infection; whereas, no significant correlation was observed between the liver enzymes (AST, ALT, GGT) and ferritin. Among 195 recruited patients, the prevalence rate of male patients was 73% and female patients was 27% (Figure 1).

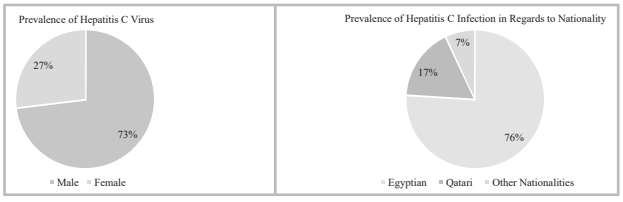

Figure-1: Gender-based prevalence of Hepatitis C Virus among 195 patients and Prevalence of HCV infection in regards to nationality among 195 patients.

(Source: Self-Generated in Microsoft Excel as per Data).

The highest rate of prevalence; i.e. 76% incidence rate, was observed among Egyptians; whereas, the prevalence rate of 17% was observed among Qatar nationals. The remaining 7% was distributed among Tunisian, Sudanese, Indian, Syrian, Somalian, Bangladeshi, Bahraini, and Canadian individuals (Figure 1).

A slight increase in ALT level was observed among patients, who received treatment for HCV infection. The ALT levels were increased to 57.00 µmol/L (positive PCR) from 55.82 U/L (negative PCR) (Figure 2). The normal range for ALT level is 6-56 U/L. Considering the ALT levels, about 37.62% of the patients had increased level of ALT, and 62.37% of the patients with positive PCR were within normal range. The ALT level for patients with negative PCR was estimated to be 48.04%.

The hepatocytes are considered as the primary site for storing iron. The gradual hepatic iron deposition, cirrhosis, and development of hepatic fibrosis characterized the acquired defect, which lead to the excessive uptake of iron. A study stated that iron overload is the major factor for complicating chronic viral hepatitis leading to various hepatic disorders of multifactorial origin[18]. According to the study, no significant correlation was observed between ALT level and HCV (r=0.40, P=0.695)[23]. Moreover, there is no significant association between ALT levels and development of HCV, even when the serum levels of ALT are increased. Another study conducted by Young[19] stated weak association between serum ALT levels and HCV.

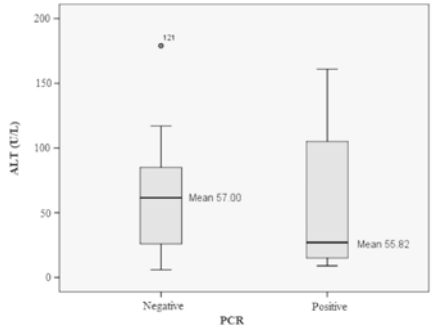

Figure-2: Effect of HCV on ALT in negative and positive PCR patients.

(Source: Self-Generated in SPSS as per Data).

Approximately 20-30% of the patients suffering from chronic HCV infection were diagnosed with normal ALT levels; and mild histological damage was seen among such patients. A study conducted by Sanai et al.[20] demonstrated ALT as a poor indicative marker for the diagnosis of inflammation and fibrosis among chronic HCV patients. An increase in ALT levels up to 27% of cases was demonstrated among the patients with normal ALT, when the patients were monitored for 5 years[21].

The results of AST levels for negative and positive PCR patients were 53.25 U/L and 48.93 U/L respectively (Figure 3). Both the values for negative and positive PCR were increased as compared to the normal value; i.e. 5-34 U/L. The patients with negative or positive PCR were observed to have increased levels of AST. The positive PCR results for 38.61% of the patients were abnormal; whereas, approximately 61.39% of the patients had positive PCR. The normal levels of AST were observed among 31.68% of the patients with negative PCR and abnormal results were observed among 68.32% of the patients with negative PCR.

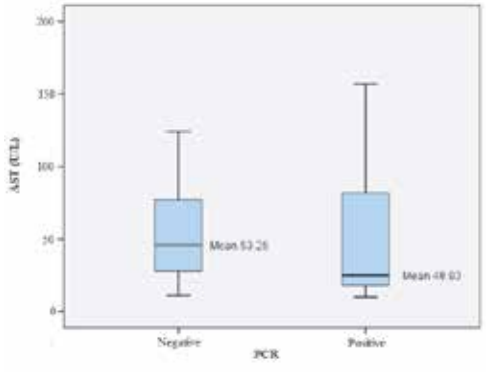

Figure-3: Effect of HCV on AST (U/L) in negative and positive PCR patients.

(Source: Self-Generated in SPSS as per Data).

The mean value of GGT for positive and negative HCV was 61.15 U/L and 62.95 U/L respectively; whereas, its reference range is between 9-64 U/L (Figure 4).

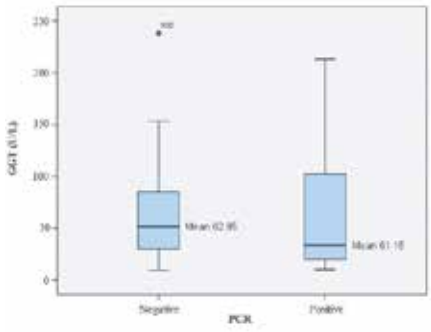

Figure-4: Effect of HCV on GGT (U/L) in negative and positive PCR.

(Source: Self-Generated in SPSS as per Data).

A slight increase for mean GGT levels was observed in HCV negative patients, as compared to the HCV positive patients. 91.55% of the patients depicted normal levels of GGT before receiving any treatment. However, the normal GGT levels were decreased to 73.24% after the treatment initiation.

Table I shows the correlation of liver enzymes (ALT, AST, GGT) and iron markers with HCV load after initiation of treatment.

Table-I: Summary of p-values and r-values for liver enzymes after receiving treatment.

Parameters	PCR	N	Mean	SD	r- value	p-value
	(Initially/	102	55.82	50.94	0.362	0.812
ALT	Positive PCR)					
(U/L)	(Follow up/ Negative PCR)	102	57.00	33.32		
	(Initially/	101	48.93	44.90	0.444	0.294
AST	Positive PCR)					
(U/L)	(Follow up /	101	53.25	28.40		
	Negative PCR)					
	(Initially/	94	61.15	51.30	0.543	0.723
GGT	Positive PCR)					
(U/L)	(Follow up / Negative PCR)	94	62.95	51.06		

Similarly, serum AST levels are not useful indicator to diagnose the degree of liver inflammation and fibrosis among the patients, suffering from chronic HCV infection. However, it may serve as a monitoring response for the patients, who received alpha-interferon treatment. However, a study revealed that the GGT levels can be considered for the prediction of advanced histological liver damage among the patients, suffering from chronic HCV infection[22,23].

Conclusion

The prevalence of HCV is higher among males as compared to the females. None of the liver function tests including the test for ALT, AST, and GGT found significant association with HCV viral load. The results concluded that a significant proportion of patients with persistent normal ALT levels represented various histological signs of fibrosis. There might be many reasons for representing minor changes in the functioning of liver enzymes; even after receiving treatment. For instance, body requires time to recover from any infection; therefore, the liver enzyme are not able to depict the dramatic changes. Although, the degree of fibrosis developing in liver might be mild, but sometimes marked changes are observed in the hepatic cells. A few cases may even reported about the presence of cirrhosis. The study has stated slight correlation between ALT, AST, and GGT with HCV viral load, but no significant correlation has been observed for p-values of ALT, AST, and GGT.

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Original Article

Spectrum of Benign Breast Diseases in Females- a 10 years study

Ahmed S[1], Awal A[2]

Abstract

The study was conducted to determine the frequency of various benign breast diseases in female patients, to analyze the percentage of incidence of benign breast diseases, the age distribution and their different mode of presentation. This is a prospective cohort study of all female patients visiting a female surgeon with benign breast problems. The study was conducted at Chittagong Metropolitn Hospital and CSCR hospital in Chittagong over a period of 10 years starting from July 2007 to June 2017. All female patients visiting with breast problems were included in the study. Patients with obvious clinical features of malignancy or those who on work up were diagnosed as carcinoma were excluded from the study. The findings were tabulated in excel sheet and analyzed for the frequency of each lesion, their distribution in various age group.

Keywords: *Spectrum, Breast Diseases, Benign, Risk, Management.*

Number of Table: 01

Number of References: 21

Number of Correspondences: 02

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Introduction

Breast is a dynamic organ which undergoes cyclical changes under the influence of hormone and growth factors throughout the reproductive life of a woman[1]. The vast majority of the breast lesions are benign and far commoner than the malignant one, but they are not given significant attention as compared to malignant one. The significance of this entity is that around 50% of women in their life time would have had the sign or symptom of benign breast disease[2]. Both the physical and specially the psychological sufferings of those females should not be underestimated and must be taken care of. In fact some benign breast lesions can be a predisposing risk factor for developing malignancy in later part of life[2,3]. So it is essential to recognize and study these lesions in detail to identify the high risk group of patients and providing regular surveillance can lead to early detection and management. As the study includes a great number of patients, this may reflect the spectrum of breast diseases among females in Bangladesh.

Aims and Objectives

The objective of the study was to determine the frequency of various breast diseases in female patients and to analyze the percentage of incidence of breast diseases and different mode of presentation.

Materials and Methods

A total of 3555 patients were diagnosed with breast lesions over a period of ten years in two private clinics were the participants of this study. This is a prospective (historical) cohort study carried out at Chittagong Metropoliton Hospital and CSCR (Centre for Specialized care and Research) Hospital over a period of ten years starting from July 2007 to June 2017. All female patients visited with breast problems from 18 to 55 years of age were included in the study. Initially 4147 patients visited with breast problems. Among them 12.23%(507/4147) patients who came mostly with the complaints of lumpiness in their breasts and a few of them who came for checkup and found normal both clinically and with imaging were excluded from the study. Another 85 patients were also excluded from the study who were diagnosed as sebaceous cysts in their breasts. So after excluding 592 patients out of 4147, total 3555 patients were included in the study. Detailed history of patients were recorded that included age, marital status, parity, age of last child, breast feeding history and age at menopause. Family history of breast diseases, specially breast cancer, history of contraception used were recorded.

Thorough examination of breast and axilla done. Ultrasonography or mammograms were done according to age. Fine needle aspiration cytology (FNAC) was advised in patients with lump to confirm the diagnosis. Core biopsy/ incision/ excision biopsy was done in patients with inconclusive FNAC report.

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The Data were tabulated in excel sheet and analyzed for the frequency of each lesion.

Results

A total of 3555 patients from 18 to 55 years were included in the study during the study period from July 2007 to June 2017. Among the patients fibroadenoma was the most common breast disease seen in 32.26% (1147/3555) of patients, followed by mastalgia in 24.22% (861/3555) patients. Fibrocystic disease was seen in 18.80% (668/3555) patients. 7.68% (273/3555) patients were presented with axillary lump, which were mostly due to accessory axillary breast tissue or lymphadenopathy. 4.59% (163/3555) patients were visited with breast abscess and acute mastitis, many of them were breastfed mothers. Most of the patients presented with nipple discharge were diagnosed as a case of duct ectasia, 3.68% (131/3555), although some young patients had galactorrhea due to hyperprolactinemia. 3.49% (124/3555) patients were diagnosed as carcinoma breast. Granulomatous mastitis was not an uncommon entity and 2.19% (78/3555) patients were diagnosed as granulomatous mastitis and among them 59 were idiopathic granulomatous mastitis and 19 were tubercular mastitis. 1.21% (43/3555) patients had cracked nipple/nipple erosion/ulcer. 0.79% (28/3555) patients came with the complaints of their unequal breast size, some of them complained of breast atrophy, some hypertrophy. Some other patients were visited who had lipoma, phyllodes, milk fistula, scar etc. The different spectrum of breast diseases with their frequency are shown in Table I.

Table-I: Frequency of breast diseases.

Serial No	Diseases	Frequency	Percentage (%)
1.	Fibroadenoma	1147	32.26
2.	Mastalgia	861	24.22
3.	Fibrocystic Disease	668	18.80
4.	Axillary lump	273	7.68
5.	Abscess & mastitis	163	4.59
6.	Duct ectasia	131	3.68
7.	Carcinoma Breast	124	3.49
8.	Granulomatous Mastitis (IGM & TB)	78	2.19
9.	Cracked Nipple/ Nipple erosion/ Nipple ulcer	43	1.21
10.	Unequal breast size	28	0.79
11.	Others	39	1.10
	Total	3555	

Discussion

A vast majority of lesions that can occur in breast are both benign and malignant. Benign breast diseases constitute a heterogenous group of lesions including developmental anomalies, inflammatory lesions, epithelial and stromal proliferations and neoplasms. Much concern is given to malignant lesions of the breast because it is one of the most common malignancy in women specially in Western countries; however benign lesions are far more frequent than malignant ones[4-12].

In our study fibroadenoma was the most common BBD seen in 1147 patients, which is 32.26% of the total 3555 patients. Murillo et al found 38% incidence of fibroadenoma in a study of about 698 patients with BBD, which is not dissimilar with our study[13]. Khanzada et al showed 27% incidence of fibroadenoma in a study of 275 patients[14]. Other two studies showed a little higher incidence of 42% and 45% respectively[15,16].

Mastalgia was the second most common (24.22%) BBD seen in our study but Khanzada et al found 11% patients with mastalgia. 25% of the referral to breast clinics in West are due to mastalgia and it affects up to 70% woman at some times during their lives[17].

The third most common disease in our study was fibrocystic disease (18.80%). In three other studies the frequency was 21%, 36% and 17% respectively[14,16,15]. Because of low literacy rate and more rural areas, the females affected with fibrocystic disease tend to see a surgeon when the symptoms are alarming.

In our study a good number of patients (273) were presented with axillary lump, mostly with accessory axillary breast tissue.

The next entity was breast abscess and acute mastitis (163 patients). This was most commonly observed in lactating females during early lactating period. Barton et al found acute bacterial mastitis common at any age but most frequently in lactating breasts[18].

In our study 3.68% patients had duct ectasia which can mimic invasive carcinoma clinically[19]. It usually presents with nipple discharge, palpable subareolar mass, pain, nipple inversion or retraction[14].

In our study 124 patients that is 3.49% of all breast patients were diagnosed as carcinoma breast. Study showed that the highest incidence of breast cancer was in Northern America and Oceania; and the lowest incidence in Asia and Africa[20].

Granulomatous mastitis was diagnosed in 78 patients (2.19%). Among them IGM in 59 patients and Tuberculosis in 19 patients. The term "Idiopathic granulomatous mastitis" is used for granulomatous lesions without an identifiable cause. Identification of etiology requires microbiologic and immunologic testing in addition to histopathologic evaluation[19]. In our study we also diagnosed the cases with microbiologic, immunologic and histopathologic testing. Though GM is rare in developed countries, this is not uncommon in Asian countries. The overall incidence is less than 0.1% of all breast lesions in developed countries and 3-4% in developing countries[21].

43 patients presented with cracked nipple, nipple erosion/ulcer. Most of them were breastfed.

28 patients visited with unequal breast size, some with macromastia and some with atrophy.

Some of the patients presented with other diseases like lipoma, phyllodes, milk fistula etc.

Conclusion

Breast diseases are one of the commonest problems in females. Breast cancer is the most common cancer in women worldwide and is the fifth most common cause of death from cancer in women. So much more concern is given for the screening, diagnosis and management of breast cancer. But BBD is far more frequent than malignancy. Our study also showed similar results. In our study fibroadenoma is the commonest breast lesion. Mastalgia is the next common problem. Fibrocystic disease also occurs in a great number of females. It is essential to give importance in assessing these benign lesions to reduce morbidity from those diseases and identify any risk for cancer development.

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Original Article

Analysis of Cardiotocography Findings in Pregnancy with Less Fetal Movement and Its Association with Perinatal Outcome

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Abstract

Less fetal movement affects perinatal outcome. To examine association between antenatal CTG findings and perinatal outcome in women with less fetal movement. This prospective observational study was conducted in the department of Obstetrics and Gynecology, Kumudini Women's Medical College and Hospital, Mirzapur, Tangail over a period of six months from January 2015 to June 2015. It included 100 pregnant women after 34 weeks of gestation. They underwent a cardiotocogram (CTG) test. Data were collected by face-to-face interview, observation and document review. The mean age of the women was 24.37±4.62 (SD) years and mean gestational age was 38.48±2.15 weeks. In this study, 82.0% of the cases presented at term pregnancy, 42.0% of the women were primi gravida and rest falls between 2nd to 4th gravida. Normal vaginal delivery was in 59.0% cases and rest were undergone caesarean sections (41.0%). Late deceleration with decreased variability was (23.5%) most common. Incidence of low birth weight was 16.0% & macrosomia was 5.0%. Birth asphyxia was found in 52.0% cases, 49.0% needed immediate resuscitation, 35.0% were admitted into neonatal unit and early neonatal death was 8.0%. Birth asphyxia was significantly higher in non-reassuring [37(72.5%)] than reassuring [15(30.6%)] on CTG. Incidence of low birth weight was higher in non-reassuring [11(21.6%)] than in reassuring [5(10.2%)] on CTG (p>0.05). Early neonatal death was more in respondents with non-reassuring [5(9.8%)] on CTG than reassuring [3(6.1%)] on CTG (p>0.05). Twenty six (51.0%) neonatal of the non-reassuring were admitted into neonatal unit whereas only 9 (18.4%) neonatal of the reassuring were admitted into neonatal unit. It can be concluded that CTG may be the first line investigation for ante and intrapartum fetal assessment.

Keywords: *CTG, Less Fetal Movement, Perinatal Outcome.*

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Introduction

A reduction of fetal movements causes concern and anxiety, both for the mother and obstetrician. Reduced fetal movement is difficult to interpret because it is a subjective complaint by the mother[1]. Decreased fetal movement affects 5 - 15% of pregnancies[2].

Currently there is no universally agreed definition of DFM. In a study of women with normal uncomplicated pregnancies, 99% of women were able to feel 10 movements within 60 minutes[3]. Studies have been conducted on the correlation between maternal perception of fetal movements and fetal movements detected on ultrasound scans, showing large variations, with correlation rates ranging from 16-90%[4,5]. This variation in maternal perception may be related to gestational age, amount of amniotic fluid volume, medications, fetal sleep state, obesity, anterior placenta, smoking and nulliparity[6,7].

Maternal perception of DFM is a common cause of unplanned antenatal presentation in the third trimester[8]. Maternal perception of DFM is associated with increased incidence of a number of adverse pregnancy outcomes including stillbirth, preterm delivery and intrauterine growth restriction[9]. Recent evidence suggests that the improved management of DFM and uniform information to women may be associated with fewer stillbirths[10].

Cardiotocography (CTG) is the graphical presentation of fetal heart activity and the uterine contraction to detect the fetal hypoxia[1]. It is the most commonly used test for antepartum and intrapartum fetal surveillance in the majority hospitals of developed countries[11]. This technology was first developed in 1950 and became commercially available in 1960[11]. The goal of antepartum

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fetal surveillance is to predict, diagnose and timely intervene the pregnancies those are complicated with fetal asphyxia and might lead to fetal and newborn morbidity and death[12]. Cardiotocography (CTG) is also termed as electronic fetal monitoring. A predictive fetal heart rate record is the principle indication that led to intervention and delivery. A prediction of fetal asphyxia that leads to intervention and delivery may prevent or modify moderate or severe newborn morbidity as the result of fetal asphyxia[13].

The fetus' health is evaluated by assessment of the fetal heart rate (FHR). This assessment involves identification of two general types of FHR patterns: those that may be associated with adverse fetal or neonatal outcomes (ie, non-reassuring patterns) and those that are indicative of fetal well-being. But there is no evidence from randomized trials that proves antepartum FHR monitoring results in a decreased risk of fetal death[14].

Materials and Methods

This hospital based prospective observational study was conducted in the Department of Obst. & Gynae, Kumudini Women's Medical College and Hospital, Mirzapur, Tangail from January 2015 to June 2015 for a period of six months. A total of 100 pregnant women with less fetal movement were included as study population. Purposive sampling technique was adopted. Pregnant women with multiple pregnancy, eclamptia or severe preeclampiac, lethal congenital abnormality, severe oligohydramnios and GA<34 weeks were excluded from the study. Written consent was taken from each study population before interview. All of the study subjects underwent a cardiotocogram (CTG) test. Data were collected by face-to-face interview, observation and document review.

Results

Sixty six percent of the study population was in the age group 20 - 29 years and 20% had an age above 30 years. The mean age was 24.37±4.62 (SD) years (Table I).

Table-I: Age distribution of the study population (n=100).

Age (years)	Frequency (n)	Percentage (%)
<20	14	14.0
20 to 30	66	66.0
30 and above	20	20.0
Mean±SD (min-max)	24.37±4.62 (18-35)	

n: Number of subject

Mean gestational age of the study population was 38.48±2.15 weeks. Present study found 82.0% of the cases term pregnancy, 42.0% were primi gravida and 58.0% falls between 2nd to 4th gravida. Regarding mode of delivery, 59.0% delivered by normal vaginal delivery and rest were undergone caesarean sections (41.0%) (Table II).

Table-II: Obstetric characteristics of study population (n=100).

Characteristics	Frequency (n)	Percentage (%)
Gestational age (weeks)		
Term (≥37 to 42 weeks)	82	82.0
Preterm (28 to < 37 weeks)	15	15.0
Post-Term (> 42 weeks)	3	3.0
Mean±SD	38.48±2.15 (34 - 44)	
(min-max)		42.0
Gravida Status		33.0
Primi	42	17.0
2nd	33	8.0
3rd	17	
4th	8	59.0
Mode of delivery		41.0
Normal virginal delivery	59	
Caesarean Section	41	20.0
Premature rupture of membrane		
≥ 24 hours	8	10.00
< 24 hours	12	4.00
Preeclampsia	10	
Diabetes Mellitus	4	

n: Number of subject

According to CTG findings 49.0% cases were reassuring and 51.0% were non-reassuring. Absent or decreased variability was 8 (8.0%), fetal bradycardia was 7 (7.0%), fetal tachycardia was 6 (6.0%), variable deceleration with fetal bradycardia was 5 (5.0%), variable deceleration was 7 (7.0%), late deceleration with decreased variability was 12 (12.0%), and late deceleration was 6 (6.0%) (Table III).

Table-III: Distribution of study population by CTG findings (n=100).

Cardiotocography findings	Frequency (n)	Percentage (%)
Reassuring	49	49.0
Non-reassuring	51	51.0
Late deceleration	6	6.0
Late deceleration with decreased variablity	12	12.0
Variable deceleration	7	7.0
Variable deceleration with fetal bradycardia	5	5.0
Fetal tachycardia	6	6.0
Fetal bradycardia	7	7.0
Absent of decreased variability	8	8.0

n: Number of subject

In this study incidence of low birth weight was 16.0 % & macrosomia was 5.0%. Birth asphyxia was found in 52.0% cases, 49.0% needed immediate resuscitation, thirty 35.0% were admitted into neonatal unit and early neonatal death was 8.0%(Table IV).

Table-IV: Perinatal outcome in study population (n=100).

Perinatal outcome	Frequency (n)	Percentage (%)
Birth Weight		
Normal (≥2.5 to <4 kg)	79	79.0
Low birth weight (<2.5 kg)	16	16.0
Macrosomia (≥4 kg)	5	5.0
Birth asphyxia	52	52.0
Needed resuscitation	49	49.0
Needed admission to neonatal unit	35	35.0
Early Neonatal Death	8	8.0

n: Number of subject

Birth asphyxia was significantly higher in non-reassuring [37(72.5%)] than that of reassuring [15(30.6%)] on CTG.

Incidence of low birth weight was higher in non-reassuring [11(21.6%)] than in reassuring [5(10.2%)] on CTG but the difference was not statistically significant (p>0.05). Early neonatal death was more in respondents with non-reassuring [5(9.8%)] on CTG than reassuring [3(6.1%)] on CTG but the difference was not statistically significant (p>0.05). Twenty six (51.0%) neonatal of the non-reassuring were admitted into neonatal unit whereas only 9 (18.4%) neonatal of the reassuring were admitted into neonatal unit (Table V).

Table-V: Association of abnormal CTG findings with birth asphyxia, low birth weight, early neonatal death and admission to neonatal unit (n=100).

	CTG finding		P value
	Non reassuring (n=51)	Reassuring (n=49)	
Birth asphyxia	37 (72.5%)	15 (30.6%)	<0.001
Low birth weight	11 (21.6%)	5 (10.2%)	>0.050
Early neonatal death	5 (9.8%)	3 (6.1%)	>0.050
Admission to neonatal unit	26(51.0%)	9(18.4%)	0.001

n: Number of subject

Discussion

In this study, 66 percent of the study population was in the age group 20 - 29 years and 20% had an age above 30 years. The mean age was 24.37±4.62 years. Similar age was seen in the study of Kumari et al[15] and Khatun et al[16].

Eighty two percent of the cases presented at term pregnancy, 42% of the cases were primi gravida and 58.0% falls between 2nd to 4th gravida. Nahar et al[17] had all the study populations of multigravida having various types of previous obstetrical history. On the other hand, Kumari et al.[15] found 32 (42.7%) nullipara (parity 0) followed by 28(37.3%) with parity 2-5, and 15(20.0%) grand multiparous (parity >5).

As regard mode of delivery, 59% delivered by normal vaginal delivery while rest were undergone caesarean sections (41.00%). In the study of Kumari et al[15], vaginal deliveries were successful in 45(60%) women, while CS was done in 30(40%) cases. Out of 45 vaginal deliveries, 33(73.3%) were spontaneous vaginal and 12(26.7%) were IVDs.

In this study, non-reassuring were 51.0% cases and reassuring were 49.0% cases. Chakrobarty et al[18] found two-third of their study population with reactive CTG and one-third with nonreactive type. In their study, Kumari et al[15] found 25 (33.3%) patients had non-reactive CTG, and 50(66.7%) had reactive CTG.

In present study, absent or decreased variability was 8 (8.0%), fetal bradycardia was 7 (7.0%), fetal tachycardia was 6 (6.0%), variable deceleration with fetal bradycardia was 5 (5.0%), variable deceleration was 7 (7.0%), late deceleration with decreased variability was 12 (12.0%), and late deceleration was 6 (6.0%). Late deceleration with decreased variability was most common. In the study of Khatun et al[16], out of 100 abnormal CTG 30.0% had fetal tachycardia, 38.0% had deceleration, 19.0% was non reactive CTG, 4.0% had fetal bradycardia and 4.0% had absent beat-to-beat variability. Present study showed that early neonatal death was more in nonreassuring CTG than reassuring CTG. Five early neonatal death was noted in nonreassuring CTG. Birth Asphyxia was found in 52.0% of the cases. Immediate resuscitation was needed 49.0% cases. Thirty five percent babies need admission in neonatal unit and early neonatal death was 8.0%. Only 16.0% babies were found LBW. In their study, Kumari et al[15] found low birth weight in 40.0% and birth asphyxia in 1.3% cases. Chakrobarty et al[18] found low birth weight in 17.1% cases.

In this study, the proportion of birth asphyxia was significantly more in non-reassuring (72.5%) than reassuring (30.6%) on CTG. The proportion of the low birth weight was higher in non-reassuring (21.6%) than in reassuring (10.2%) on CTG but not statistically significant. Early neonatal death was more in respondents with non-reassuring (9.8%) on CTG than reassuring (6.1%) on CTG but not statistically significant. This study also showed more than fifty percent of the non-reassuring 26 (51.0%) required admission to neonatal unit. On the other hand, less than twenty percent of the reassuring 9 (18.4%) required admission to neonatal unit. Statistically this difference was found significant. Birth weight was significantly lower and admission into neonatal care unit was significantly higher in non-reassuring group than that of reassuring group[19].

Conclusion

Though abnormal CTG findings showed significant relationship only with birth asphyxia and admission to neonatal unit, CTG monitoring along with timely obstetrical intervention and can reduce associated complications and improve fetal outcome. So it can be concluded that CTG can be the first line investigation for ante and intrapartum fetal assessment.

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Original Article

Effect of Rhesus Negative in Pregnancy

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Abstract

Hemolytic disease of the newborn due to Rh-isoimmunisation is a major cause to perinatal morbidity & mortality. Erythroblastosis fetalis is a disease of fetus and newborn due to incompatibility between fetal and maternal blood group. Diagnosis and therapy for Rh immunization improved considerably. Its prevention by immunoprophylaxis has been responsible for the reduction in the incidence of perinatal mobility. Still Rh immunization and erythroolastosis fetalis is responsible for many obstetric mishaps in our country. To see the pregnancy outcome of Rhesus negative women. This prospective study was carried out from October 2013 to March 2014 in Obstetrics & Gynecology department of Sylhet MAG Osmani Medical College & Hospital, Sylhet. 50 Rh-negative pregnancies were selected those who got admitted in department of Obstetrics & Gynecology, SOMCH. 30.62% of the fetuses had blood group B+ve, 24.40% 0+ve and 20.40% A+ve. Regarding the perinatal outcome 76% were healthy, 4% still birth, 4% neonatal death, 14% with erythroblastosis foetalis and 4% developed hydrops. Mild anaemia and oedema was common in primi and multigravida patients. PET was found 6.2% in multigravida patients. APH and Hydramnios with congenital anomalies were 3.1% and 3.1% respectively. This study was undertaken to evaluate the outcome of pregnancy in Rh -ve women. It is preventable. Primary prevention of isoimmunization by giving combined antenatal and postnatal prophylaxis.

Keywords: *Outcome, Pregnancy, Rhesus Negative.*

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Number of References: 14

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Introduction

Fetus inherits antigenic determinats both from father & mother. Rh antigen on the surface of the red cell may cause hemolytic reaction when Rh negative mother bears Rh positive fetus Fetomaternal ABO incompatibility is clinically more important because it causes disease of greater severity. (Froster J. 1996)[1]. In the past, Rh incompatibility used to be a very serious problem. Affected newborns were gravely ill or died from Rh disease. Of all infants 10-20% dies in utero or in the early neonatal period before effective therapy possible. 50% of affected infants need treatment during neonatal period (Contreras M. Lubinco A. 1991)[2]. In the developed countries incidence of morbidity and mortality due to Rh incompatibility in pregnancy is greatly reduced due to prenatal Rh screening, obtaining maternal antibody titre, ultrasound guided amniocentesis. Rh immunoprophylaxis, and postnatal emergency care by umbilical cord blood transfusion for erythroblastosis fetalis, hydrops fetalis or kernicterus (Salem, 2005)[3]. Anti-D has been routinely use as postpartum prophylaxis since 1968 in Canada, and routine ante partum prophylasis was introduced in 1976. (Fung KF, Eason E. Crane J. Ronde S. Armos, Willson D. 2003)[4]. In a developing country most of the fetal and neonatal deaths due to Rh incompatibility remains undiagnosed, 2% of women are at risk of becoming Rh immunized after having sopntaneous or therapeutic abortions. The risk grows by 2.5 fold after 20 weeks. A blood sample should be taken from every women at her first antenatal visit for Rh blood grouping and antibody screening (Kausar 2005)[5].

Materials and Methods

This study was a hospital based prospective cross-sectional study, carried out in IPD (inpatient department) of Obstetrics and Gynecology of Sylhet M.A.G Osmani Medical College and Hospital, Sylhet in between October 2013 to March 2014. Total 50 cases were enrolled in this study. Data was collected by using a preformed questionnaire and check list. Cases were selected according to inclusion and exclusion criteria. Relevant infromations (according to questionnaire) were taken from patients. After data collection all data was entered in master sheet and Statistical analysis were carried out by using the Statistical package for Social Sciences version 16.0.

Results

In SOMCH 203 Rh negative patients out of 7150 obstetrics patients who were admitted from October 2013 to March 2014, giving the incidence of 2.83%. Among them 50 cases were included in this study. Table I shows most of the patients (62%) belong 21-30 years and their mean age found was 25.5 years with range from 18-36 years.

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Table-I: Details of patients (age and parity distribution) (n=50).

Age (in years)	Numbers of patients	Percentage
≤20	11	22
21-30	31	62
31-36	8	16
Mean	25.5	
Range (min-max)	18-36	

Table-II (A) shows 36% of the patient were B^{-ve}, 30% of the patients were A^{-ve}, 24% of the patients were O^{-ve} ,10% of the patients were AB^{-ve}.

Table-II: (A) Blood group of the patients: (n=50).

Blood Grouping & Rh Typing	Number of patients (n=50)	Percentage
B^{-ve}	18	36
A^{-ve}	15	30
O^{-ve}	12	24
AB^{-ve}	05	10

Table-II (B) shows 98% of the husband's blood group were Rh^{+ve} and 2% were negative.

(B) Husband's blood Group:

Blood Grouping & Rh Typing	Number of patients (n=50)	Percentage
B^{+ve}	16	32
O^{+ve}	15	30
A^{+ve}	12	24
AB^{+ve}	06	12
A^{-ve}	01	02

Table-II(C) shows 81.61 % of the newborn babies were Rh^{+ve} and 18.37 were Rh negative.

(C) Blood group of the fetuses:(detected from the cord blood sample).

Blood Grouping & Rh Typing	Number of patients	Percentage
B+ve	15	30.62
O+ve	12	24.49
A+ve	10	20.40
AB+ve	03	6.12
B-ve	03	6.12
O-ve	02	4.08
A-ve	03	6.12
AB-ve	01	2.04

Table-III Shows the no. of primi and multigavida patients who came with complication in this current pregnancy.

Table-III: Complication in current pregnancy: (n=50).

Complications	Primi		Multi		Total	
	n	Percentage	n	Percentage	n	Percentage
Anaemia						
Mild	8	16	22	44	30	60
Moderate	04	8	04	8	08	16
Severe	01	2	02	4	03	6
Oedema	09	18	15	30	24	48
Mild	02	4	02	4	04	8
Moderate						
APH	00	0	01	2	01	2
Hydramnos with congenital anomaly	01	2	01	2	02	4
IUD	01	2	02	4	03	6

Table-IV shows 2% Spontaneous abortion, 32% vaginal delivery and 58% Caesarean section.

Table-IV: Mode of termination of pregnancy.

Delivery	Primi		Multi		Total	
	n	Percentage	n	Percentage	n	Percentage
Spontaneous Abortion			1	2	1	2
Spontaneous Vaginal delivery	07	14	09	18	16	32
Induced VD	03	6	03	6	06	12
Caesarean section	08	16	21	42	29	58

Table-V shows 76% healthy baby, 10 % developed jaundice and 4% neonatal death.

Table-V: Outcome of baby.

No. of patients	Health baby	Abortion	Stillbirth	Jaundice (mild)	Born with Erythroblastosis	Developed Hydrops	Neonatal death
pimigravida.	17	0	01	05	0	0	0
multigravida	21	01	01	0	07	02	02
Total	38	01	02	05	07	02	02
percentage	(76%)	(2%)	(4%)	(10%)	(14%)	(4%)	(4%)

Table-VI shows Increase antibody titre increase adverse outcome of foetus.

Table-VI: Antibody titre during current pregancy and outcome of the baby (in immunized pregnancy).

Antibody titre	No. of case	Outcome of baby in current-pregnancy
1:4	01	Health baby slightly enteric on 3rd day
1:8	02	Squired exchange transfusion once
1:16	02	Required exchange transfusion twins
1:32	01	Required exchange transfusion twins
1:64	02	I baby wash healthy as blood group was Rh negative.
1:128	02	Required exchange transfusion three times and died neonatally.
1:256	02	I intrauterine death due to Hydrops.
		I Developed hydrops and died within I hour of delivery

Discussion

A total number of 50 pregnant patients with Rh negative blood group who admitted in department of obstetric and gynaecology, Sylhet MAG Osmani Medical College & Hospital, during the period of October 2013 to March 2014 were included in this study. The present study findings were discussed and compared with previously published relevant studies. The study of M. Rahman (1978)[6] showed that the incidence of Rh-ve blood group in general population were 2.56% where as the incidence of Rh negative pregnant patients in present study was 2.84% which was higher. Another study made by Dr. Fatema (1986)[7] showed even higher incidence which was 3.6% at BSMMU. Analysis of husband's blood group showed the incidence which was almost similar to that of general population (M. Rahman 1978)[6]. Labour and fetal outcome was not significantly different from other normal pregnant patients. Hemolytic disease of the fetus and newborn due to Isoimmunization now accounts for only 4-5 deaths per 1000,000 births in USA[8]. In the present study the fetal outcome in sensitized patients showed that overall fetall loss due to Rh immunization was 14% which was nil in the primigravid patients, Incidence was higher because of lack of facility for neonatal management. According to the Bowman[9] work about 17% of Rh negative women become isoimmunized without preventable measures after the delivery of her first child (Harrod et al 2003)[10]. This number is very high possible because the sample size was small and most of the immunized patients had history of repeated unprotected deliveries. About the complication in the current pregnancy of these study patients it was observed that mild anaemia and oedema was common in primi and multigravida patients. Mild anaemia was found 44.4% in primi and 68.7% in multigravida patents. Mild oedemia was 50% and 46.8% in primi and multigravida patients respectvely. APH was found 3.1% in multigravida

patients but not found in primipara group. Hydramnions with congenital anomaly was found 3.1% in multigravida patients but not found in primipara patients, which was compitable with study of Roman[11]. Neonatal deaths and morbidity due to Rh sensitization have decreased dramatically since the introductions of Anti-D immunoglobulin According to the Centre for Disease Control and prevention, the incidence of HDN was 40.5 per 10,000 births in 1970. Today, the incidence has dropped to less than 5 cases per 10,000 birth. Despite the marked success of lgG, postpartum only administration has resulted in a failure rate of 1% to 2%. Routine antenatal prophylaxis reduces the rate of sensitization during pregnancy to 0.2%. Trolley found no alloimmunization with anit-D 300 microgram, compared to 1.9% sensitized with no anti-D at 28 weeks. Tovey compared anti-D 100 microgram at 28 and 34 weeks to a cohort without antepartum prophylaxis, and found 02% treated and 1.4% untreated women become alloimmunized later. This study 5.5 failure rate. The likely reason for this high failure rate was that out of 32 patients to whom anti-D was given only 20 patients visited. Also, given dose of lgG was possibly inadequate for the volume of feto-maternal hemorrhage[12,13,14].

Conclusion

Although Rh isoimmiminzation and erythroblastosis fetalis due to Rh incompatibility has now become a preventable disease. Yet the problem of Rh negative pregnant patients still remains as a major problem for poor developing country like Bangladesh. This is because most of our patients do not get any antenatial advice and facility for hospital delivery. To make it a real success there must be awareness about the problem of Rh negative blood group in the general population.

Acknowledgement

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Original Article

Pattern of Presentation of Chronic Venous Insufficiency in CVI Clinic of CMCH

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Abstract

Chronic venous insufficiency (CVI) is a common but often ignored problem in primary health care, sign and symptoms may ranges from mild leg heaviness or aching, dilated or unsightly veins, or troublesome odema to fibroses subcutaneous panniculitis associated with recurrent cellulitis and chronic ulceration. The prospective observational study was carried out department of surgery, Chittagong Medical College & Hospital, Chittagong. The primary purpose of the present study was to evaluate the impact of the diagnostic approach on patient of chronic venous insufficiency, varicose vein to difference primary and secondary venous insufficiency. Most common sign flebedema found in 56 (65.12%) patients was followed by dermo-hypodermatitis in 15(17.44) patients, stasis eczema in 09(10.47) patients and thrombophlebitis in 06(6.98) patients. Most frequent lower leg symptoms are heaviness 82 (95.35%) & the lowest is Throbbing 55(63.95%). The others are according to order of frequency cramps 66 (70.0%), Itching (73.26%), burning 61(70.93%), tiredness (80.23%), restless leg (82.55%), pain aching 76 (88.37%). CVI (chronic venous insufficiency) studied 04 (4.65%) were in C1, 54(62.79%) were in C2, 03(3.49%) were in C3, 11(12.79%) were in C4, 6 (6.98%) were in C5 and 8(9.30%) were in C6 according to clinical CEAP classification. Majority of patients presented with the complains of heaviness of leg and unexplained leg swelling, sex predilection is almost same for male and female but advanced stages are more common in male patients. Increasing age is associated with more advanced stage of the disease.

Keywords: *Chronic Venous Insufficiency, CVI Clinic, Pattern of CVI.*

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Introduction

The term chronic venous insufficiency refers to the venous valvular incompetence in the superficial, deep and/or perforating veins. Incompetence of the vein valves permits reversal of flow and promotes venous hypertension in the distal segments. This form of venous dysfunction may be the result of recanalisation of thrombosed venous segments, pathological dilation of the vein or due to congenital absence of competent valves[1]. Chronic venous insufficiency (CVI) is one of the most prevalent, frequently unrecognized and underestimated disease world wide[2]. It is a progressive disease[3]. Chronic venous insufficiency includes all changes resulting from dilatation of veins of the lower limb, incompetence of their valves and resultant venous hypertension. Presentation of CVI varies, ranging from incomplecated ankle oedema to the most severe form of post thrombotic syndrome[4]. Typical symptom of Chronic venous insufficiency includes aching pain, tightness, skin irritation, purities, heaviness, tingling, muscle cramps, cosmetically unsatisfying varicose vein. In Europe, the Prevalence of venous diseases in subjects aged 30 to 70 has been estimated at between 25% and

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50%[5-7] venous leg ulcer is certainly one of the most sever complication of CVI. Its prevalence in general population is between 0.1% and 3.2%[8]. Prevalence estimates vary widely by geographic location, with the highest reported rates in Western countries. Reports of prevalence of chronic venous insufficiency vary from < 1% to 40% in females and from < 1% to 17% in males. Prevalence estimates for varicose veins are higher, <1% to 73% in females and 2% to 56% in males[9]. A lower prevalence has been observed in men but some recent surveys have suggested that the occurrence in men may be comparable to that in women[10]. This study was designed to see various modes of presentation of chronic venous insufficiency, to find out the risk factors and to see relationship to various symptoms of chronic venous insufficiency with age, sex and body mass index of the patient.

Materials and Methods

This prospective cross sectional study was carried out Dept of Surgery, CMCH. Chittagong during July' 2008 to June' 2009 patients who attended in CVI clinic at Chittagong Medical College Hospital. Patients who were aged 18 years and above and willing for treatment and given informed written consent were included this study and patients below 18 years of age were excluded in this study. Data collected with a pre-tested structured questionnaire containing history, clinical, laboratory investigations, pre-operative, post operative complications and post operative follow up findings. Data collected, compiled and tabulated according to key variables. The analysis of different variable done according to standard statistical analysis by using SPSS-19.

Results

The mean age was 54.68(±7.45) years, minimum age was 18 years and maximum age was 75 years. Among 86 patients, majority of the patients in this study was male which was 45(52.33%) rest of 41(47.67%) were female. Male female ratio 1.09: 1. Most of the patients 34(39.53%) showed both symptoms & sign of venous diseases for less than 5 years (Table -I).

Table-I: Demographic characteristics of the study population.

Demographic characteristics	Number	Percentage
Age in years (Mean ±SD)	54.68(±7.45)	Range 18-75 years
Sex		
Male	45	52.33%
Female	41	47.67%
Time of diagnosis by years		
0-5 yrs	34	39.53%
6-10 yrs	28	32.56%
> 10 yrs	24	27.91%

BMI of all patients were calculated and it shows that 20(44.44%) male patients are obese and 30(73.17%) were female patients obese (Table-II).

Table-II: Distribution of patients according to BMI (Body Mass Index).

BMI (kg/m^2)	Number of Patients	Percentage
Male (n=45)		
>25	20	44.44
20-25	24	53.33
<20	02	4.17
Female (n=41)		
>24	30	73.17
19-24	09	21.95
<19	02	4.88

Among 86 Patients, 56 gave history of prolonged standing. Most of the patients 36 (64.30%) gave history of standing more than 8 hrs/day (Table-III).

Table-III: Prolonged standing position.

Group	Total no of patients	Percentage
< 4 Hrs/day	06	10.71%
4-8 Hrs/Day	14	24.99%
> 8 Hrs/ Day	36	64.30%
Total	56	100.00%

Determinants of chronic venous insufficiency majority 48(55.81%) were varicose disease; followed by 35(40.70%) were deep thrombophlebitis, 03(3.49%) were venous dysplasia cases (Table-IV).

Table-IV: Determinant factors distribution.

	Number	Percentage
Varicose disease	48	55.81
Deep thrombophlebitis	35	40.70
Venous dysplasia	03	3.49
Total	86	100.00

The most frequent lower leg symptoms are heaviness 82 (95.35%) & the lowest is throbbing 55(63.95%). The others are according to order of frequency cramps 66 (70.0%), Itching (73.26%), burning 61(70.93%), tiredness (80.23%), restless leg (82.55%), pain aching 76 (88.37%) (Table-V).

Table-V: Lower leg symptoms.

Symptoms	Total no of patients	Percentage
Pain aching	76	88.37%
Heaviness	82	95.35%
Swelling	79	91.86%
Cramps	66	70.00%
Burning	61	70.93%
Itching	63	73.26%
Tiredness	69	80.23%
Restless Leg	71	82.55%
Throbbing	55	63.95%
Total	86	100.00%

Among 85 cases of CVI (chronic venous insufficiency) studied 04 (4.65%) were in C1, 54(62.79%) were in C2, 03(3.49%) were in C3, 11(12.79%) were in C4, 6 (6.98%) were in C5 and 8(9.30%) were in C6 according to clinical CEAP classification. Analysis of Doppler ultrasound finding of 59 patients shows 46 patients had involvement of superficial venous system (78%). Among than 15 patients had superficial venous incompetence (25.42%), 13 Patients had perforators incompetence (22.03%), & 18 patients had both superficial venous & proportions incompetence (30.51%), 13 patients had deep venous

involvement. Among than 11 patients had venous incontinence (18.64 %), 2 patients had deep venous thrombosis (3.40%) (Table-VI).

Table-VI: CEAP Classification.

CEAP Classification	Total no of patients	Percentage
C0	--	0.00%
C1	04	04.65%
C2	54	62.79%
C3	03	03.49%
C4	11	12.79%
C5	06	06.98%
C6	08	09.30%
Total	86	100.00%

Discussion

The venous system is one of the largest organs of the body, and venous disease is a burden for the society and a cause of much disability[11]. Chronic venous insufficiency may affect globally 25-50% of adult population and its costs both personal to individual and economic to society are well documented[12-20]. Many contributing factors are involved in the genesis of varicose disease of the lower limbs such as age, sex, heredity, sedentary life style, number of pregnancies, overweight etc[21]. In present study showed the most frequent lower leg symptoms are heaviness 82 (95.35%) & the lowest is Throbbing 55(63.95%). The others are according to order of frequency cramps 66 (70.0%), Itching (73.26%), burning 61(70.93%), tiredness (80.23%), restless leg (82.55%), pain aching 76 (88.37%). Shahin-Ul-Islam MM et al[22] study showed according to presentation, 87(87%) patients have heaviness in leg, 75(75%) patients have aching pain in leg, 70 (70%) have leg swelling, 68 (68%) have cramping leg pain, 48 (48%) have tiredness, 43 (43%) have burning pain, 39 (39%) have engorged leg vein, 21 (21%) have restless leg at night, 18 (18%) have throbbing leg pain, 13 (13%) have itching, 7(7%) have various skin changes including lipodermatosclerosis, eczematization, white atrophy etc and only 3 (3%) patients have active leg ulcer. In present study showed BMI of all patients were calculated and it shows that 20(44.44%) male patients are obese and 30(73.17%) were female patients obese. In Shahin-Ul-Islam MM et al[22] study searching obesity, 63 patients (63%) out of 100 were obese/ overweight having BMI >25 kg/m^2 in case of male and >24 kg/m^2 in case of female. This finding is comparable with the study conducted at the Straub Clinic and Hospital in Hawaii[23]. They studied 272 patients and found that 61% of patients were overweight. Out of 63 overweight patients, 42 were female and 21 were male, this is also comparable with analysis of the Balse[24], the Framingham[25] and the Edinburgh[26] studies, which shows association between varicose vein and obesity or overweight, is more marked in female than in male. In this study shows among 85 cases of CVI (chronic venous insufficiency) studied 04 (4.65%) were in C1, 54(62.79%) were in C2, 03(3.49%) were in C3, 11(12.79%) were in C4, 6 (6.98%) were in C5 and 8(9.30%) were in C6 according to clinical CEAP classification. In study of Shahin-Ul-Islam MM et al[22] observed among 100 cases of CVI (chronic venous insufficiency) studied, 3 (3%) were in C0, 11 (11%) were in C1, 16 (16%) were in C2, 60 (60%) were in C3, 5 (5%) were in C4, 2 (2%) were in C5 and 3 (3%) were in C6 according to clinical CEAP classification. We know from previous description that C3 means edema of legs without skin changes. But in the community based study of Tecumseh shows 20% of subjects affected by CVI presents with leg edema[27]. Number of patients presented with active leg ulceration i.e. C6 were 3 (3%), this finding is comparable with the study conducted by Cornwall JV, Dore CJ, Lewis JD, they shows 0.1 - 3.2% patients presented with leg ulceration[28]. In current study showed determinants of chronic venous insufficiency majority 48(55.81%) were varicose disease; followed by 35(40.70%) were deep thrombophlebitis, 03(3.49%) were venous dysplasia cases. Compare with Florea I et al.[22] study, they showed the determinants of chronic venous insufficiency were varicose disease 582(67.36) cases; deep thrombophlebitis 273(31.60) cases, venous dysplasia 9(1.04) cases.

In this study shows ulcer location unilateral leg ulcers were 59(68.60%) cases and bilateral leg ulcers were 27(31.40%) cases. Florea I et al[29] study showed ulcer location unilateral leg ulcers 618 cases (71.5%); bilateral leg ulcers 246 cases (28.5%).

In this study the contributory factors in our group of patients with chronic venous insufficiency of were diabetes mellitus 13(15.12%) cases, surgical factors 7(8.14%) cases, hypothyroidism 12(13.95%) cases, obesity 05(5.81%) case, cardiovascular disease vascular 5(5.81) cases, digestive disease 06(6.98%) cases, osteo-articulary pathology 15(17.44%) cases, genetic predisposition 02(2.33%) cases, multiple pregnancies 14(16.28%) cases, inactivity 05(5.81%) cases. Florea I, et al.[29] study showed associated diseases chronic venous insufficiency of were diabetes mellitus 129(14.93%) cases, surgical factors 68(7.87%) cases, hypothyroidism 122(14.12%) cases, obesity - 51(5.90%) case, cardiovascular disease vascular 46(5.32%) cases, digestive disease - 59(6.83%) cases, osteo-articulary pathology 148(17.13%) cases, genetic predisposition - 25(2.89%) cases, multiple pregnancies - 137 (15.86%) cases, inactivity - 53(6.13%) cases. In present study showed the most common sign flebedema found in 56 (65.12) patients was followed by dermo-hypodermatitis in 15(17.44) patients, stasis eczema in 09(10.47) patients and thrombophlebitis in 06(6.98) patients. Florea I, et al[29] study showed the most common sign flebedema found in 65.74% patients was followed by dermo-hypodermatitis in 19.09% patients, stasis eczema in 9.49% patients and thrombophlebitis in 5.67% patients.

Conclusion

CVI (Chronic Venous Insufficiency) is not uncommon in our country. Among precipitating factors of chronic

venous insufficiency, majority were varicose disease. Others are diabetes mellitus, surgical factors, hypothyroidism, obesity, cardiovascular disease, osteo-articulary pathology, multiple pregnancies. Most common sign were flebedema, dermo-hypodermatitis, stasis eczema and thrombophlebitis. The most common symptoms were cramps, Itching, burning, Tiredness, restless leg, pain aching. In CVI (chronic venous insufficiency) studied most were in C2 group according to clinical CEAP classification. Majority of patients presented with the complains of heaviness of leg and unexplained leg swelling. Sex predilection is almost same for male and female. But advanced stages are more common in male patients. Increasing age is associated with more advanced stage of the disease.

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Original Article

Study on Clinical and Histopathological Changes of Alopecia Areata

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Abstract

Alopecia areata is a common, unpredictable, non-scarring form of hair loss. It is characterized by rapid and complete loss of hair in one or more round or oval patches, usually on the scalp, bearded area, eyebrows, eyelashes and less commonly on other hairy areas of the body. The present study was undertaken in the department of Dermatology and Venereology of Ibn Sina Medical College, Dhaka from July 2014 to June 2015 to observe the histopathological changes in different stages of alopecia areata. For this purpose 30 patients with age ranged from 18 to 45 years were enrolled. Of them 17 were males and 13 were females. A 4 mm punch biopsy from the involved scalp taken from each patient and histopatological changes were examined. The study revealed that anagen hairs decreased but catagen and telogen hair increased in all stages of alopecia areata. Telogen hairs increased in acute and chronic stage and catagen hair increased markedly in subacute stage. Although miniaturized (atrophic) follicle was frequently found in chronic stage. It was absent in acute and subacute stages. Moderate to dense peribulbar infiltration of lymphocytes were observed in acute stage and mild to moderate infiltration in subacute stage. In chronic stage either no or mild infiltrations were observed. Peribulbar infiltration of eosinophils and macrophages was seen in all stages of alopecia areata. Thus we can conclude that alopecia areata can be diagnosed with some confidence, even when inflammatory infiltrate is absent, based on increasing numbers of telogen hairs in the acute and subacute stages and increasing miniaturized hairs in chronic stage.

Keywords: *Alopecia Areata, Anagen, Catagen, Telogen, Histopatology.*

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Introduction

Alopecia areata is a common, unpredictable, non-scarring form of hair loss[1]. It is characterized by rapid and complete loss of hair in one or more round or oval patches, usually on the scalp, bearded area, eyebrows, eyelashes and less commonly on other hairy areas of the body[2].

The incidence of alopecia areata in the United States (Minnesota) is 20.2/100,000 person- years and the lifetime risk is estimated to be approximately 1.7%[3]. It accounts for about 2 or 3% of new patients presenting at dermatology clinics in the U.K. and U.S.A[4]. It occurs in both sexes in all racial groups. Alopecia areata can occur at any age from birth to the late decades of life. Congenital cases have been reported. Peak incidence appears to 15-29 years. As many as 44% of people with alopecia areata have onset at younger than 20 years. Onset in patients with older than 40 years is seen in fewer than 30% of patients with alopecia areata5.The pathophysiology of alopecia areata remains unknown. The most widely accepted hypothesis is that alopecia areata is a T-cell mediated autoimmune condition that is most likely to occur in genetically predisposed individuals[5].

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In the histological assessment of scalp biopsy specimens from alopecia areata, the diagnostic pathologic feature is peribulbar lymphocytic inflammation ("Swarm of bees") affecting anagen follicles or follicles in early catagen[6].

The histopathologic features of alopecia areata vary with the stages of the lesion. In the acute stage, a dense or moderate infiltrate develops around the anagen hair bulb. The infiltrate comprises lymphocytes and Langerhans cells, with eosinophils and plasma cells occasionally[7]. The inflammatory assault on anagen follicles induces a premature conversion of catagen. Consequently the number of catagen and telogen follicles found may be marked, approaching 100%. One may also see nanogen hairs, that combine characteristics of both catagen and telogen follicles[13].

In the subacute stage, an increasingly large numbers of catagen hairs are seen and some telogen hairs will appear after a few weeks as the hair bulb retracts upward in its journey to telogen level, the inflammatory infiltrate may persist in or around follicular stelae[7].

In the chronic stage, there is a reversal of the terminal-vellus ratio and many more miniaturized hairs will be seen at the expense of terminal hairs. The terminal vellus ratio is likely to be 1:1 rather than the usual 7:1. A variable amount of inflammation will be seen and if present, is more likely to be in the papillary dermis around miniaturized hair bulbs than in the reticular dermis or subcutaneous tissue because many terminal hairs have miniaturized and ascend to the upper dermis[7]. The purpose of this cross sectional study is to observe the histopathologic changes of alopecia areata at different stages by means of vertically sectioned scalp biopsy specimens.

Materials and Methods

It was a cross sectional study carried out in Department of Dermatology and Venereology of Ibn Sina Medical College and Department of Pathology of Bangubandhu Sheikh Mujib Medical University from alopecia areata of scalp with or without involvement of other sites. Total 30 samples were included in this study. Data were collected by structured questionnaire. A careful history was taken from each patient regarding the presence of atopy or other autoimmune diseases. A family history of alopecia areata, atopy and autoimmune diseases were also recorded. At the initial visit, one 4-mm punch scalp biopsy specimen was taken from an area of hair loss by application of local anesthetics with aseptic precaution. None has received any treatment for at least 3 months before the biopsy. Biopsy specimens were send in a test tube filled with formalin to the department of Pathology, BSMMU where tissue were processed, section cutting vertically by microtome (2-5μm). The haematoxylin and eosin stain are used. This allowed examining the hairs from the isthmus to the bulbar portion and thereby differentiating anagen, catagen and telogen hairs. Statistical analysis was performed with SPSS (Statistical package of social science) win 16 software packages.

Results

Table -I: Demographic characteristics of the patients.

Characteristics	Frequency	Percent
Age in years		
10-19	4	13.3
20-29	16	53.3
30-39	7	23.3
40-49	3	10.0
Mean±SD	27.00±7.92	
Sex		
Male	17	56.7
Female	13	43.3

Table-II: Distribution of respondents by sites of hair loss.

Site of hair loss	Frequency	Percent
Scalp	30	100.0
Eyebrows	6	20.0
Eye lashes	3	10.0
Other area	0	0.0

Table-III: Exclamation point hair and stages of alopecia areata.

Stages of alopecia areata	Exclamation point hair		Total	P value
	Present	Absent		
Acute	3 (75)#	1 (25)	4 (100)	
Subacute	5 (71.4)	2 (28.6)	7 (100)	0.962
Chronic	13 (68.4)	6 (31.6)	19 (100)	
Total	21 (70)	9 (30)	30 (100)	

Table-IV: Percentage of different types of hair in different stages of alopecia areata.

Stages of AA	Anagen Mean±SD	Catagen Mean±SD	Telogen Mean±SD
Acute	17.5 (±11.9)	32.5 (±8.7)	50 (±8.2)
Subacute	26.2 (±7.7)	46.7 (±10)	27.14 (±14.7)
Chronic	24.7(±17.8)	34.2 (±25.3)	41.1 (±30.5)

Table-V: Miniaturization of hair follicles.

Stages of alopecia areata	Miniaturization of hair follicles		Total	P value
	Present	Absent		
	0 (.0)#	4 (100)		
Acute	0 (.0)	7 (100)	4 (100)	
Subacute	18 (94.7)	1 (5.3)	7 (100)	0.001
Chronic	18 (60)	12 (40)	19 (100)	
Total			30 (100)	

Table-VI: Peribulbar lymphocytic infiltration.

Stages of alopecia areata	Peribulbar lymphocytic infiltration				Total	P value*
	Nil	Mild	Moderate	Dense		
Acute	0 (.0)	0 (.0)	2 (50)	2 (50)	4 (100)	
Subacute	0 (.0)	2 (28.6)	5 (71.4)	0 (.0)	7 (100)	0.001
Chronic	4 (21.1)	13 (68.4)	2 (10.5)	0 (.0)	19 (100)	
Total	4 (13.3)	15 (50)	9 (30)	2 (6.7)	30 (100)	

Discussion

This study was conducted with a view to see the variations of histopathologic changes in different stages of alopecia areata in the scalp. Thirty patients were enrolled in this study. Among them 17 were male and 13 were female. Mean age of this study participant was 27 years with a standard deviation of 7.92 years with a range of 18 to 45 years.

From the present study it was found that alopecia areata is more common among the age group of 20-29 years. Among respondents 16 (53.3%) were within this group. This finding is comparable with Bolduc[5]. He showed that peak incidence appears to occur from age 15 to 29 years. But differ from Sharma et al[8]. They observed the peak age of onset was 20 to 29 years constituting 32.3% of the total cases.

It was revealed that males (56.7%) were predominant than that of females (43.3%). This result is supported by Sharma et al[8]. They showed that 61.2% patients were male and 38.8% were female in their study.

From this study it was also found that among the respondents students were predominant. Total 53.3% respondents were student. Due to lack of relevant literature it could not be compared with other study findings. Probably it is due to awareness to seek medical care and also due to the fact that they are usually in the age group 20-29 years.

Although alopecia is commonly seen on the scalp it may occur on other body sites. In the present study it was found eyebrows (20%) and eyelashes (10%) were the site of affected area of alopecia areata along with scalp. Sharma et al (1988) reported eyebrows alopecia in 5.2% of their patients along with scalp alopecia. This result is not consistent with the present study.

Present study revealed that most of the patients, 19 (63.3%) were in the chronic stage. This finding is consistent with the work of Whiting,[7] they studied 50 patients among them 31 (62%) patients were in chronic stage of alopecia areata.

From the present study it was revealed that 6.7% respondent had autoimmune disease. This finding is not consistent with Whiting[7]. He found that in 20% to 30% of patients were associated with other autoimmune disease.

This study revealed that atopy was associated in 10% of respondents whereas family history of atopy was associated in 6.7%. This finding is consistent with Sharma et al[9]. They found 8.4% for personal atopy and 6.8% for family history of atopy.

From the present study it was revealed that 16.7% respondents had nail involvement. This finding is accord with Drake et al[10]. They reported 10% patients of alopecia areata had nail involvement.

A common finding of a patchy alopecia areata is 'exclamation point' hair present at the margin. Present study revealed that exclamation point hair was present in 3 (75%) respondents in acute stage, 5 (71.4%) in subacute stage and 13 (68.4%) in chronic stage. Difference was not found statistically significant (P>0.05). Due to scarcity of relevant literature it could not be compared with present study.

The present study revealed that in the acute stage percentage of anagen hair were decreased whereas catagen and telogen hair were increased. In the subacute stage decreased anagen hairs and markedly increased catagen hair and slightly increased telogen hair. In chronic stage percentage of anagen hair also decreased and increased catagen and telogen hairs were found. These findings were quite consistent with Whiting,[7] and Sperling & Lupton[11], Stefanato[12].

Though miniaturized hair follicles were absent in all acute and subacute cases. It was present in 18 (94.7%) of chronic cases. This observation was found statistically significant (P<0.05). This result is supported by Whiting[7], Stefanato[12]. They stated that miniaturized hairs were found in chronic stage of alopecia areata. Sperling and Lupton[11] also observed that in longstanding (chronic) stage of disease almost all hairs are miniaturized. The present study is totally accord with their study.

Dense lymphocytic infiltration was only seen in acute 2 (50%) stage whereas moderate infiltration was found in acute (50%), subacute (71.4%) and chronic stage (10.5%). This observation was found statistically significant (P<0.05). This result is supported by Whiting[7] and Ioffreda[6]. They described in acute stage a dense or moderate infiltrate develops around the terminal hair bulb.

Conclusion

Thus we can conclude that alopecia areata can be clinically diagnosed with some confidence, even when inflammatory infiltrate is absent, based on increasing numbers of telogen hairs in the acute and subacute stages and increasing miniaturized hairs in chronic stage. It can be recommended that transverse histologic section of the biopsy specimen may be taken to see the alterations of terminal and vellus hair ratio which is also helpful to differentiate the chronic stage from other stages of alopecia areata.

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Original Article

Low Serum Vitamin D is Independently Associated with Acute Ischemic Stroke

Majumder MMI[1], Chowdhury MNH[2], Khan AR[3], Ahmed T[4], Ahmed S[5]

Abstract

Low serum vitamin D levels have been associated with various vascular diseases. Very little is known its association with acute stroke in Bangladeshi population. We therefore sought to assess whether low serum 25-hydroxyvitamin D, a marker of vitamin D status is associated with acute stroke. We performed a prospective study in Comilla Medical Collage, Comilla, from November 2016 to November 2017. All the patients diagnosed as acute ischemic stroke on the basis of CT scan or MRI of brain. Patients were eligible for inclusion if they were admitted with onset of symptoms within 24 hours. Estimation of 25(OH)D level was done at presentation. The patients were stratified by vitamin D status, >30 as vitamin D sufficient, vitamin D 20-20.9 as insufficient and finally vitamin D<20 as deficient. Multivariate logistic regression analysis revealed that out of the desired 7 variables, smoking, hypertension and low serum vitamin D were found independent predictors for acute stroke with ORs being 1.44, 4.23 and 2.39 respectively. Vitamin D deficiency represents an important risk factor for acute stroke and it might play a causal role in the development adverse events associated with stroke.

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Number of Correspondences: 05

Introduction

Stroke is the second leading cause of disability in Europe and sixth leading cause worldwide[1]. Women have a higher lifetime risk of stroke than men. It is estimated that about one in five women (20% to 21%) and one in six men (14% to 17%) will suffer from a stroke in their lifetime[1]. Low serum 25 hydroxy vitamin D [25(OH)D] is independently associated with larger infarct volume, which may partially explain worse outcomes in ischemic stroke patients[2]. This poor stroke outcome possibly due to inhibition of thrombogenic influences and mitigation of endothelial dysfunctionin vitamin deficiency[3]. It also triggers secondary hyperparathyroidism which promotes myocyte hypertrophy, vascular remodeling and has pro-inflammatory effects[4-5].

Body vitamin D status is measured by estimation of serum 25(OH)D because of its long half life[6]. Early reports shows link between vitamin D deficiency and easily treatable cardiovascular risk factor such as hypertension, diabetes mellitus, obesity, metabolic syndrome, left ventricular hypertrophy, heart failure, coronary heart disease and renal disease[7-8]. Despite evidence suggesting that vitamin D deficiency may lead to elevated cardiovascular disease risk but the association of 25(OH) D levels with ischemic stroke risk is inconclusive. Recent reports of the association of hypovitaminosis D with multiple cardiovascular (CV) conditions have been of great interest suggesting the need for prospective validation and extended observations. We conducted a prospective study to examine the relationship between plasma 25(OH)D levels and risk of stroke.

Materials and Methods

We performed a prospective study in Comilla Medical Collage on the patients presented with acute stroke from November 2016 to November 2017. Patients were eligible for inclusion if they were admitted to the emergency department with onset of symptom within 24 hours[9].

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Acute ischemic stroke was diagnosed by with computed tomography (CT) and/or magnetic resonance imaging. Estimation of 25(OH)D level was done at presentation. A single vitamin D level provides an estimate of long-term vitamin D status[10-11]. Patients suffering from malignant tumor, renal insufficiency (creatinine>1.5 mg/dl), febrile disorders, acute or chronic inflammatory disease at study enrolment and autoimmune diseases were excluded from this study. The patients who used vitamin and/or calcium supplementation before stroke onset were also excluded. All the laboratory data, comorbidities, preadmission medications and stroke etiology after completion of diagnostic evaluation were collected. Written informed consent was obtained from all subjects. This study was reviewed and approved by our institutional review board. Serum levels of 25(OH)D were analyzed using 25-hydroxy chemiluminescent immunoassay. We trichotomized vitamin D status as sufficient (≥30 ng/mL [75 nmol/L]), insufficient (20-29.9 ng/mL [50-75 nmol/L]), and deficient (□20 ng/ mL [50 nmol/L]) according to the Endocrine Society criteria[9]. In addition, we dichotomized vitamin D status as 25(OH)D concentration of 30 ng/mL or more versus less than 30 ng/mL and 20 ng/mL or more versus less than 20 ng/mL, respectively.

During Statistical analysis continuous variables are reported as mean ± standard deviation or median (interquartile range), and categorical variables are reported as proportions. Between-group comparisons for continuous variables were performed using Student's t test, ANOVA analysisas appropriate. Categorical variables were compared using the chi-square test or the Fisher exact test. Univariable regression models were constructed to examine associations of serum 25(OH)D concentrations and acute stroke. The following prespecified variables were included in the multivariable linear regression model with backward elimination to identify independent predictors for a final acute stroke model as they have been associated with acute stroke: age, sex, smoking, diabetes mellitus, hypertension and dyslipidaemia[7]. All statistical analyses were performed using SPSS statistics version 16 Windows 2007. All the authors vouch for the completeness and accuracy of data and analyses presented.

Results

The study patients were stratified by vitamin D status>30 as vitamin D sufficient, vitamin D 20-20.9 as insufficient and finally vitamin D<20 as deficient. Patients having vitamin D deficient were more older than vitamin D insufficient and sufficient respectively with statistically significant difference (p=0.04) by ANOVA test. Male patients were higher in vitamin D sufficient than that of vitamin D insufficient and deficient with statistically significant difference (p=0.04). Female patients were found higher in vitamin D deficient than that of vitamin insufficient and sufficient with statistically significant difference (p=0.04). Smoking habit was found higher in vitamin D deficient patients than that of vitamin insufficient and sufficient with statistically significant difference (p=0.04).

Hypertension was found higher in vitamin D deficient patients than that of vitamin insufficient and sufficient with statistically significant difference (p=0.04).The remaining factors such as diabetes mellitus, IHD, dyslipidaemia and obesity were observed more in vitamin D deficient patients but did not reach the level of significance (p>0.05) (Table - I).

Table- I: Participants baseline clinical characteristics of the study patients as stratified by vitamin D status (n=116).

Variables	Total patients (n=116)	Vitamin D sufficient (n=26)	Vitamin D insufficient (n=42)	Vitamin D deficient (n=48)	P value
Age, years	61.7±11.3	58.1±12.8	60.6±12.1	64.7±9.0	0.04[s]
Sex (Male)	70 (60.3%)	20 (76.9)	27 (64.3%)	23 (47.9)	0.04[s]
Sex (Female)	46 (39.7%)	6 (23.1%)	15 (35.7%)	25 (52.1%)	0.04[s]
Smoker	57 (49.1%)	11 (42.3%)	17 (40.5%)	29 (60.4%)	0.03[s]
Diabetes mellitus	38 (32.8%)	5 (19.2%)	13 (31.0%)	20 (41.7%)	0.09[ns]
Hypertension	52 (44.8%)	8 (30.8%)	17 (40.5%)	27 (56.2%)	0.04[s]
IHD	37 (31.9%)	7 (26.9%)	12 (28.6%)	18 (37.5%)	0.54[ns]
Dyslipidaemia	35 (30.2%)	6 (23.1%)	10 (23.8%)	19 (39.6%)	0.17[ns]
Obesity	15 (12.9%)	3 (11.5%)	4 (9.5%)	8 (16.7%)	0.58[ns]

Data were expressed as mean±SD. p:probability value reached from Chi Square test for qualitative data and ANOVA test for quantitative data. Ns = Not significant (p>0.05), Bold indicates significant (p<0.05).

Vitamin D status of patients in percentage with smoking habit, diabetes mellitus, hypertension, IHD, dyslipidaemia and obesity are plotted in bar diagram in figure-1.

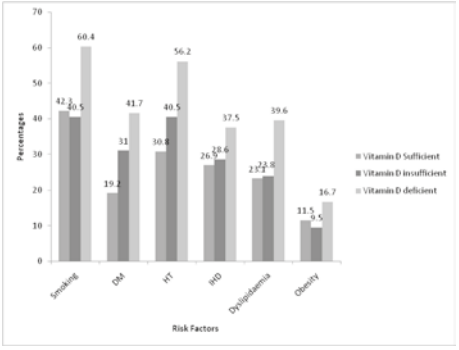

Figure-1: Bar diagram showing risks factors of the study patients according to Vitamin D status.

The following table displays the binary logistic regression analysis of odds ratio (OR) for characteristics of the subjects likely for having stroke. Multivariate analysis revealed that out of the desired 7 variables smoking, hypertension and low serum vitamin D were found to be the independently significant predictors for having stroke with ORs being 1.44, 4.23 and 2.39 respectively. The table revealed that smoking habit, hypertension and low

serum vitamin D is associated more than 1 time, 4 times and 2 times for having stroke than non smoker, normotensive and raised serum vitamin D ≥ 20 ng/ml (Table- II).

Table-II: Multivariate binary logistic regression analysis of having stroke by low serum vitamin D and other variables (n=116).

Variables of interest	Multivariate	
	OR (95% CI)	P value
Advance age>55	0. 98 (0.689 - 4.274)	0.12^{ns}
Sex (female)	0. 92 (0.409 - 5.274)	0.15^{ns}
Smoking	1.44 (1.241 - 6.101)	0.03^{s}
Hypertension	4.23 (1.247- 14.210)	0.02^{s}
Dyslipidemia	1.11 (0.241 - 6.222)	0.19^{ns}
Diabetes mellitus	1.20 (1.189 - 13.112)	0.008^{s}
Low serum Vitamin D (<20 ng/ml)	2.39 (1.101-6.201)	0.03^{s}

s = Significant (p<0.05), ns = Not significant (p>0.05)

OR= odds ratio p: probability value, n= number of the subjects

Discussion

In the present prospective observational study, we assessed serum levels of 25(OH)D with regard to their accuracy to predict acute stroke. A large body of evidence from epidemiological studies indicates that vitamin D deficiency is associated with an increased risk of stroke[12], and Stepwise decrease in plasma 25(OH)D concentrations were associated with stepwise increasing risk of ischemic stroke[1]. To the best of our knowledge, no previous work has focused on the association between 25(OH)D and acute stroke in Bangladeshi population. In the present study, we found that serum levels of 25(OH)D were substantially lower in patients with acute stroke. Vitamin D deficiency and insufficiency (77.5%) was very common in our patients. Median baseline 25(OH)D levels 14.03ng/ml in our patients were similar compared with other studies 15.2ng/ml[14] and 14.1 ng/ml[15]. Pathophysiological mechanisms remain speculative, but several possible biological mechanisms might explain the association of low 25(OH)D with poor outcome[16]. Low 25(OH)D levels may contribute to pro-atherosclerotic changes of vascular smooth muscle cells, endothelial dysfunction and increased macrophage to foam cell formation[17]. High dose oral vitamin D supplementation produced short-term improvement in endothelial function in stroke patients with well controlled baseline blood pressure[14]. Finally, low 25(OH)D levels are known to influence macrophage and lymphocyte activity in atherosclerotic plaques and to promote chronic inflammation in the artery wall[18]. Various studies suggest that vitamin D may exert anti-inflammatory effects. Reduced 25(OH)D levels might be associated with overall increased inflammatory activity[19].

Low level of vitamin D has been associated with an increased future risk of stroke and acute myocardial infarction during 10 years of follow-up[20] and was independently predictive for fatal stroke in patients who were referred for coronary angiography at baseline[19]. In a prospective population-based cohort study, individuals with severe 25(OH)D deficiency (<20 nmol/l) had higher risk of ischemic stroke (hazard ratio 1.36, 95% CI 1.09-1.70) compared with individuals with optimal 25(OH)D level (>75 nmol/l) during 21 years of follow- up[20]. Daubail et al found that the mean 25(OH)D level was lower in ischemic stroke patients[14]. In our study, we found that circulating serum 25(OH)D levels were deficient and insufficient in 77.5 % of patients with acute stroke. Another study in Chinese patients also found that vitamin D deficiency (78.6 %) was very common[15]. Tu et al also suggested that 25(OH)D was an independent predictor of major disability and death within 90 days after onset of ischemic stroke with ORs (95% CIs) of 0.79 (0.73-0.85) and 0.70 (0.50-0.98) respectively[16]. Strengths of the present study relate to the extensive measurement of covariates and rigorous adjustment for variables that have been associated with acute stroke. There are some limitations relate to the retrospective study design like. Uncontrolled or unknown factors that may affect the incidence of stroke. For example, we did not collect information on nutritional habits. However, surrogate markers for the nutritional status were not associated with stroke incidence or vitamin D status in our study. This may assuage concerns that the noted association of vitamin D with acute stroke was a spurious finding related to overall poor nutritional health. Nevertheless, careful assessment of the nutritional status should be done in future studies assessing these associations. Although our data show a significant association between 25(OH)D and acute stroke, a causal relationship remains to be established. Large scale prospective studies in tertiary level hospital in different region of this country is necessary to establish this relationship.

Conclusion

In the context of our observations, vitamin D deficiency represents an important risk factor for acute stroke and it might play a causal role in the development adverse events associated with stroke.

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Case Report

Persistent Mullerian Duct Syndrome (PMDS) Presenting as a Malignant Tumour

Islam MR[1], Ali MS[2], Azam SMG[3]

Abstract

Persistent Mullerian duct syndrome is a condition in which there is presence of Mullerian duct structures (uterus, fallopian tube, vagina etc.) in an otherwise phenotypically, as well as genotypically, normal man. This patient usually presents with unilateral or bilateral cryptorchidism associated with inguinal hernia and ectopic testis. There is the chance of developing malignancy in ectopic testis (incidence being 15%), as well as infertility in case of bilateral cryptorchidism. Our patient suffers from PMDS presents with malignant tumour. The aim of the presentation of this case is to draw the attention in case of unilateral or bilateral cryptorchidism associated with or without inguinal hernia; the possibility of PMDS should be kept in mind to prevent infertility as well as malignancy.

Keywords: *Persistent Mullerian Duct Syndrome (PMDS).*

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Number of Correspondences: 03

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Introduction

Persistent Mullerian duct syndrome is a rare form of male pseudo-hermaphroditism characterized by the presence of Mullerian duct structures in an otherwise phenotypically, as well as genotypically, normal man; only a few cases have been reported in the world wide literature. We report the case of a 22 year old man with bilateral cryptorchidism, presents with a lump at lower abdomen. After laparotomy there was a well developed uterus, both Fallopin tubes, apparently normal left gonad with a large tumour arising from right gonad. He was diagnosed as a case of PMDS.

Case Report

Mr. Sumon, age 22 years was admitted to a private clinic at Khulna city with a complaint of intra abdominal mass. According to the statement of the patient he was alright one month back. Then he developed a mass in the lower abdomen. This is about 15 cm in diameter, smooth surface, freely mobile, non tender. No abnormality in bowel and bladder habit.

On examination the boy was good looking, healthy, masculine in get up (Fig-1).

Figure-1: Facial appearance of the patient.

(Images are taken by mobile phone camera during operation.)

Secondary sex characters are well developed including male genitalia. His scrotum contains soft tissue without definitive testis on either site. All investigations are found within normal limit except Ultrasonography. Ultrasonography shows a large intra abdominal mass at the lower abdomen with mixed echogenicity. He was diagnosed clinically as a case of mesenteric tumour. He was decided for laparotomy. Abdomen was opened through a paramedian incision. A large mass was detected arising from right gonad, uterus and both fallopian tubes (Fig- 2) were found normal, left testis was atrophied and embedded in broad ligament. Upper part of vagina ends on apparently prostatic tissues.

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Figure-2: Uterus at the lower abdomen.

Total abdominal hysterectomy with excision of the tumour (Fig-3) was done. Abdomen was closed with a drain. His external genitalia were further examined. Penis and scrotum were well developed, scrotum contains soft tissue like structure, no testis was found. Specimen sent for histopathological examination. He was diagnosed as a case of PMDS.

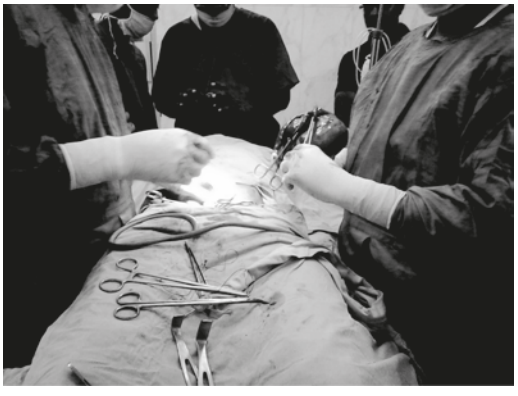

Figure-3: Specimen of tumour after resection.

Histopathological report shows uterine muscular tissue with cavity lined by atrophied endometrial tissue. Left testis showing atrophy with hyalinised seminiferous tubules with complete arrest of maturation, tumour at right testis shows malignant testicular tumour (germ cell tumour).

Discussion

In true hermaphrodites, both ovarian and testicular tissue is present in one or both gonads[4]. In female pseudo-hermaphroditism, the gonads are the ovaries, but male tendencies are seen in the organ of reproduction[5]. Conversely, male pseudo-hermaphroditism is a condition in which the gonads are the testes but the internal genitalia are not completely virilized. Male intersex may present (1) with masculine external genitalia with fully developed uterus (as in our patient's), (2) with purely feminine external genitalia, or (3) With external genitalia of equivocal sexuality.

The exact cause of PMDS in not known, however it is thought to rest from a defect of the synthesis or release of MIF, or from defects in the MIF receptor (2). MIF is released by the Sertoli cells in fetal tissue from seven weeks of gestation onwards, and is responsible for the regression of the Mullerian duct in the male fetus.

The female form, seen in 10% to 20 % of cases, is characterized by bilateral cryptorchidism. The gonads are fixed within the pelvis, with the testes fixed within the round ligament in the ovarian position with respect to the uterus[3].

PMDS is usually coincidently detected during surgical operation, as in our patient's case. However pre-operative Ultrasonography, computerized tomography and MRI allow possible pre-operative diagnosis[2].The prognosis depends upon the integrity of the testicular tissue and successful correction of cryptorchidism.

The risk of malignancy in an ectopic testis in a case of PMDS is similar to that in a healthy male, with the incidence being 15%. There have been case reports of embryonal carcinoma, seminoma, yolk sac tumor and teratoma in patients with PMDS, whereas tumors of the Mullerian duct derivatives are very rare[1,3]. Infertility is common, with an absence of spermatozoa observed during semen analysis[3].

Excision of tumour along with total excision of the uterus with bilateral fallopian tubes and left testis was performed and the operation was completed with a drain in pelvic cavity.

Our patient recovered well post-operatively. The patient was referred to oncologist for further management of cancer and long-term follow-up.

Conclusion

PMDS is a rare form of male psedo-hermaphroditism characterized by the presence of Mullerian duct structures in an otherwise phenotypically, as well as genotypically, normal man. The patient with PMDS has unilateral or bilateral cryptorchidism and is usually assigned to the male sex at birth without hesitation. Since patients are phenotypically male, the diagnosis is usually not suspected until surgery is performed for cryptorchidism or hernia repair. In cases of unilateral or bilateral cryptorchidism possibility of persistence Mullerian duct syndrome should be kept in mind in order to prevent further complications such as infertility and malignant change.

Acknowledgement

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Case Report

Laurence Moon Bardet Biedle Syndrome

Islam MN[1], Akhter S[2], Kamal SM[3], Chowdhury SN[4]

Abstract

Laurence Moon Bardet Biedle syndrome is a rare, autosomal recessive genetic disorder involving multiple systems and has wide spectrum of clinical features. Characteristic features of this disorder are retinitis pigmentosa, polydactyly, truncal obesity and learning difficulties. It may also be associated with hypogonadism in male and complex genitourinary abnormalities in female. We present a case of 33 years male patient having obesity, decreased vision, polydactyly, hypogonadism and retinitis pigmentosa. These clinical features are consistent with Laurence Moon Bardet Biedle syndrome.

Keywords: *Polydacytyly, Retinitis Pigmentosa, Brachydactyly, Syndactyly, Hypogonadism, Hypodontia.*

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Introduction

Laurence-Moon syndrome is caused by changes (mutations) in the PNPLA6 gene and is inherited in an autosomal recessive manner[1]. PNPLA6 gene encodes neuropathy target esterase, critical in phosphatidylcholine metabolism, membrane phospholipid trafficking and axonal integrity[2].

The incidence is much higher in some populations with a high level of consanguinity of marriage or those that are geographically isolated. The syndrome is more often seen in the Arab population especially in the Bedouin population of Kuwait, affecting about 1 in 13,500 newborns and also on the island of Newfoundland (off the east coast of Canada), where the prevalence is 1 in 17,000 newborns[3,4].

Larger studies in Bangladeshi population are needed and the literature review has revealed only few cases[5].

The Laurence moon bardet biedle is a rare autosomal recessive disorder, which is characterized principally by cardinal symptoms of marked central obesity, retinal dystrophy, polydactyly, mental retardation and hypogonadism and renal dysfunction.

Other features not always present include hepatic fibrosis, diabetes mellitus, neurological, speech and language deficits, behavioral traits, facial dysmorphism, dentalanomalies and developmental delay.

The authors present a case of LMBBS presented with hypogonadism, marked central obesity, retinitis pigmentosa and polydactylyetc along with a brief review of the literature.

Case Report

A 33 years-old-male patient from Fulbarigate, Khulna has presented with the complaints of progressive dimness of vision more marked at night from his childhood. On query he gives history of nocturia, polydipsia, loss of libido, absent penile erection. There is no history of consanguity of marriage; no developmental delay. No other family member has similar problem. He is diabetic for 20 years and is on regular insulin therapy.

On examination his height is 141 cm, weight 58 kg; resulting BMI = 29.2. He has short stature and short neck. There is bilateral gynaecomastia (Fig-1), testicular atrophy and small penis (2 cm).

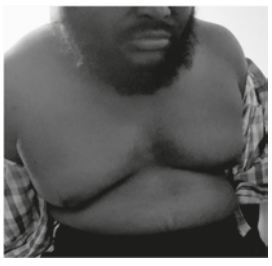

Figure-1: Gynaecomastia, Obesity. (Source: The reporting case).

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There is polydactyly involving both upper limbs and right lower limb. There is also brachydactyly in right foot and syndactyly of left foot (3rd and 4th toes) (Fig -2 & 3).

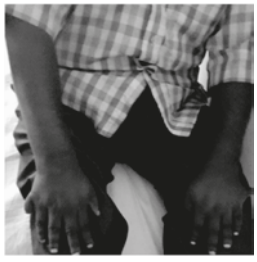
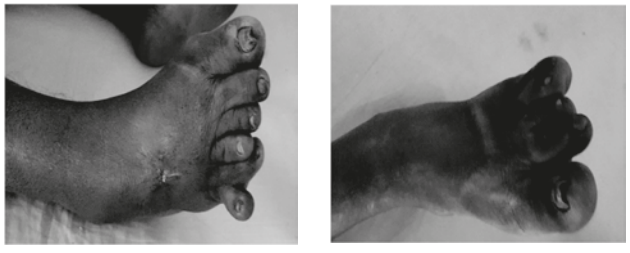


Figure-2: Polydactyly.
(Source: The reporting case).



(a) (b)

Figure-3 :(a & b) Polydactyly, Bachydactyly, Syndactyly.

(Source: The reporting case).

His pulse is 80 /min; BP- 120/70 mm Hg. There is no anaemia, jaundice, cyanosis, clubbing or koilonychia. He has no thyromegaly or lymphadenopathy.

His eyes are small and deep seated. On ophthalmoscopy there is bilateral retinitis pigmentosa. Optic disc, vessels were normal. His fundal photograph was taken and shows bilateral retinitis pigmentosa (Fig-4).

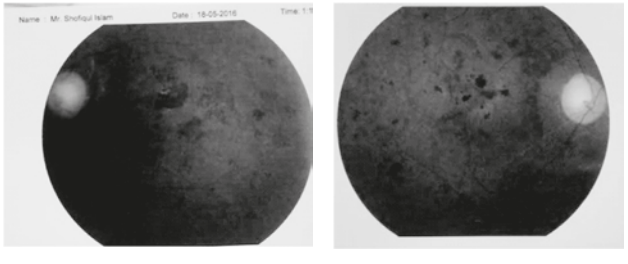


Figure-4: Retinitis Pigmentosa (a) right eye; (b) left eye.

(Source: The reporting case).

Others systemic examinations reveals no abnormality.

His Blood TC DC ESR, urine R/M/E and USG of whole abdomen is normal. X ray chest and ECG reveals normal findings. Blood sugar is normal with insulin therapy. Urine Routine and microscopic examination reveals - normal. USG of testes reveals bilateral small testes. Serum testosterone level is markedly reduced (0.1ng/ml).

Discussion

In 1866 Laurence and Moon described a disease characterized by adiposity, genital dystrophy, retinitis pigmentosa, and mental deficiency, affecting four members of one family. In 1920 Bardet described a similar syndrome in a child with polydactyly. In 1922 Biedl reported a similar condition in a brother and a sister. In 1925 Solis-Cohen and Weiss suggested the name Laurence-Moon-Biedl syndrome for this condition[6].

Five cardinal signs were considered the major components of LMBB syndrome. They were retinitis pigmentosa, mental retardation, polydactyly, syndactyly and obesity.

Along with the characteristic features, the patients with this syndrome at times present with other findings like intellectual impairment, cardiovascular abnormalities, deafness and dental anomalies[7,8].

Our patient was 33 year old. Polydactyl has been reported in upper or lower limbs. Most of the reported cases were females, whereas our patient was male. Our patient hadpolydactyly, brachydactyly, syndactyly in lower limb. In 75 % cases obesity was found with mean BMI to be 33 kg/m^2. Our patient was also obese with BMI 29.2.

As the clinical variability of the syndrome is very large, Klein and Amman have adopted the following classification:

1. Complete form:
2. Incomplete form:
3. Atypical form
4. Extensive form

Modified diagnostic criteria for Bardet-Biedl syndrome[9].

Primary features

- Rod-cone dystrophy
- Polydactyly
- Obesity
- Learning disabilities
- Hypogonadism in males
- Renal anomalies

Secondary features

- Speech disorder/delay
- Strabismus/cataracts/astigmatism
- Brachydactyly/syndactyly
- Developmental delay
- Polyuria/polydipsia (nephrogenic diabetes insipidus)
- Ataxia/poor coordination/imbalance
- Mild spasticity (especially lower limbs)
- Diabetes mellitus
- Dental crowding/ hypodontia/small roots/high arched palate
- Left ventricular hypertrophy/congenital heart disease
- Hepatic fibrosis

For diagnosis of this syndrome the patients should have either four primary features or three primary and two secondary features[10,11,12,13].

Our patient had 4 primary features (Rod-cone dystrophy, Polydactyly, Obesity, hypogonadism) and 2 secondary features (brachydactyly/syndactyly, diabetes mellitus). Hence we diagnosed the patient to be suffering from Laurence Moon Biedl Bardet syndrome.

Initial investigation and follow up recommendations for a person with Bardet-Biedl syndrome[14].

Baseline

- Electroretinogram (ERG)/Visually Evoked Responses (VER)
- Renal ultrasound
- Intravenous pyelogram (IVP) or DMSA/DPTA scan
- ECG & echocardiogram
- Prader-Willi syndrome exclusion by molecular testing

Consider

- CT/ MRI of brain
- Electroencephalogram (EEG)
- Statementioning of educational needs
- Registration of blindness
- Speech assessment & therapy

Six monthly

- Urine analysis (dipstick)

Conclusion

It has got poor prognosis. Quality of life and survival of patient depends on these verities of the condition and treatment provided.

Acknowledgement

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Case Report

'Atypical Localized Not Well-Specified Cases' a case study of a rare type of Localized Lichen Myxedematosus

Hye MA[1], Quyum MA[2], Begum RA[3]

Abstract

Lichen Myxedematosus (LM) is an uncommon and distinct disease entity characterized by cutaneous mucin deposition in dermis. It is classified in several subtypes depending on many factors including the monoclonal gammapathy, pattern of skin involvement and systemic involvement. We now present a case of LM which is localized in respect of skin involvement but according to recent classification it falls into a diagnosis of 'atypical localized not well- specified cases'. This is a very rare case and to the best of our knowledge, it is the first case report in medical literature until now. We treated the case with a short course of oral Prednisolone and got excellent result. Patient has been followed up in every 6 month for last 13 yrs and observed no progression to scleromyxedema.

Keywords: *Lichen Myxedematosus, Scleromyxedema, Mucin Deposition, Atypical Type, Treatment.*

Number of Figures:06

Number of References: 05

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Introduction

Lichen Myxedematosus (LM) is a rare idiopathic cutaneous disorder characterized by an abnormal accumulation of mucin in the dermis. Its classification dates back to 1953, when Montgomery and Underwood distinguished 4 types of LM. Still now, there is no consensus regarding type or classification of mucinosis. Rongioletti and his colleagues[1,2] studied the disease extensively and classified it primarily into three clinico pathologic subsets: (i) a generalized and sclerodermoid form associated with monoclonal gammapathy and systemic, even lethal manifestations (the only one which should be called scleromyxedema) (ii) localized forms, in the absence of monoclonal gammapathy and systemic involvement, and it is subdivided into 4 subtypes: (1) a discrete popular form involving any site; (2) acral persistent popular mucinosis involving only the extensor surface of the hands and wrists; (3) papular mucinosis of infancy, a pediatric variant of the discrete form or the acral form of persistent papular mucinosis; and (4) nodular form. (iii) A third group of atypical or intermediate forms, not meeting the criteria for either scleromyxedema or the localized form, includes cases of (1) scleromyxedema without monoclonal gammopathy, (2) localized forms with monoclonal gammopathy and/or systemic symptoms, (3) localized forms with mixed features of the subtypes, and (4) not well-specified cases. In the literature, many forms of LM are reported. However due to its rarity, it is still a poor documented disease. In this paper authors describe a case of LM which does not fit with any subtypes of localized LM. We categorized it as a'atypical localized non- specified cases' depending the type and distribution of lesions.

Case Report

A 41 years old man presented himself with skin lesions in trunk and extremities for 7 months [Fig 1,2,3].

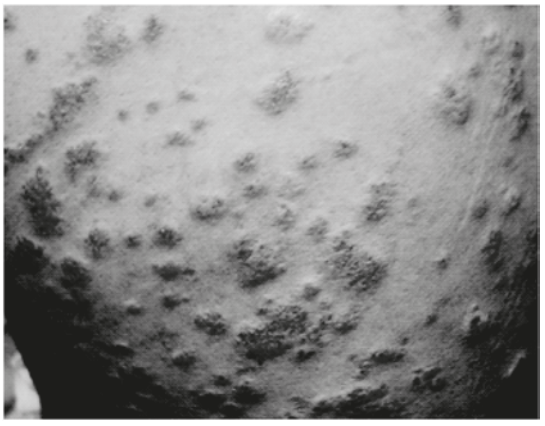

Figure-1: Erythematous Papules and Plaques in left side of trunk.

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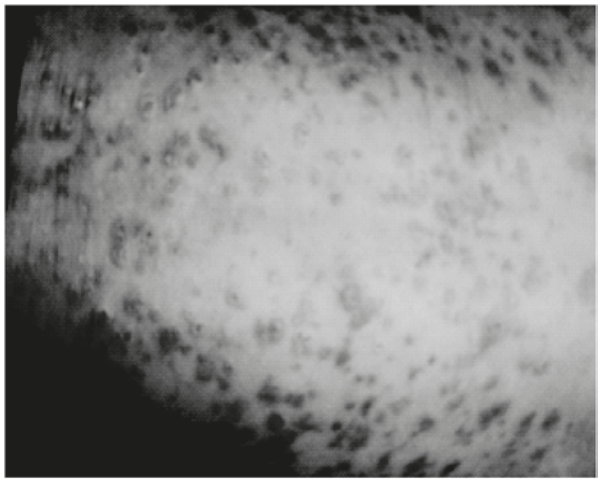

Figure-2: Linear pattern of lesions in back.

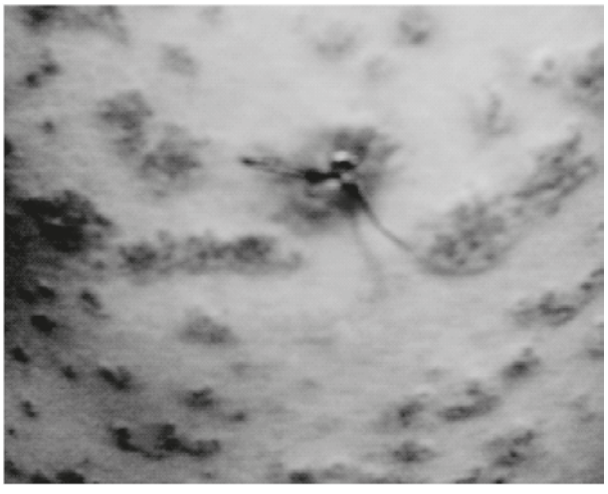

Figure-3: Site of biopsy.

He complained that the lesions were static for last five month without any discomfort except occasional pruritus. He also informed that he had no systemic disease.

Cutaneous examination showed multiple, well defined skin coloured to erythematous papule and plaques scattered over the trunk, thigh and arms. The lesions are few millimeter to few centimeter in diameter and confluent in trunk. Linear patterns of lesions were also noted in back of trunk [Fig:2].

On palpation, the lesions were non-tender, waxy and slightly hard in consistency. In general, thickening of skin, face involvement or systemic symptoms were not apparent. Laboratory evaluation showed a normal blood count, blood chemistry, HIV serology and thyroid hormones. Ig G paraprotein was absent.

A skin biopsy Revealed normal epidermis but moderate deposit of mucinous material in the upper and middle dermis separating the collagen bundles [Fig:5,6].

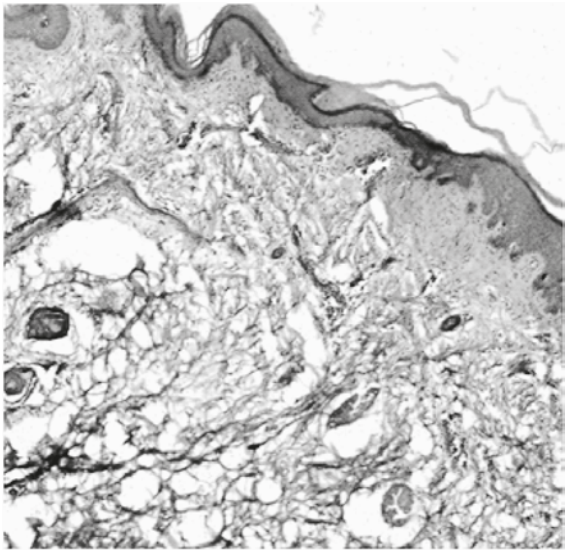

Figure-5: Collagen fibers were separated in upper dermis without epidermal changes (H&E100x).

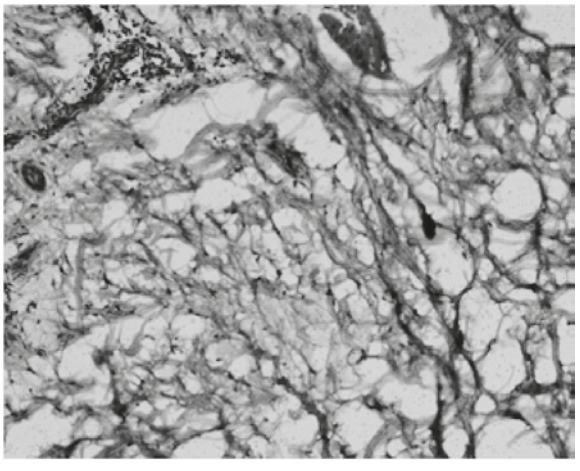

Figure-6: Mucin deposits between collagen fibers with proliferation of fibroblasts (H&E 400x).

A slight increase in fibroblasts with accompanying inflammatory infiltrate were also observed. According to Rongioletti and his colleagues, above mentioned histopathologic criteria are diagnostic for LM. He opined that neither collagen deposition nor sclerosis are typical features of LM[3].

The type and distribution of lesions of our patient did not match with any subtypes of localized form of LM. So in the light of Rongioletti classification, this LM case was categorized as 'Atypical Localized Not Well specified Cases'[1].

The patient was treated with oral prednisolone 20 mg for 10 days with tapering dose of 10mg for another 4 days. The patient was examined after 1 month and it was found that lesions were cured absolutely. Patient returned back after 3 month with a minor relapse and again he was treated with same doses of prednisolone.

In follow up examination after 1 month, [Fig:4] it was found that lesions were almost cured and left behind scars only.

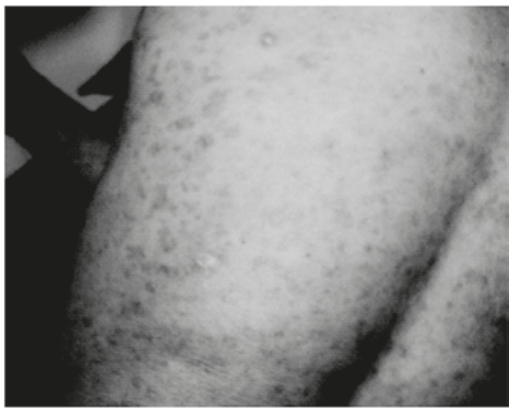

Figure-4: After 1 month of treatment.

The patient has been followed-up every 6 months for last 13 years. We did not observed any relapse and also there was no progression of the disease to sclerormyxedema or other systemic disease.

Discussion

Lichen Myxedematosus is one of the rare disease in dermatology. Until now less than 200 cases are documented in medical literature. Among the three major form, localized variants are benign in nature. Localized LM is further subdivided into the following four subtypes: (1) discrete LM, which has firm, smooth, waxy or flesh-colored papules of 2 to 5 mm in size, numbering a few to hundreds on the limbs and trunk in a symmetric pattern. The papules are isolated or form confluent nodules or plaque and rarely resolve spontaneously[1]; (2) acral persistent papular mucinosis, which is characterized by a few to multiple, ivory to flesh colored papules of 2 to 5mm in size on the back of the hands, wrists, and occasionally the distal aspect of the forearms. Papules persist or increase without spontaneous resolution and occur predominantly in females[4] (3) cutaneous mucinosis of infancy, characterized by firm, opalescent papules located on the upper arms, especially the elbows, and the trunk without spontaneous resolution[1], and (4) nodular-type LM, characterized by multiple nodules on the limbs and trunk, with a mild or absent papular component[2].

Due to its rarity, only few numbers of studies are available which focus on pathogenesis, clinical variants and management of the disease. Our case did not match with any subtypes of localized LM and according to Rongioletti classification it categorized into 'Atypical Localized Not Well-specified Cases'. In a Medline search, there is no single report is found on 'atypical localized non specified cases' of LM.

To the best of our knowledge, this is the first case report of the condition in medical literature until now. Treatment of LM is always a challenge to physician. Different drug or treatment modalities are tried. But still there are no consensus regarding its treatment. However, localised form of LM is benign in nature and many drugs are successfully tried. There was no documentation or guideline for the treatment of atypical localized case.We treated our case successfully with systemic prednisolone.

Conclusion

Lichen Myxedematosus is a rare but a distinct entity with wide varieties of clinical feature. It is not well documented in medical literature and may be under diagnosed. Different types of disease are not well studied. There are also lacking of knowledge in cause and treatment of the disease. We have to work a lot to unveil the many facts of this distinct disease entity.

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