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ORIGINAL ARTICLE

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Frequency of bacterial infections in patients with cirrhosis of liver due to Hepatitis B virus

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Abstract

Patients with cirrhosis have increased risk of bacterial infection, sepsis, sepsis induced organ failure and death, are 2 times more likely to die from sepsis than individuals without cirrhosis, mortality reaches 38%, with septic shock may exceed 70%. The type of infection that occurs in Bangladesh may not be similar to other countries which is important to know for early and effective intervention to reduce morbidity and mortality. The aims and objectives of the study was to see the frequency of bacterial infections and association of type of infections with severity of liver disease in Bangladeshi patients of cirrhosis of liver due to Hepatitis B virus. The Cross sectional study was conducted at Department of Gastroenterology, BSMMU from February 2013 to March 2014 in patients with cirrhosis of liver due to Hepatitis B virus infection. Total 185 patients were enrolled. Cirrhosis due to other causes, HCC, associated DM, malignancy, secondary peritoneal infection were excluded. Severity of liver disease was assessed according to Child- Pugh criteria. Infections were identified by appropriate investigations.

Child-pugh class C, B, A were present in 118 (63.78 %), 49 (26.48 %), and 18 (9.72 %) cases respectively. Common infections were urinary tract infections (UTI) 40(21.60%), spontaneous bacterial peritonitis (SBP) 32(17.20%), pulmonary TB 20(10.80%), pneumonia 7(3.70%), and bacteremia 5(2.70%). There were no association between Child-Paugh classes and infective cases (Chi-square - 4.83, p =0 .089).UTI was more common than SBP. Decompensated cirrhosis (Child-pugh C) had more frequent episodes of bacterial infections than those with compensated cirrhosis.

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Introduction

Bacterial infections are common and often recurrent in cirrhosis, with high mortality [1]. It is the first cause of death in decompensated cirrhosis[2] and 7% death in compensated cirrhosis[3]. About 30% of patients with cirrhosis develop bacterial infection at the time admission or during hospital staying period [2]. High Child-Pugh score, variceal bleeding, low ascitic fluid protein level and prior episodes of spontaneous bacterial peritonitis (SBP) are associated with high bacterial infection[2]. The current prevalence of bacterial infections is 25% - 30% causing 30%-50% death in these patients[4]. 60% of bacterial infections are community-acquired and 40% are nosocomial[5].

The most common infections in cirrhosis are spontaneous bacterial peritonitis (SBP) (25%), urinary tract infections (UTI) (20%), pneumonia (15%), bacteremia and cellulitis (2%). Approximately 75% of bacterial infections are caused by gram-negative bacteria, e.g. Escherichia coli, Klebsiella spp. Enterobacter spp, P. aeruginosa, Vibrio spp. Aeromonas spp., 20.2% with gram positive, only 3.2% anaerobes [6].Prevalence of multiresistant bacteria infection is increaseing[2].

Due to altered and diminished immunity, increased shunting of blood away from the liver, qualitative dysfunction of the reticuloendothelial system, decreased opsonisation capacity of the ascitic fluid, increased intestinal permeability of bacteria, associated endotoxins – all increase susceptibility of infection in cirrhosis[1].

Once an overt infection occurs, it may lead to systemic inflammatory response syndrome (SIRS) or sepsis which can precipitate hypotension, renal dysfunction,

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encephalopathy, coagulopathy, and multiorgan failure[7].Cirrhosis increases risk to develop bacterial infection, sepsis, sepsis induced organ failure and death[8]. Cirrhotic patients are 2 times more likely to die from sepsis than individuals without cirrhosis[9]. The mortality reaches 38%[10], with septic shock may exceed 70%[11].

Bacterial infections can be asymptomatic or pauci-symptomatic, and have to be suspected in any cirrhotic patient with a sudden impairment of liver function[12]. Infection is independently associated with uncontrolled and early recurrent variceal bleeding[13]. Antibiotic prophylaxis decreases infections, rebleeding, mortality and improve prognosis. Early diagnosis of infection, appropriate antibiotic with appropriate dose and duration reduces mortality[4].

Cirrhosis of liver is common in Bangladesh, 61.15% case is due to hepatitis B virus [14]. The type of infection that occurs in our country may not be similar to other countries. This study was aimed to see the frequency and type of bacterial infections and association of type of infections with severity of liver disease in Bangladeshi patients of cirrhosis of liver due to Hepatitis B virus so that early and effective intervention can be done to reduce morbidity and mortality.

Materials and Methods

It is a cross sectional study conducted to observe the frequency of bacterial infections among patient with cirrhosis of liver due to Hepatitis B virus infection in department of Gastroenterology, BSMMU from February 2013 to March 2014. Cirrhosis was diagnosed by clinical and laboratory data or by liver biopsy. Cirrhosis due to other causes (e.g HCV), associated immunosuppressive condition that leads to infection (e.g Diabetes mellitus, Malignancy), hepatocellular carcinoma, secondary peritoneal infection was excluded.

Total 185 patients were enrolled in this study according to selection criteria. Informed written consent was taken. The particulars of the patients and clinical data were recorded in a pre-design data sheet. Patients were grouped into several child-pugh classes. For diagnosis of infection detail history, clinical examination and relevant investigations were done. For liver status alanine-aminotransferase (ALT), aspertate-aminotransferse (AST), alkaline phosphatase (ALP), Serum bilirubin, albumin, Prothrombin time (PT), Ultrasonogram of abdomen, endoscopy of upper gastrointestinal tract was done. Serological markers for Hepatitis B virus, HBsAg, HBeAg, Anti-HBc, were assessed. Anti-HCV, ferritin, ceruloplasmin were done to exclude other cause of cirrhosis of liver.

For diagnosis of infection one blood sample for culture and one sample for urine culture collected routinely in all patient of cirrhosis of liver due to hepatitis B virus either compensated or decompensated in the first 48h of admission. Blood and ascitic fluid collected into blood culture bottles at the bed side and incubated for 24 hours at 37 degree celcius. Afterwards blood sample were put in chocholate agar media and evaluated every 48 hours until 10th day. The ascitic fluid collected in patients with ascites for biochemical evaluation and total leukocytes count with percentage of neutrophil count as well as culture was made. Urine samples were incubated on MacConkey-agar media. Diagnosis of spontaneous bacterial peritonitis was made when the ascitic fluid presented with more than 250 neutrophils and /or positive cultures (irrespective of positive culture) and exclusion of other secondary causes of peritonitis[15].

Urinary tract infections was diagnosed mainly by the isolation of bacteria in the urine culture above 10^5 colony forming unit/ml but also by clinical symptoms and signs(dysuria, fever) and presence of pus cells (more than 10 leukocytes per high power field) in the urine[16,17].

The diagnosis of respiratory tract infections (pulmonary tuberculosis, pneumonia) was made by clinical symptoms and signs (fever, cough, productive sputum), positive radiological signs (consolidation, patchy opacities) and/or positive bacteriologic examination (sputum or blood culture)[2].

To diagnose Bacteremia- positive blood culture and symptoms and signs like fever, shivers and hypotension were used[18]. Other types of infections diagnosed by specific methods in accordance with the infectious process.

Child-Pugh score used to measure the severity of cirrhosis of liver. The score 7 = Child's A, 7-9= Child's B, 9= Child's C. Child's C was the worst form cirrhosis where decompensation raised with bad prognosis.

Statistical analysis:

The data collected during the study procedure presented in the form of table for quantitative data (e. g Frequency table) and Graphs and Charts. Mean, standard deviation and 95% confidence interval of bacterial infections calculated by using the statistical package for social science (SPSS) program 17.0. The data was expressed as frequency, mean, standard deviation (SD) and percentages and Chi square was done to see the association of bacterial infection with Child-Pugh classes. The continuous variables were expressed as mean and standard deviation

Results

Total 185 patients were enrolled in this study. Highest numbers of respondents were from 41-50 years of age covering 35.10% of the respondents. The mean age of the respondents was 47.89 years and SD ± 11.82. The lowest and highest ages of the patients were 21 years and 80 years. 170 (91.90%) were male and 15 (8.10%) were female.

Table I: History of the presenting complaints (N=185)

Presenting Complaints	Frequency	Percentage
Fever	145	78.40
Abdominal distension	145	78.40
Oedema	120	64.90
Jaundice	102	55.14
Cough	51	27.57
Haematemesis	42	22.70
Melaena	28	15.13
Haemoptysis	27	14.50
Disorientation	25	13.50
Dysuria	13	7.00
Polyuria	12	6.48
Unconsciousness	10	5.40

Common presenting complaints are shown in table 1, fever 145 (78.40%), abdominal distension 145 (78.40%), oedema 120 (64.90%), jaundice 102 (55.14%) was most common. Other complaints were cough 51 (27.57%), haematemesis 42 (22.70%), melaena 28 (15.13%), haemoptysis 27 (14.50%), disorientation were 25 (13.50%), dysuria 13 (7.00%), polyuria 12 (6.48%) and unconsciousness were 10 (14.50%).

Table II: Findings of Clinical examination(n=185)

Clinical examination	Frequency	Percentage
Ascitis	140	75.68
Fever	130	70.27
Oedema	120	64.90
Splenomegaly	106	57.30
Hepatomegaly	97	52.40
Jaundice	90	48.65
Testicular atrophy	90	48.65
Anaemia	82	44.32
Abdominal collateral veins	70	37.80
Gynaecomastia	50	27.00
Hair loss	50	27.00
Palmar erythema	45	24.30
Spidernaevi	40	21.60
Breast atrophy in female	3	1.62

On clinical examination, we found ascitis 140(75.68%), fever 130(70.27%), oedema 120 (64.90 %), splenomegaly 106 (57.30 %), hepatomegaly 97 (52.40%), jaundice 90 (48.65%), testicular atrophy 90(48.65%), anaemia 82(44.32%), abdominal collateral veins 70(37.80%), gynaecomastia 50(27.00%), hair loss 50(27.00%), palmar erythema 45(24.30%), spidernaevei 40(21.60%) and breast atrophy in female 3(1.62%) among the respondents.

Important laboratory findings were listed below in Table III

Table III: Laboratory findings among participants

Laboratory findings	Mean	Standard deviation ±SD)
ALT	81.84	13.3
AST	84.10	9.22
ALP	90.00	8.00
S. Bilirubin	1.90	1.44
S. Albumin	29.74	7.64
PT	15.08	2.85

Mean± SD ALT was 81.84±13.3 U/L, Mean±SD AST was 84.10±9.22 U/L, Mean± SD ALP was 90.00 ±8 U/L, Mean± SD S.Bilirubin 1.90 ±1.44mg/dl, Mean± SD S. Albumin 29.94 ±7.64gm/L, Mean± SD PT 15.08±2.85.

Table IV: Serological tests findings among participants:(n=185)

Serological tests	Frequency	Percentage
HBs Ag	170	91.90
HbeAg	110	59.46
Anti HBc	90	48.60

In Table-IV serological tests among 185 participants was shown in frequency and percentage in which HBsAg was positive 170 (91.90%) cases, HBeAg was present 110 (59.46%) cases and Anti HBc was present 90 (48.60%). Severity of cirrhosis was assessed with Child-Pugh score (table V)

Table V: Child- Pugh score among Participants (n=185)

Child- Pugh score	Frequency	Percentage
Child's A Below 7)	18	9.72
Child's B 7-9)	49	26.48
Child's C Above 9)	118	63.78
Total	185	100.00

Among 185 patients Child-pugh class C was present 118 (63.78 %) cases, Child-pugh class B was 49 (26.48 %), and Child-pugh class A was 18 (9.72 %) were present.

Table VI: Upper Gastrointestinal Endoscopy findings among participants (n=185)

Upper Gastrointestinal Endoscopy findings		Frequency	Percentage
Oesophageal varices	Yes	170	91.80
	No	15	97.20
Congestive gastropathy	Yes	57	30.80
	No	128	69.20

Oesophageal varices and Congestive gastropathy were present 170 (91.80%) and 57 (30.80%) cases respectively.

In USG ascites was detected in 140(75.68%) patients. In all biochemical and cytological analysis of ascetic fluid was done.

TableVII: Ascitic fluid study (Biochemical evaluation)

Biochemical evaluation				
	Minimum	Maximum	Mean	Standard deviation (±SD)
Protein	7.5 gm/l	45 gm/l	27.39gm/l	8.56 gm/l
Albumin	9 gm/l	43 gm/l	25.89 gm/l	8.23 gm/l
Glucose	3.60 mmol/l	9.50 mmol/l	7.5 mmol/l	1.14 mmol/l

In Table- VII, biochemical evaluation of ascitic fluid revealed mean protein was 27.39±8.56 gm/l, mean albumin 25.89±8.23 gm/l and mean glucose 7.5±1.14.

TableVIII : Ascitic fluid study (neutrophil count cut off value 250/cmm and lymphocyte count)

Ascitic fluid neutrophil count cut off value 250/cmm and lymphocyte count				
Ascitic fluid neutrophil count	Frequency	Percentage	Mean	Standard deviation (±SD)
>250 /cmm	32	22.85	231.00/cmm	75.00 /cmm
<250/cmm	108	77.15		
Total	140	100.00		
Lymphocyte			33.97 cells/mm^3	8 cells/mm^3

In table-8 mean neutrophil count was 231±75/cmm and mean lymplocyte count was 33.79±8 cells/cmm. 32(22.85%) had neutrophil count more than 250/cmm and 108(77.15%) had neutrophil count less than 250 cells/cmm.

Ascetic fluid culture was done in 140 patients and culture was negative.

Table IX: Blood Culture among Participants (n=185)

Blood Culture Result	Frequency	Percentage
No growth	180	97.30
E. coli	5	2.70
Total	**185**	**100.00**

In Table-IX Blood Culture was done in 185 patients, among them E. coli found in 5 (2.70%) cases and no growth of bacteria found in 180 (97.30%) cases.

Table X: Urine study among Participants:(n=185)

Urine R/M/E Findings	Frequency	Percentage
Pus cells >10/ HPF	40	21.63
Pus cells <10/ HPF	145	78.37
Total	**185**	**100.00**
Urine Culture Findings	**Frequency**	**Percentage**
Growth (E. coli >10^5 CFU /ml)	17	9.19
No growth	168	90.81
Total	**185**	**100.00**

CFU:Colony Forming Unit

In Table- X urine culture and routine and microscopic e amination (/ /E) was done in 185 patients. us cells >10/H F was found in frequency and percentage 40(21.63%) patients and pus cells <10/H F was found 145(78.37%) cases. Urine culture showed *E.coli* >10^5 CFU/ml in 17(9.19%) cases and no organisms in 168(90.81%) cases.

Table XI: Chest X-ray findings among Participants: (n=51)

Chest X-ray findings	Frequency	Percentage
Normal	24	47.00
Fibrosis in lungs	2	3.90
Patchy opacity in lung fields	6	11.76
Apical opacity	4	7.84
Pleural effusion	8	15.68
Consolidation	7	13.72
Total	**51**	**100.00**

Table-XI shows that among 185 Cirrhotic patients X-ray chest was done 51 pateints on the basis of clinical features (cough, fever and haemoptysis), among them 27 patients were found to have changes in Chest X ray, consolidation 7 (13.72%), fibrosis 2(3.90%), patchy opacity in both lung fields 6(11.76%), apical opacity

4(7.84%), and pleural effusion 8(15.68%).Normal X-ray findings was 24(47%) cases.

Table XII: Sputum findings among Participants: (n=51)

	Gram staining positive	Gram Staining negative	Total	AFB staining positive	AFB staining negative	Total
Frequency	7	44	51	20	31	51
Percentage (%)	13.73	86.27	100	39.22	60.78	100

In Table-XII among 185 patients sputum Gram and Acid Fast Bacilli (AFB) staining were done in 51 patients. Gram staining positive were 7 (13.73%) and AFB staining positive were 20 (39.22%).

Table XIII: Total Bacterial infections among Participants: (n=185)

Infections		Frequency	Percentage
Infection absent		81	43.75
Infection present		104	56.25
	Urinary tract infections(UTI)	40	21.60
	Spontaneous bacterial peritonitis(SBP)	32	17.20
	Pulmonary Tuberculosis(TB)	20	10.80
	Pneumonia	7	3.70
	Bacteremia	5	2.70

Table- XIII Among 185 cirrhotic patients, 104(56.25%) patients had infections. The frequency and percentage of bacterial infections were Urinary tract infections (UTI) 40(21.60%), Spontaneous bacterial peritonitis (SB) 32(17.20%), ulmonary TB 20(10.80%), neumonia 7(3.70%), and Bacteremia 5(2.70%).

Table XIV: Causative organisms in Infected Cirrhotic patients: (n==104)

Causative organisms	Frequency	Percentage
Organism not isolated	55	52.88
Organisms isolated	49	47.12
E.Coli (urine & blood culture)	22	21.15
Mycobacterium Tuberculosis (AFB staining of sputum)	20	19.24
Strepto pneumoniae (Gram staining of sputum)	7	6.73
Total	104	100.00

Table-XIV among 104 infected cases causative organisms were detected in 49 patients. Among them were *E.Coli* 22(21.15%), *Mycobacterum tuberculosis* 20(19.24%), *Strepto pneumoniae* 7(6.73%).

ycobacteria tuberculosis are aerobic acid fast bacilli. Acid-fast staining (Ziehl-Neelsen staining) of sputum it shows the red carbol fuchsin stain. *Escherichia coli (E.Coli)* are Gram negative rods.It grows on acconkey's agar media .E.Coli colonies have a characteristics green sheen. Streptococci (*Streptococcus pneumonia*) are Gram positive cocci arranged in pairs or short chains.In sputum it was seen ovel shape Gram positive diplococcic in Gram stain smears.

Table XV: Bacterial infections among Child- Pugh classes:

Child-Pugh class	Child's A (Below 7)	Child's B (7-9)	Child's C (Above 9)	Total
UTI	4(10.00%)	13(32.50%)	23(57.50%)	40((100.00)
SBP	1(3.10%)	11(32.50%)	20(62.50%)	32(100.00%)
Pulmonary TB	3(15.00%)	6(30.00%)	11(55.0%)	20(100.00%)
Pneumonia	1(14.30%)	5(71.40%)	1(14.30%)	7(100.00%)
Bacteremia	1(20.00%)	1(20.00%)	3(60.00%)	5(100.00%)
Total	10	36	58	104

Among 185 patients Child-pugh class A was 18 (9.72%) cases, class B was 49 (26.48%) and class C was 118 (63.78%). Bacterial infections found in child-pugh class A, UTI were 4(10.00%) cases, SB - 1(3.10%), pulmonary tuberculosis were 3(15.00%) cases, pneumonia were 1(14.30%) case and Bacteremia found 1(20.00%) case. In child-pugh class B UTI were found in 13(32.50%) cases, SB were 11(32.50%) cases, pulmonary TB were 6(30.00%) cases, pneumonia were 5(71.40%) cases and Bacteremia found in 1(20.00%) case. In child-pugh class C, UTI found in 23(57.50%) cases, SB were 20(62.50%) cases, pulmonary TB were 11(55.00)% cases, pneumonia were 1(14.30%) cases and Bacteremia were 3(60.00%) cases.

Table XVI: Association between Child- Pugh classes with infective cases:

Child Pugh	No infection n(%)	Infection n(%)	Total n(%)	Chi-square P-value
A	8(9.98%)	10(9.62%)	18(9.73%)	
B	13(16.05%)	36(34.62%)	49(26.49%)	$X^2=4.83$
C	60(74.06%)	58(55.76%)	118(63.78%)	
Total	81(100.00%)	104 (100.00%)	185 (100.00%)	p-value : 0.089 df=2

There were no association between Child- augh classes and infective cases. Chi-square value was found 4.83, p value was 0 .089 which was not significant at p-value < 0.05.

Discussion

In recent studies the prevalence of bacterial infections was present in cirrhosis of liver ranges between 25% and 30%[7,19]. This study showed the frequency of bacterial infections 104 (56.25%) and the most frequent types of infection was urinary tract infection (UTI), spontaneous bacterial peritonitis (SB), pulmonary tuberculosis, pneumonia and Bacteremia.

Spontaneous bacterial peritonitis (SB) is one of the most frequent types of infection in cirrhotic patients due to a deficiency of immune system, associated with factors which promote infection of the ascitic fluid such as the presence of previous upper gastrointestinal bleeding. It acts as a trigger for a number of severe complications such as hepatic encephalopathy and renal failure[18].

The identification of the infection of ascitic fluid is based on the result of diagnostic paracentesis. A polymorphonuclear leucocyte (N) count >250 cells/mm^3 is an important parameter for the diagnosis of SB as responsible bacteria in the ascitic fluid culture very infrequent. The low proportion of positive ascitic fluid cultures is probably due to the relatively low concentration of bacteria in the ascitic fluid as compared with the infections in the other organic fluid(e.g. urine)[20].

The data in literature concerning the frequency of bacterial infection suggest that SB is the most common infection (over 25% of cases) followed by urinary tract infection (20.00%) and pneumonia (15.00%).[21,22] But results in this study concerning cirrhotic patients are not similar in order and frequency: urinary tract infections was the most frequent (21.60%) followed by spontaneous bacterial peritonitis (17.20%) pulmonary tuberculosis (10.80%) pneumonia (3.70%) and Bacteremia (2.70%). Pulmonary tuberculosis were more frequent than in the literature.

Aetiologic agents of SBP were not isolated whereas 50% of aetiologic agents were isolated from other studies[23]. The low isolation rate can be e plained by low concentration of organisms in ascitic fluid and used non-automated culture methods.

The frequency of urinary tract infections in literature was the second most common bacterial infections in cirrhosis 16-18% after SB [2]. In this study, the frequency of UTI was the most common 21.60%.The aetiologic agent were isolated Gram negative organisms (*E.coli*).

ulmonary infections are common in cirrhotic patients. In literature the frequency of pneumonia was 21.37%[23]. In this study the frequency of pneumonia was 3.70%.The aetiologic agents were identified Gram positive cocci. In this study, pulmonary tuberculosis was found in 10.80% of cases.

Bacteremia without particular organ-specific source is increasingly common in cirrhosis.It is often caused by Gram negative enteric bacilli, enterococci and streptococcus spp[2,24]. In this study Bacteremia was found in 5(2.7%) cases.

The causative organisms isolated in infected cirrhotic patients were E.coli 22(21.15%), *Mycobacterium tuberculosis* 20(19.24%) and streptococci 7(6.73%).

Among 185 patients Child- ugh class A was 18 cases (9.72%), class B was 49 cases (26.48%) and class C was 118 cases (63.78%). Bacterial infections found in Child- ugh class A, UTI was in 4(10.00%) cases, SB was in 1(3.10%), pulmonary tuberculosis was in 3(15.00%) cases, pneumonia was in 1(14.30%) case and Bacteremia was found 1(20.00%) case. In Child- ugh class B UTI was found in 13 (32.50%) cases, SB was in 11(32.50%) cases, pulmonary TB was in 6 (71.40%) cases, pneumonia was in 5 (71.40%) cases and bacteremia was found 1(20.00%) case. In Child- ugh class C, UTI found in 23(57.50%) cases, SB was in 20 (62.50%) cases, pulmonary TB was in 11 (55.00%) cases, pneumonia was in 1(14.30%) case and Bacteremia was in 3 (60.00%) cases.

Bacterial infections were more frequently found in child-pugh class C. Chi-squre tests were done to see the association of bacterial infections with Child-pugh class. No statistically significant association was found (-value was 0.089, which was not significant at -value <0.05).

In conclusion, bacterial infections in patients with cirrhosis of liver due to hepatitis B virus are common. In this study, the most frequently found bacterial infections were urinary tract infections (UTI) than spontaneous bacterial peritonitis (SB). In literature, SB was the most commonly found bacterial infections. In this study, pulmonary tuberculosis was found. atients with decompensated cirrhosis (Child-pugh class C) were more frequent episodes of bacterial infections than those with compensated cirrhosis.

ecommendations:

- Early detection of infection.

- Use of early and effective Antibiotic prophyla is.
- Classical symptoms might not be present in infected cases, a clear & in depth investigations might help to find the infection process.
- In future more study will be required in large sample size or in population to better understand the pathogenesis of bacterial infections among cirrhotic patients.

Limitations :

In this study sample size was small, and anaerobic culture facility was not available.

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ORIGINAL ARTICLE

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Seroprotection level in Hepatitis B vaccinated medical students and nurses in Sylhet MAG Osmani Medical College and Hospital

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Abstract

This study was carried out with an aim to determine antibody levels and evaluate seroprotection in hepatitis B vaccinated medical students and nurses.In our study medical students and nurses who had completed 3 dose schedule of hepatitis B at least 5 years ago were enrolled. Total 80 serum samples of 40 hepatitis B vaccinated medical students and 40 vaccinated nurses of SOMCH were taken. Anti-HBs levels of the serum samples were detected by ELISA Method in the department of Microbiology, Sylhet MAG Osmani Medical College. Results Showed that out of eighty participants seventy six (95%) had anti-HBs above the protective level ie. ≥ 10 mIU/ml whereas four (5%) of the participants had antibody titre below the protective level. Group, time since vaccination, gender, age during first dose of vaccination in relation to Anti-HBs titre showed no significant difference. After > 15 Years protection conferred by Hepatitis B Vaccine still persisted as shown by high titre of Anti-HBs found in the study.

From this study it can be concluded that all medical students and nurses should not only receive and complete the three dose schedule of hepatitis B vaccine but also should have post-vaccination testing for the anti-HBs levels to document immunity.

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Introduction

HBV infection leads to a wide spectrum of liver disease ranging from acute hepatitis (including fulminant hepatic failure) to chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). Hepatitis is a major health problem in both developed and under developed countries as it affects about 3.5 billion individuals globally[1].

Bangladesh lies in an intermediate endemic region with a prevalence of 5% in the general population and this population is at high risk of acquiring infection. Hepatitis B (HB) vaccination is the most effective measure to prevent HBV infection and its consequences. Center for disease control and prevention (CDC) recommended HBV vaccination for all health care workers (HCW) in 1997. Recombinant hepatitis B vaccine for the prevention of hepatitis B virus infection is in practice in different parts of the world since its availability in 1986. Government of Bangladesh has also included hepatitis B vaccine in EPI schedule since 2005[2].Although the practice of vaccination against HBV has been started in our country for quite a few years but up till now there is no published data regarding the immunity level among the recipients of HB vaccines of different commercial brands available [3].

To achieve hepatitis B virus protection, two types of vaccines have been used- a plasma-derived vaccine and a recombinant hepatitis B vaccine. Both the vaccines were proven to be safe and effective in preventing HBV infection. The most licensed recombinant DNA hepatitis vaccine is a product of S gene consists of 226 amino acids.The recombinant vaccine most widely used is produced in yeast by inserting S gene in plasmid downstream to three genes of Saccharomyces cerevisiae, yeast that serves to promote production of HBsAg.

The protective immunity of Hepatitis B vaccine is directly related to the development of anti-HBs titre with a minimum level of 10mIU/ml whichis considered as protective level. On the basis of immune response (anti-HBs titre) to Hepatitis B vaccine that develops within one to si months after completion of vaccine schedule,

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vaccinated individuals are categorized into good responder (titre>100mIU/ml), hypo-responder (titre between 10-100 mIU/ml) and non-responder (titre<10mIU/ml)[4]. Both good and hyporesponder are protected against HBV infection but non-responder remains susceptible to HBV infection. Although antibody titres decline with time it should be reasonably 10mIU/mLat any time for acquiring immunoprotection against vaccinated individual[5].

Healthcare personnel represent a high risk population for HBV infection. Hepatitis caused by HBV is the most important infectious occupational hazard which medical students and nurses encounter. The factors responsible for thehigh risk of being infected by HBV are the high prevalence of HBV carriers in the population and the high contagiousness of HBV.

The practice of sero-testing after HBV vaccination is applied in the vast majority of European countries, not only for doctors and nurses but also paramedical, technical, and cleaning staff [6]. Serotesting after HBV vaccination is not widespread in our country and is not included in local vaccination strategy. A few studies in abroad reported the immune status against hepatitis B in health care workers but to the best of my knowledge there is no reported study vaccinated medical students and nurses. So, the present study was designed to assess seroprotection status of these two vulnerable groups.

Material and Methods

This observational study was carried out in the department of Microbiology Sylhet M.A.G Osmani medical college. Serum samples from eighty vaccinated individuals forty from each group were taken. Relevant data regarding vaccination status were taken in a predesigned questionnaire. Informed written consent of the participants were taken. The study was approved by the ethical review committee of Sylhet M.A.G Osmani medical college.

Collection of specimen

Approximately, 50 micro liter of serum was required. After proper aseptic precaution 4-5ml of venous blood was collected in a vaccutainer tube and was allowed to clot. Then it was centrifuged at 3000 rpm for 30 min. The serum layer was transferred carefully in to eppendorf tubes, properly capped, labeled and stored in -20^{0}c and analysis was done later.

Estimation of Anti-HBs level

The quantitative ELISA kit for measurement of Anti-HBs titre was manufactured by Enzo Diagnostics Inc, USA. For detection of anti-HBs in the kit, antigen "sandwich" ELISA method was used in which polystyrene microwell strips were pre-coated with recombinant HBsAg. Patient's serum or plasma sample was added to the microwells together with a second HBsAg conjugated to Horseradish Peroxidase (HRP-Conjugate). In case of presence of anti-HBs in the sample, the pre-coated and conjugated antigens were bound to the two variable domains of the antibody and during incubation, the specific immunocomplex formed was captured on the solid phase. After washing to remove sample and unbound HRP-Conjugates, Chromogen solutions containing Tetramethylbenzidine (TMB) and urea peroxide were added to the wells. In presence of the antigen- antibody-antigen (HRP) "sandwich" complex, the colorless Chromogens were hydrolyzed by the bound HRP-Conjugate to a blue-colored product. The blue color turned yellow after stopping the reaction with sulfuric acid. The amount of color intensity was measured and was proportional to the amount of antibody captured in the wells.

Results

A total of 80 serum samples from vaccinated medical students and nurses were estimated for Anti-HBs levels. Amongst the 80 samples 76 showed Anti-HBs level above the protective level ie.≥10 mIU/ml whereas four of the participants had antibody level below the protective level . The 80 participants in the study included both gender. Most of the participants were female 65% (n=52). The Anti-HBs titres between 10-100 mIU/ml was found in 27 (33.75%) of the participants, 49 (61.25%) individuals had titres>100 mIU/ml. 4(5%) had titres<10 mIU/ml.

Table I: Anti-HBs status of vaccinated participants in relation to time since vaccination. Chi square test was done to analyze the data.

Years elapsed after completion of vaccination	Anti-HBs titre mIU/ml			P value
	<10	10-100	>100	
5-9 (n=56)	4	17	35	NS
10-15 (n=23)	0	10	13	
>15 (n=1)	0	0	1	
Total	4	27	49	

NS: not significant

Out of the 80 subjects who were vaccinated 56 had completed vaccination 5-9 years ago, 23 had completed vaccination 10-15 years ago and 1 individual completed vaccination >15 years ago.

Table II: Mean Anti–HBs titre of male and female participants (n=80).

	Gender	Number	Mean
HBsAbTitre	Female	52	149.7173
	Male	28	159.3893

Table II shows Mean antibody titre was more in male than female participants.

Table III: Comparison of serum concentration of HBsAb level between students and nurses.

HBsAb level mIU/ml	Medical students (n=40)		Nurses (n=40)		P value
	Number	%	Number	%	
<10	1	2.5	3	7.5	NS
10-100	14	35	13	32.5	
>100	25	62.5	24	60	

NS: not significant

TableIII shows out of 80 participants one medical student and 3 nurses had titre below the protective level i.e. <10 mIU/ml. 14 medical students and 13 nurses had titre between 10-100 mIU/ml. 25 medical students and 24 nurses had a titre of >100 mIU/ml. No significant difference in Anti-HBs titre was seen between both groups.

Table IV: Anti-HBs titre of the participants in relation to age of starting of vaccination.

Age of starting of vaccination	Anti-HBs titre HBsAb level mIU/ml			P value
	<10	10-100	>100	
<18 (n= 41)	1	16	24	NS
18-25 (n=24)	1	7	16	
26-33 (n=15)	2	4	9	
Total	4	27	49	

NS: not significant

Table IV shows that 41 of the participants started vaccination at <18 years. 24 of the participants started vaccination between the age of 18-25 years and 15 between the age 26-33 years. There was no significant difference in Anti-HBs titre in relation to age at starting of vaccination.

Discussion

In this study the Antibody level of forty medical students and forty nurses who were vaccinated at least five years back were evaluated. Out of 80 participants four (5%) had titre below the protective level i.e. <10mIU/ ml rest had antibody titre above the protective level. Several factors may be attributed for decreased Anti-HBs status in vaccinated. Non response or hyporesponse at the time of vaccination or simply waning of Anti-HBs titre with time are the possible causes of Anti-HBs being below the protective level in the vaccinated four. Unresponsiveness to HB vaccine has been attributed to a number of environmental and genetic factors; the most important ones being the haplotype of HLA antigen and immunological tolerance. Other factors include male gender, old age, smoking, immunosupression and chronic disease[7].Inappropriate methods of vaccine preservation and administration, lax monitoring, frequent power outage, ignorance regarding expiry date also results in loss of vaccine potency.

Protection defined as Anti-HBs level ≥10 mIU /ml after three doses of HB vaccine has been reported to be 90-95% [8]. This finding is similar to the finding of our study in which 95% of the participants had titre above the protective value. No significant difference was seen between the anti-HBs titre of vaccinated participantsand time elapsed since vaccination in this study. In a study conducted on vaccinated medical students in Iran there was no significant association between immunity level and time since vaccination [9]which supports the finding of the present study.

Previous studies have demonstrated that the protection given by HBV vaccine during childhood and adulthood lasts at least 15–22 years in immunocompetent individuals [10,11].The present study findings also show that the immunity against Hepatitis B persists for several years. In the present study Anti-HBs levels >100 mIU /ml were found in a participant even 15 years after completion of vaccination (Table I). In a similar study conducted in the university of Peradeniya, Sri-Lanka showed that participants had Anti-HBs >100 mIU /ml even 14 years after last dose [12]. A study in India on Medical Students and other HCW's by Tripathi et al., (2011) found that 85% had protective levels even after 10 years of completion of vaccination[13].

In this study the mean anti-HBs titre of male and female participants were 159,38 mIU/ml and 149.71 mIU/ml respectively (Table II) .In a similar study conducted in Iran on vaccinated medical students Jahromi et al., (2013) found that there was no significant association between gender and HBs-Ab Level[9]. In this respect three studies conducted in Yasuj, Shahrekord and Rasht

cities of Iran, showed that females had higher titre than male[14,15,16]. In a cross sectional study on 150 vaccinated medical interns in India the average anti-HBs titer found among the male (561.7 IU/L) and female (665.33 IU/L) revealed no co-relation between the Immunological memory and gender[17]. Zamani et al., (2011) also found that there was no association between gender and anti-HBs titer[18].

Comparison of serum concentration between medical students and nurses in the present study showed no significant difference. Out of four participants with titre below the protective level 3 were nurses and one medical student. In terms of titre students had slightly higher titre than nurses. 62.5% students had titre>100 whereas 60% nurses had titre>100mIU/ ml (Table III). A study conducted on humoral response of HCW's 5 years post vaccination conducted in Israel showed no association between profession and Anti-HBs titres and supports the present study finding[19].

Anti-HBs titre of the participants showed no significant difference in relation to age of starting of vaccination in the present study (TableIV).The finding of the study is in concordance with a study conducted in Philadelphia on vaccinated HCW's were no statistical significance between titre and starting age of vaccination was seen [20].

As part of global strategy Bangladesh included HB vaccine in the National Expanded programme on immunization (EPI) and formed national policy. At present there is no policy programme to vaccinate adult population. Although three doses are sufficient to provide immunity booster doses are frequently given in our country without prevaccination screening or post vaccination serotesting. In USA, UK and other developed countries there is policy that clearly states these aspects of vaccination.Medical students and nurses due to their professional work are expected to be exposed to HBV from time to time. Boosting effect of this natural exposure to HBV on the immune status obtained through vaccination is not known. So it may be that the high titre Anti-HBs observed in health care workers after years of vaccination is due to the boosting effect of exposure to HBV encountered while handling HBV infected patients. This may not be the case in general population. So, the value of booster doses to boost immunity and to know persistence of immunity requires further evaluation with larger sample size encompassing different geographical location as it has financial implications for a poor country like Bangladesh.

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Effects of oral iron with folic acid supplementation on haematological status in pregnancy with anaemia

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Abstract

Iron deficiency anaemia (IDA) is the most wide-spread of all nutritional deficiencies in pregnancy.Routine screening and supplementation for IDA in anaemic pregnant women could improve maternal and infant health outcomes.Anaemia is more marked in second trimester and continued through the third trimester.This study was undertaken to see the effect of oral iron with folic acid supplementation initiated between 16 and 24 weeks of gestation for 12 weeks to meet the iron requirements of second and third trimester. A non-randomized uncontrolled trial was conducted on pregnant women attending the Outpatient Department of Obstetrics and Gynaecology, Sylhet MAG Osmani Medical college Hospital, Sylhet during the period from 1st July 2013 to 30th June 2014. Forty- six pregnant women with gestational age of 16-24 weeks having anaemia were treated with ferrous sulfate 200 mg and folic acid 0.5 mg three times daily orally for 12 weeks. Haematological studies included RBC parameters (e.g. Haemoglobin, PCV, MCV, MCH, MCHC, RBC count) and iron status (e.g serum iron and serum ferritin) level were measured before and after 12 weeks iron supplementation. Among forty-six, 14 patients dropped out. The study was carried out on 32 pregnant women with a mean age was 23.91 ± 4.52 (range, 18-35) years; 53.1% of patients were primiparas and mean gestational age was 20.22 ± 2.62 (range, 16-24) weeks.

The RBC parameters and iron status were changed in course of iron therapy. The mean haemoglobin, PCV, MCV and RBC count were increased by 9.83% ($p<0.001$), by 10.21% ($p<0.001$), by 3.42% ($p<0.001$) and by 6.52% ($p<0.001$) respectively after 3 months of iron supplementation.The mean MCH tended to increase (by 1.66%; $p=0.064$), while the mean MCHC level significantly decreased (by 1.7% $p=0.023$). Serum iron and serum ferritin level were increased significantly by 23.8% $p<0.001$) and by 101.9% ($p<0.001$) after 3 months treatment compared to pre-treatment level.

Our study suggest that oral iron supplementation given to pregnant women with anaemia for 12 weeks at gestational age of 16 to 24 weeks improved the haematological status throughout the second and third trimester of pregnancy.

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Introduction

Pregnancy is not just a matter of waiting to give birth but a joyful and a fulfilling period in a woman's life. It can also be one of the experiences of misery and suffering when complications or adverse circumstances compromise the pregnancy, causing ill health or even death.[1]Pregnancy complications are the important causes of maternal and infant mortality. Worldwide, anaemia contributes to 20% of all maternal death.[2] Around 2 billion people, amounting to over 30% of the world's population are anaemic, mainly due to iron deficiency. In developing countries of South Asia this proportion appear to be as high as 80%.[3] The prevalence of anaemia among pregnant women in Bangladesh is 39%.[4] Of all the nutritional causes of anaemia, iron deficiency is perhaps the most common and important because the physiological changes during pregnancy exert a demand for additional iron needed for delivery to the foetus.[5]

Maternal anaemia increases the risk of fetal growth retardation, prematurity, intrauterine death, premature rupture of membrane and infection. Maternal effects on pregnancy being abortion, preterm labour, pre-eclampsia, sepsis, postpartum haemorrhage and maternal

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and infant mortality.[6,7,8,9] There is a high demand for iron during pregnancy, daily requirement is 2–5 mg & total requirement throughout the pregnancy is 800-1000 mg.[10]This amount is difficult to obtain from the average diet. Several effects of pregnancy-nausea, vomiting, motility disorder with reflux esophagitis, indigestion make this even more problematic.[11] Diagnosis of IDA during pregnancy is difficult due to the morphological changes occur at a later stage.Serum ferritin has been regarded as the gold standard in establishing iron deficiency & is the most reliable and higher accuracy test than RBC indices although its cutoff point remains an issue.[7,11]

Anaemia is marked in second trimester (because of maximum haemodilution) and continued through third trimester. The challenge with injectable iron therapy is that free ferric iron produced severe dose-dependent toxicity including anaphylaxis as compared to oral therapy.In Bangladesh, oral iron along with folic acid supplementation is usually given routinely throughout the pregnancy. However, oral iron supplementation in first trimester is often associated with troublesome side effects resulting in failure and compliance. The present study was undertaken to see the effect of oral iron with folic acid supplementation during the period of 2nd and 3rd trimester on RBC parameters & iron status in a outpatient department setting.

Materials and Methods

A non-randomized uncontrolled trial was done to see the effect of oral iron with folic acid supplementation. Forty- six pregnant women of gestational age of 16-24 weeks with anaemia attending the Outpatient Department of Obstetrics and Gynaecology, Sylhet M.A.G. Osmani Medical College Hospital, Sylhet fulfilling the inclusion and exclusion criteria were selected.Inclusion criteria were pregnant women with haemoglobin concentration 8.0-11.0 gm/dl and serum ferritin less than 15 ng/ml. Exclusion criteria were pregnant women who are already on iron supplementation, twin pregnancy, other known co-morbidities like (e.g. thyroid, liver, rheumatic, renal, cardiovascular, pulmonary or neoplastic disease). Informed written consent was obtained from the patients after detailed explanation of purpose of the study and the study process. The clinical histories of the patients were noted. Each patient was examined thoroughly. All the findings, previous history and reports and investigations were recorded in a preformed data collection sheet prepared for this purpose.

Gestational age was calculated from the first day of last menstrual cycle. Haemoglobin level was estimated by cyanomethaemoglobin method.Before initiation of therapeutic intervention haemoglobin, PCV, MCV, MCH, MCHC and RBC count were estimated by CELL-DYN 3200 automated haematology analyzer (Abbott, USA) and were confirmed by conventional methods and formulas. Serum iron was estimated using biochemistry end point method by semi-auto biochemistry Analyser (Humalyzer 3000, Human Germany).Serum ferritin estimation were carried out by AxSym System Random Access Multibatch Immunoassay Analyzer (Abbott, USA).

Oral iron with folic acid (Ferrous sulphate 200 mg and folic acid 0.5 mg) supplementation were given 3 times daily starting between 16 and 24 weeks of gestation for 12 weeks.12 weeks following oral iron and folic acid supplementation when the study participants attended the OPD for second antenatal visit, 5 ml blood was again collected for study of the haematological parameters. At the end of 2nd and 6th weeks the patients were inquired for any adverse effects over cell phone and also finally at the second visit following 12 weeks of oral iron supplementation. All relevant findings were recorded in a preformed data collection sheet designed for the study. Quantitative data were expressed as mean and standard deviation and comparison were performed by paired t test. Qualitative data were expressed as frequency and percentages and comparison was performed by Chi-Square (X^2) test. Statistical analysis was performed by using SPSS (Statistical package for social science) for windows version 16.0.

Results

In this study, 46 patients fulfilled exclusion and inclusion criteria. Among them 14 patients dropped out. Of them 9 patients failed to attend follow up visit after 12 weeks and 5 patients did not satisfy study protocol (irregular intake of drug, stop due to ignorance). The study was carried out on 32 pregnant women with a mean age was of 23.91±4.52 (range 18 to 35) years. 53.1% of patients were primiparas and mean gestational age was 20.22±2.62 (range, 16-24) weeks.

Table- I shows, the comparison of different RBC parameters in pregnant women before and at the end of 12 weeks iron treatment. The mean haemoglobin level was 10.45±0.66 gm/dl before initiation of iron supplementation and at the end of 3 months iron therapy the mean haemoglobin level was 11.47±0.84 gm/dl resulting in increase of 9.83%. The haemoglobin

mean gestational age of our study was 20.22±2.62 weeks. On the other hand Subhadra et al found the mean gestational age was 23.94 weeks.[16]

Before initiation of iron supplementation the mean haemoglobin level was 10.45±0.66 gm/dl and at the end of iron treatment the level was 11.47±0.84 gm/dl. Halimi et al found that the mean haemoglobin level was 9.35±1.62 gm/dl and after treatment it was 11.20±0.28gm/dl.[17]In this study the mean PCV level of the pregnant women was 30.79 ± 2.70 percent and after 12 weeks iron supplementation 33.87±2.81 percent, p<0.001, which was statistically significant. This result was similar with the study of Kumar et al. that mean PCV level was 30.07±2.53 percent and increased significantly to 33.40±3.24 percent. The mean MCH level was increased from pre-treatment level to end point of iron supplementation but did not attain the level of significance (MCH=29.49±1.50 pg; p=0.064). Kumar et alfound that the MCH level of the pregnant women increased significantly from pre-treatment level to end point of iron supplementation (30.26±3.23 pg).[18]

The mean MCHC level of the pregnant women was recorded 34.47±1.63 gm/dl and after treatment the MCHC level decreased significantly (MCHC=33.85 ±1.42 gm/dl; p=0.023), while Kumar et al observed that the MCHC level of the pregnant women with iron deficiency anaemia increased significantly from pre-treatment level to end point of iron supplementation (34.68±3.16 gm/dl).[18] Kochhar et al also observed that MCHC level of the pregnant women with iron deficiency anaemia increased significantly from baseline level.[14]The mean RBC count increased significantly from initial level (3.89 ±0.35 mil/ µl) (p<0.001). This result was consistent with the study findings of Neeruet al.[19]

The present study showed that the mean serum iron level of the pregnant women was 30.31±10.05 µgm/dl and after 12th weeks (mean serum iron level of 37.53±7.20 µgm /dl; p<0.001) which was significant. This result was correlated with the study of Dede et al. that the mean serum iron level (before 34.5±12.4 mg/dl and after 67.8±32.2 mg /dl).[20] In our study the serum ferritin level of the pregnant women with iron deficiency anaemia was 10.46±4.38 ngm/ml and increased significantly from baseline treatment (21.12±9.36 ngm/ml;p<0.001). Neeru et al. found that the serum ferritin level of the pregnant women was 14.74±7.55 ngm/mland after treatment it was 27.33±7.55 ngm/ml.[19]Inthis study 11 (34.4%) patients experienced adverse effects. The recorded adverse effects were epigastric pain in 6.3%, nausea or vomiting in 15.6%, constipation 9.4% and diarrhoea in 3.1% patients. These findings were almost similar to the study of Kochhar et al that oral iron supplementation developed headache in 2.0%, nausea in 6.0%, Heartburn in 4.0%, constipation in 8.0% and diarrhoea in 4.0% of patients.[14]

In conclusion, iron supplementation for IDA in anaemic pregnant women improve maternal haematological parameters. RBC parameters e.g. haemoglobin concentration, packed cell volume, mean corpuscular volume, red blood cell count and iron status e.g. serum iron and serum ferritin increased; while the mean corpuscular haemoglobin concentration decreased at the end of 12 weeks iron supplementation. Our study suggests that oral iron therapy may be given safely to pregnant women with iron deficiency anaemia to improve haematological status.

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ORIGINAL ARTICLE

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Effect of Pitavastatin and Atorvastatin on Lipid profile, Troponin and C-reactive protein in Diabetic Dyslipidemic Patients.

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Abstract

This prospective comparative study was conducted in the outpatient department of Medicine of Sylhet MAG Osmani medical college hospital, Sylhet and Sylhet Diabetic hospital, Sylhet during the period from July 2013 to June 2014. Total 40 diabetic dyslipidemic patients attending the above mentioned outpatient departments were selected and were grouped into Group-A and Group-B. Patients of group-A were given Atorvastatin 10 mg daily and patients of group-B were given Pitavastatin 2 mg daily for 6 months. Each patient was followed up at 3rd month and at 6th month of treatment. At each follow up fasting lipid profile, serum troponin-I and serum CRP were assessed along with baseline fasting lipid profile. Serum total cholesterol level ($p<0.001$), serum triglyceride level ($p<0.001$) and serum LDL-cholesterol level ($p<0.001$), serum C-reactive protein and troponin-I were decreased significantly from baseline to end point of treatment in both groups. But there was no significant difference in percentage elevation of serum HDL at 6th month of treatment ($p=0.860$) in Atorvastatin treated group while a significant difference in percentage elevation of serum HDL at 6th month of treatment ($p=0.001$) was observed in Pitavastatin treated group. Thus Pitavastatin at a dose of 2 mg/day is not inferior to Atorvastatin at a dose of 10 mg/day in treating patients with diabetic dyslipidaemia rather it is superior in the percent elevation of HDL.

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Introduction

Cardiovascular disease (CVD) is a major health problem throughout the world and a common cause of premature morbidity and mortality.[1] The incidence of cardiovascular disease (CVD) is more common in patients with type 2 diabetes than in the general population.[2] Dyslipidemia, including elevated low-density lipoprotein cholesterol (LDL-C), triglyceride (TG) concentrations and low high-density lipoprotein cholesterol (HDL-C) concentration, are risk factors for coronary heart disease(CAD).[3] High concentration of LDL cholesterol and low levels of HDL cholesterol are able to promote atheroma formation.[4] Therapy with HMG-COA reductase inhibitors or statins, has provided the principal pharmacological innovation in the treatment of hypercholesterolemia for prevention of CAD in recent years.[5] During the past few years, paradigm shifts have witnessed understanding of the role of inflammation in atherosclerosis and its complications.[6] High-sensitive C-reactive protein (CRP), a marker of inflammation, has been identified as an independent predictor of adverse cardiac events in healthy populations and in patients with coronary artery disease.[7] Statins have a wide range of biologic effects in addition to lipid lowering including reductions in the levels of C-reactive protein (CRP)[8]. Multiple studies have demonstrated that elevated levels of CRP are clearly associated with increased CV risk.[9, 10] Minute myocardial damage, which can become detectable with cardiac sensitive and specific biomarkers such as troponin I, has been documented in patients with heart failure and stable coronary artery disease. Elevated serum troponin level is directly

proportional to the disease severity and prognosis.[11, 12] Pitavastatin, a potent inhibitor of HMG-CoA reductase, is now available in several Asian countries. In a human cell line (HepG2), Pitavastatin inhibited cholesterol synthesis 2.9 and 5.7 times more potently than Simvastatin and Atorvastatin respectively.[13] On the other hand, Pitavastatin increases serum levels of HDL-C although it does not have harmful effects on glucose tolerance.[14] Little is known about the role of Pitivastatin and Atorvastatin on dyslipidaemia, CRP and troponin-I in diabetic dyslipidemic patients.[15] We performed the present study to compare the effectiveness of Pitivastatin and Atorvastatin in diabetic dyslipidemic patients with a low HDL-C level, and to evaluate whether Pitavastatin could affect the lipid profile, inflammatory marker and biomarkers indicating myocardial stress and injury in these patients.

Materials and Methods

This prospective comparative study was conducted in the outpatient department of Medicine of Sylhet MAG Osmani medical college hospital, Sylhet and the outpatient department of Sylhet Diabetic hospital, Sylhet during the period from July 2013 to June 2014. Study population was diabetic dyslipidemic patients attending the above mentioned outpatient department during study period and study sample were 40 selected on the basis of inclusions and exclusion criteria after a thorough history taking, physical examination and fasting lipid profile. By simple random sampling they were divided into two groups (group-A and group-B) with 20 patients in each group. Informed written consent was obtained from each patient. Along with fasting lipid profile, serum troponin-I and serum C-reactive protein were assessed in all at baseline. Patients of group-A were given 10 mg Atorvastatin daily for 6 months and patients of group-B were given 2 mg Pitavastatin daily for 6 months. Each patient was followed up at 3rd months and at 6th month of treatment period. At each follow up (3rd and at 6th month of treatment) fasting lipid profile, serum troponin-I and serum C-reactive protein were assessed along with clinical data review and treatment-emergent adverse events (TEAEs) recording for efficacy assessment. Standard enzymatic methods were adopted for measurement of fasting serum total cholesterol and triglyceride. The serum HDL-C level was measured using the direct method. The LDL-C level was determined using Friedwald's equation as follows: LDL-C= TC - (HDL-C + TG/5). Troponin-I were measured using a fluorecence immunoassay and CRP was measured by a dry chemistry microslide method. Primary variables were HDL, LDL, Total cholesterol, Triglyceride, Troponin-I and CRP. Secondary variables were age and sex.

Data were processed and analyzed with the help of computer program SPSS (Statistical package for social sciences) 21.0 version. Quantitative data is analyzed by mean and standard error and comparison are done between the groups by unpaired t-test and within the groups of before and after measurement by paired t-test. Qualitative data is analyzed by frequency and percentage and comparison are done between the groups by Chi-Square (χ^2) test. A probability (p) value of < 0.05 is considered statistically significant.

Results

In course of study period 2 patients from group-A and 1 patient from group-B failed to complete the follow up. So, 18 patients of group-A and 19 patients of group-B were analyzed in this study. There were 7 (38.9%) male and 11 (61.1%) female in the Atorvastatin treated group; while 6 (31.6%) male and 13 (58.4%) female in the Pitavastatin treated group. The sex difference between the groups was not significant (x^2=0.217; p=0.642) suggesting the study was a sex matched one.The mean age of Pitavastatin and Atorvastatin treated group were 47.05 ± 1.81 (mean ± SE) and 47.89 ± 2.11 years respectively. The mean age of Atorvastatin and Pitavastatin group did not differ (t=0.320; p=0.764) suggesting the study was an age matched one.Results are presented in tables(Table I –Table V).

Table I: Effect of Atorvastatin and Pitavastatin on serum total cholesterol and triglyceride.

Lipid parameter		Atorvastatin group(n=18)	Pitavastatin group(n=19)	*p value
Total Cholesterol (mg/dl) (Mean ± SE)	At 0 month	201.11 ± 7.63	202.89 ± 16.63	p=0.923
	At 3rd month	187.50 ± 7.63	191.26± 13.37	p=0.811
	At 6th month	169.89 ± 7.50	166.32± 11.17	p=0.798
	†p value	p<0.001	p<0.001	
Triglyceride (mg/dl) (Mean ± SE)	At 0 month	257.00 ± 27.34	195.47± 19.67	p=0.074
	At 3rd month	229.39± 22.10	174.74± 15.44	p=0.048
	At 6th month	189.44 ± 15.26	156.58± 12.96	p=0.108
	†p value	p<0.001	p<0.001	

†p –ANOVA and *p- Unpaired t test

Table II: Effect of Atorvastatin and Pitavastatin on serum LDL and HDL

Lipid parameter		Atorvastatin group(n=18)	Pitavastatin group(n=19)	*p value
LDL (mg/dl) (Mean ± SE)	At 0 month	133.17± 11.92	138.68± 12.56	p=0.753
	At 3rd month	120.39± 11.26	122.37± 9.02	p=0.981
	At 6th month	111.28± 9.82	111.68± 8.68	p=0.975
	†p value	p<0.001	p<0.001	
HDL (mg/dl) (Mean ± SE)	At 0 month	37.67± 1.11	35.68± 0.89	p=0.162
	At 3rd month	38.83± 0.58	37.58± 0.85	p=0.238
	At 6th month	38.89± 1.13	38.94± 0.64	p=0.964
	†p value	p<0.001	p<0.001	

†p –ANOVA and *p- Unpaired t test

Table III: Effect of Atorvastatin and Pitavastatin on serum CRP and troponin-I

Lipid parameter		Atorvastatin group(n=18)	Pitavastatin group(n=19)	*p value
Serum C-reactive protein (mg/L) (Mean ± SE)	At 0 month	4.48± 0.22	4.36± 0.21	p=0.706
	At 3rd month	4.30± 0.21	4.15± 0.21	p=0.615
	At 6th month	4.10± 0.21	4.06± 0.20	p=0.891
	†p value	p<0.001	p<0.001	
Serum troponin I (ng/ml) (Mean ± SE)	At 0 month	0.027± 0.008	0.021± 0.003	p=0.439
	At 3rd month	0.020± 0.007	0.015± 0.003	p=0.495
	At 6th month	0.012± 0.003	0.012± 0.003	p=0.906
	†p value	p<0.001	p<0.001	

†p –ANOVA and *p- Unpaired t test

Table–IV: Percentage change in serum HDL

Study group	Serum HDL % elevation		*p-value
	At 3rd month	At 6th month	
Atorvastatin group (n=18)	3.89±1.76	4.42±3.69	p=0.860
Pitavastatin group (n=19)	5.42±1.02	9.60±1.27	p=0.001
†p- value	p=0.452	p=0.184	

†p –Unpaired t test and *p- Paired t test

Table V: Effect of Atorvastatin and Pitavastatin on percentage change in serum cholesterol, triglyceride and LDL

Lipid parameter		Atorvastatin group(n=18)	Pitavastatin group(n=19)	†p-value
Serum cholesterol % reduction (Mean ± SE)	At 3rd month	–6.70±1.48	–4.67±0.93	p=0.248
	At 6th month	–15.57±1.70	–17.06±1.50	p=0.514
	*p value	p<0.001	p<0.001	
Serum triglyceride % reduction	At 3rd month	–9.52± 1.55	–9.08±1.66	p=0.849
	At 6th month	–22.64 ±1.73	–17.68±1.88	p=0.139
	*p value	p<0.001	p<0.001	
Serum LDL % reduction (Mean ± SE)	At 3rd month	–9.17±2.31	–9.18±2.29	p=0.998
	At 6th month	–15.41±2.69	–17.23±2.32	p=0.609
	*p value	p=0.005	p<0.001	

†p –Unpaired t test and *p- paired t test

Discussion

Elevated low-density lipoprotein cholesterol (LDL-C) and non–high-density lipoprotein cholesterol (total cholesterol minus HDL-C) are recognized as major risk factors for cardiovascular disease (CVD).[16] Most cardiovascular risk reduction strategies for individuals with dyslipidemia focus on controlling LDL-C and non–HDL-C levels, with specific targets based on a person's global risk.[17,18] Again epidemiological studies consistently showed that low HDL cholesterol to be an independent risk factor for coronary heart disease.[19] In our study at baseline level no significant differences were found between Atorvastatin group and Pitavastatin group regarding age and sex related characteristics, so confounding the results by these factors was excluded. In this study serum total cholesterol level (p<0.001), serum triglyceride level (p<0.001), and serum LDL-cholesterol level (p<0.001) were decreased significantly from baseline to end point of treatment of Atorvastatin at 6th month; while serum HDL-cholesterol level (p<0.001) was increased significantly from baseline to end point of treatment of Atorvastatin at 6th month. Furthermore the percentage reduction of serum cholesterol (p<0.001), serum triglyceride level (p<0.001), and serum LDL-cholesterol level (p=0.005) were substantially decreased from baseline to end point of treatment of

Atorvastatin at 6th month but there was no significant difference in percentage elevation of serum HDL at 6th month of treatment (p=0.860). A study by Goudevenos et al. observed greater reduction of total cholesterol, LDL-cholesterol and triglyceride while HDL-cholesterol level did not significantly changed from baseline. The greater lipid lowering effects might be due to higher dose (20mg) of Atorvastatin used by this author.[20]Another study by Shukla et al. reported almost similar effects on dyslipidemia. Their study design and doses schedule was identical to our study. They observed 13.9% fall of LDL-cholesterol, 9.7% fall of total cholesterol and 16% fall of serum triglyceride; while HDL-cholesterol did not increases markedly from baseline to end point of study.[21]

On the other arm of this study, serum total cholesterol level (p<0.001), serum triglyceride level (p<0.001) and serum LDL-cholesterol level (p<0.001) were decreased significantly from baseline to end point of treatment of Pitavastatin at 6th month; while serum HDL-cholesterol level (p<0.001) was increased significantly from baseline to end point of treatment of Pitavastatin at 6th month. Furthermore the percentage reduction of serum cholesterol (p<0.001), serum triglyceride level (p<0.001) and serum LDL-cholesterol level (p<0.001) were substantially decreased from baseline to end point of treatment of Pitavastatin at 6th month; while a significant difference in percentage elevation of serum HDL at 6th month of treatment (p=0.001) was observed. Similarly, a study by Budinski et al. with Pitavastatin showed that the percentage reduction of serum cholesterol, serum triglyceride level and serum LDL-cholesterol level were significant from baseline to end point of treatment of Pitavastatin; while a significant difference in percentage elevation of serum HDL at end point of treatment was also observed.[22]

In the present study, the reductions in LDL-C from baseline to end point of treatment of Atorvastatin group was 15.41% and 17.27% in Pitavastatin group. The percentage reduction in LDL-C between Atorvastatin and Pitavastatin group did not differ significantly (p=0.609). Similar findings was found by Lee et al.[23]In this study the percentage reduction of serum total cholesterol from baseline to end point of treatment of Atorvastatin group was 15.57% and was 17.57% in Pitavastatin group. The percentage reduction in serum total cholesterol between Atorvastatin and Pitavastatin group did not differ significantly (p=0.514).But another study by Sansanayudh found reduction of total cholesterol (TC) levels from baseline was significantly different between the Pitavastatin (28%) and Atorvastatin (32%) groups (p = 0.005).[24] In the present study, the percentage reduction of serum trigyceride from baseline to end point of treatment of Atorvastatin group was 22.65% and was 17.68% in Pitavastatin group. The percentage reduction in serum trigyceride between Atorvastatin and Pitavastatin group did not differ significantly (p=0.139).A study by Sasaki et al. found that there was no significant differences between the Pitavastatin and Atorvastatin groups in terms of the mean (SD) percent change in trigyceride at the end of the study (-9.9 [41.7] vs -11.0 [56.9] mg/dL; p=0.68).[25] In the current study the percentage change of serum HDL-C from baseline to end point of treatment of Atorvastatin group was 4.42% and was 9.60% in Pitavastatin group. The percentage change in serum HDL-C between Atorvastatin and Pitavastatin group did not differ significantly (p=0.184).A study by Budinski et al. found no significant percentage reduction of serum HDL-C between Atorvastatin and Pitavastatin group (p=0.840).[22]

Statins have a variety of pleiotropic properties, including their ability to induce dose-dependent decreases in the levels of CRP and other inflammatory biomarkers.[8,26]In this regard the present study showed significant reduction (p<0.001) of serum C-reactive protein at the end point of treatment with both Atorvastatin and Pitavastatin but no significant difference was observed between two treatment groups before initiation of treatment (p=0.706), 3rd month (p=0.615) and 6th month (p=0.891) of treatment. Similarly Matsubara et al. found that pitavastatin 2mg/day decreased the level of hs-CRP significantly in patients with metabolic syndrome.[27]

Our study also showed significant reduction of serum troponin-I at the end point of treatment with both Atorvastatin (p<0.005) and Pitavastatin (p<0.001)but no significant difference was observed between two treatment groups before initiation of treatment (p=0.706), 3rd month (p=0.615) and 6th month (p=0.891) of treatment. In a study by Ibuki et al., they observed no significant changes in the hsTnT for six months after the commencement of pitavastatin treatment.[15]

In Atorvastatin treated group, 7 (33.3%) patients experienced adverse effect and in Pitavastatin treated group, 6 (31.6%) patients experienced adverse effect. There was no statistical significant difference between the groups in respect to the adverse effects (p=0.737). Adverse effects reported in this study were mild and

no discontinuation was needed. The most frequently reported treatment-related adverse effect being nasopharyngitis (3.2% in Pitavastatin 2 mg; 3.9% in Atorvastatin 10 mg).Both Atorvastatin and Pitavastatin were well tolerated in studies by Sansanayudh et al. and Sasaki et al.[24, 25]

Finally it can be concluded that, Pitavastatin at a dose of 2 mg/day is as effective as Atorvastatin at a dose of 10 mg/day in reducing LDL-C, TG, TC, troponin -I and C-reactive protein; and increasing HDL-C concentrations in the management of diabetic dyslipidaemia. The safety and tolerability profiles of both drugs were similar, with no significant dose-related adverse effects. Thus Pitavastatin at a dose of 2 mg/day is not inferior to Atorvastatin at a dose of 10 mg/day in treating patients with diabetic dyslipidaemia rather it is superior in the percent elevation of HDL. Overall, this study suggests that Pitavastatin could be considered an effective alternative to Atorvastatin in the treatment of diabetic dyslipidaemia.

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Study of risk factors of retinal venous occlusive diseases

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Abstract

Retinal vein occlusion is a cause of significant loss of vision. This case-control study was conducted in the Department of Ophthalmology, BIRDEM, Dhaka during the period from May 2009 to September 2009 to find out risk factors for Retinal Vein Occlusion. Patients with retinal vein occlusion attended in the Department of Ophthalmology, BIRDEM, Dhaka and fulfilling the inclusion & exclusion criterias were included in this study. Control were age and sex matched patients without retinal vein occlusions attending the Department of Ophthalmology, BIRDEM, Dhaka.

Thirty three patients with retinal vein occlusions were included in case group [19 (57.6%) male and 14 (42.4%) female; mean age, 62.4 (SD ± 10.0) years] and 33 patients without retinal vein occlusions in control group [15 (45.5%) male and 18 (54.5%); mean age, 61.6 (SD ± 8.5) years]. Both groups were similar in age and sex (p>0.05 each).

The patients with hypertension were 6.5 times more likely to develop retinal venous occlusion compared to that of control group (21 (63.6%) vs 7 (21.2%); OR=6.500; 95% of CI=2.174–19.435; p<0.001) and patients with glaucoma were 4.3 times more likely to develop retinal venous occlusion as compared to that of control group (10 (30.3%) vs 3 (9.1%); OR=4.348; 95% of CI=1.072–17.629; p=0.030).

Risk of development of retinal venous occlusion in smoker, over weight patients (BMI ≥25 Kg/M^2) (OR=1.129; 95% of CI=0.429-2.971; p=0.805) and hypercholesterolaemia (OR=1.282; 95% of CI=0.482–3.410; p=0.618) were statistically not significant.

Hypertension and glaucoma are significant risk factors in the development retinal venous occlusion.

[OMTAJ 2016; 15(1)]

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Introduction

Retinal vein occlusion (RVO) is a common retinal vascular disorder that is characterized by intraretinal hemorrhages, dilation and increased tortuosity of the retinal veins, capillary telangiectasis, cotton wool spots, optic disk swelling, and retinal edema. Decreased visual acuity is very common in RVO[1].

RVO is the most common retinal vascular disease after diabetic retinopathy. It has been associated with an increased risk of cardiovascular mortality and stroke[2,3]. RVO is an obstruction of the retinal venous system by thrombus formation.

Epidemiological studies, mostly in white populations, indicate that the prevalence of RVO ranges from 0.3% to 1.6% in the general population[4,5,6] RVO occurs especially in middle-aged and older individuals[7].

Depending on the area of retinal venous drainage effectively occluded it is broadly classified as either central retinal vein occlusion, hemispheric retinal vein occlusion, or branch retinal vein occlusion. Hayreh (2005)[8] observed that each of these has two subtypes. The former two can be subdivided into ischemic and nonischemic central retinal vein occlusion or hemispheric retinal

Systemic risk factors associated with retinal vein occlusion include hypertension [3,6,9,10,11], diabetes mellitus[3,6,9], cerebrovas cular disease [3,11], cardiovascular disease, increased body mass index, smoking [12], and peptic ulcer [3]. Ocular risk factors associated with retinal vein occlusion include glaucoma [9,10,12], shorter axial length[11] and focal arteriolar narrowing and arteriovenous (AV) nicking [6,7]. Hematologic factors reportedly associated with retinal vein occlusion include elevated erythrocyte sedimentation rates[9] and elevated hematocrits [2].

In our country a good number of patients suffer from RVO either branch retinal veins occlusion or central retinal veins occlusion. For management purpose it is essential to identify the risk factors for causing retinal vein occlusions. This study will help to set a management protocol for retinal vein occlusion patients in our country.

Materials and methods

This case-control study was conducted in the Department of Ophthalmology, BIRDEM, Shahbag, Dhaka from May 2009 to September 2009 in patients with retinal vein occlusion fulfilling the inclusion criteria were the study population in this study. The protocol was approved by institutional ethical committee of BIRDEM, Shahbag, Dhaka before the commencement of the study. Informed written consent was obtained from the patients. A total of 33 patients with retinal vein occlusion were selected according to inclusion criteria(by purposive sampling technique) and enrolled as cases (group-A); and age and sex matched 33 subjects without retinal vein occlusion attending the Department of Ophthalmology were taken as control (group-B). All the patients were evaluated by detailed history and clinical examination. Complete ophthalmological examination was done. It included Visual acuity by Snellel's Chart. Slit lamp examination for anterior segment examination. Measurement of intraoccluar pressure were done by Applanation tonometer. Fundus examinations were carried out by direct and indirect ophthalmoscope. Relevant findings were recorded in the pre-designed data collection sheet. Fasting blood of patients were analysed for lipid profile. Fundus- fluorescent angiography was used to detect Branched retinal vein Occlusion (BRVO) and Central Retinal Vein Occlusion (CRVO). Perimetry (Humphey) was done. Clinical and laboratory data were recorded systematically in a predesigned data sheet.

Statistical Analysis: Data Collection: Data were collected in a pre-designed data collection sheet & they were processed and analyzed with the help of SPSS (Statistical package for social sciences) Version 16.0.

Results

This case-control study was conducted with a total of 66 patients were selected during the study period from May 2009 to September 2009 according to inclusion criteria. Thirty three patients with retinal vein occlusion were enrolled in case group and another 33 patients other than retinal vein occlusion, attending the Department of Ophthalmology, BIRDEM, Shahbagh, Dhaka were enrolled in control group. The results of the study were as follows: The age of the patients ranged from 42 to 80 years with the mean age of 62.4 (SD ± 10.0) years in group-A; while the age of the patients ranged from 43 to 79 years with the mean age of 61.6 (SD ± 8.5) years in group-B. There were 19 (57.6%) male and 14 (42.4%) female in the group-A; whereas 15 (45.5%) male and 18 (54.5%) female in group-B. Group-A and group-B did not show any statistically significant difference in relation to sex (χ^2=0.971; p=0.325).

Table-I: Distribution of patients by side of involvement

Laterality	Study groups		*P* value
	Group-A (n=33) Frequency (%)	Group-B (n=33) Frequency (%)	
Left	15 (45.5)	17 (51.5)	P=0.805
Right	18 (54.5)	16 (48.5)	
Total	33 (100.0)	33 (100.0)	

*Chi –Square (χ^2) Test was applied to analyze the data. Figure in the parenthesis indicates corresponding percentage.

Distribution of patients according to visual acuity was shown in figure-1. Visual acuity was >6/18 to 6/60 was in 12 (36.4%) patients, >3/60 to PL PR was in 10 (30.3%) patients, >6/60 to 3/60 was in 7 (21.2%) patients and 6/6 to 6/18 was in 10 (30.3%) patients.

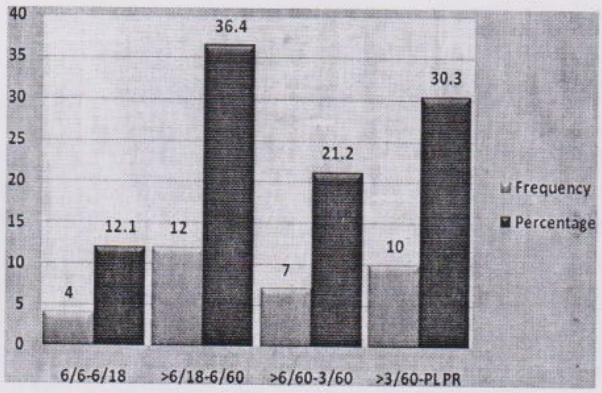

Figure-1. Distribution of patients according to visual acuity (n-33)

Distribution of patients according to type of RVO was shown in figure-2. BRVO was most common type of RVO [24 (72.7%)] and CRVO was 9 27.3%).

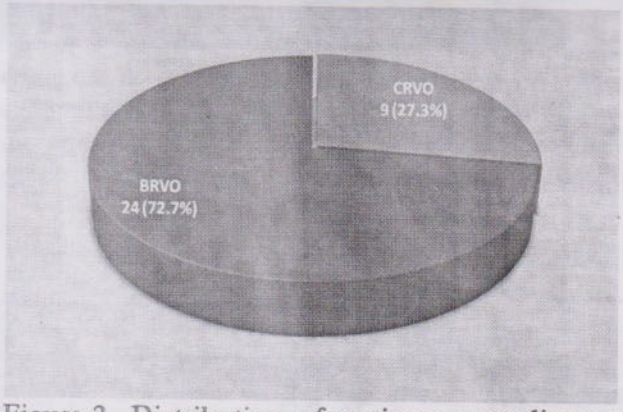

Figure-2. Distribution of patients according to type of RVO (n=33)

Table-II: Distribution of patients according to status of blood pressure

Status of blood pressure	Study subjects		Odds Ratio (95% of CI)	*p-value
	Group-A (n=33)	Group-B (n=33)		
Hypertensive	21 (63.6)	7 (21.2)	6.500 (2.174–19.435)	<0.001
Normotensive	12 (36.4)	26 (78.8)		
Total	33 (100.0)	33 (100.0)		

OR: Odd ratio, CI: Confidence interval

Distribution of patients according to status of intraocular pressure:

Distribution of patients according to status of intraocular pressure was shown in table-VI. In group-A 10 (30.3%) patients had glaucoma and 23 (69.7%) had normal intraocular pressure; while in group-B, 3 (9.1%) patients had glaucoma and 30 (90.9%) had normal intraocular pressure. The patients with glaucoma were 4.3 times more likely to develop retinal venous occlusion (OR=4.348; 95% of CI=1.072–17.629; p=0.030).

Discussion

Retinal vein occlusion (RVO) is an important sight-threatening eye disease, for which currently available treatment options remain limited[13]. In addition to its threat to vision, RVO has also been associated with increased risk of deaths, from cardiovascular diseases[14].

In the current study retinal vein occlusion was found more common in male than in female (57.6% vs 42.4%) and regarding sex of the patients of both groups did not vary statistically significant difference indicating this study was sex matched. This result was supported by Peduzzi *et al.* (1982)[15] and Hayreh *et al.* (2002)[16]. Male preponderance was reported by some other studies[17,18,19,20,21].

Regarding the of eye involvement Beaumont and Kang (2002)[10] found nearly equal frequency of eye involvement in retinal venous occlusion but in this study right eye was more affected little more than left eye (54.5% vs 45.5%).

In the current study BRVO was most common type of RVO [24 (72.7%)] and CRVO was 9 (27.3%). This result was consistent with the study of Thapa *et al.* (2010)[21] that BRVO was most common type of RVO [155 (71.1%)] and CRVO was 63 (28.9%) among their series of RVO.

In this study 36.4% patients of RVO were smokers and the risk of smokers to develop retinal venous occlusion in both groups was almost similar. This result was supported by Xu *et al.* (2010)[22] that 39.4% of their patients with retinal vein occlusion were smoker. They also reported that retinal vein occlusions were not significantly associated with smoking. But Klein *et al.* (2006)[19] reported retinal vein occlusions were significantly associated with smoking.

This study showed that 63.6% of patients were hypertensive in patients of retinal vein occlusion. The patients with hypertension were 6.5 times more likely to develop retinal venous occlusion compared to that of control group. This result was supported by Koizumi *et al.* (2007)[1]. Other studies also reported hypertension was present in 44.1 to 89.2% among the patients with retinal vein occlusion[6,14,23].

Several studies assessed the strength and significance of hypertension that may be associated with retinal vein occlusion. Kawasaki *et al.* (2010)[24] reported hypertension was significantly more frequent in patients with retinal vein occlusion than in controls and supported the present study result. Other studies also found hypertension was significantly more frequent in patients with retinal vein occlusion.[1,18,25]

In this study 30.3% of patients had glaucoma and the patients with glaucoma had 4.3 times more likely to developed retinal venous occlusion as compared to that of control group. This result was consistent with the study of Koizumi *et al.* (2007)[1] that glaucoma was present in 30.6% among the patients with retinal vein occlusion and glaucoma was significantly more frequent in patients with retinal vein occlusion than in controls. Mitchell *et al.* (2009) [26] also found glaucoma was significantly more frequent in patients with retinal

vein occlusion than in controls. Both this studies supported the present study.

As systemic hypertension and glaucoma are significant risk factors in the development RVO following are recommended. All patients with retinal vein occlusion should be evaluated for cardiovascular risk factors & effect of control of systemic hypertension and glaucoma by medications on the development of retinal vein occlusion should be evaluated in a prospective study.

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ORIGINAL ARTICLE

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Evaluation of the results of subaxial cervical spine injury with incomplete cord injury treated by anterior decompression, stabilization by cervical plate & screws and fusion by auto genous tricortical bone graft.

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Abstract

The purpose of this study was to evaluate the efficacy of anterior decompression, fusion and plate fixation in the lower cervical spine injury in respect of neurological outcome, post-operative stability, functional outcome and complications.This study was conducted at NITOR, Dhaka from January 2013 to December 2014.Patients with incomplete lower cervical spine injury who underwent anterior decompression, fusion by autogenous tri-cortical bone graft from iliac crest and stabilization by cervical plate and screws were study population. A total of 27 patients over 15 years of age were included in the study. All cases were evaluated by clinical features, neurological status by ASIA impairment scale, imaging by X-ray and MRI. Preoperative Tong traction was applied to all the patients.Follow up was done with clinical and radiological assessment for up to 4-12 months, mean follow up period was 7.6 months. The age range of patients was from 35-60 years, with mean age of (47.7± 9.1) years. Majority of the patients were male (78%) and most commonly affected people were farmers (44.44%), bearing load on the head was the most common cause (45%), and most involved level of spine was C5/C6 (66.66%). Complications included neck pain (33%), dysphagia (22%), and donor site pain (22%) and there was no infection or implant loosening. Re-do surgery was not required. Overall improvement was noted in 88.88% patients, result of bony fusion was highly satisfactory having 100% success rate. No death occurred in the series. Evaluation of final outcome revealed 78% satisfactory result and unsatisfactory (fair) in 22% patients.Anterior decompression, stabilization by cervical plate and screw and fusion by tri-cortical autogenous bone graft from iliac bone is a safe, technically simple effective method with good neurological and radiological outcome.

[OMTAJ 2016; 15(1)]

Introduction

The cervical spine is functionally the most important region of the spine. The complex anatomy, spinal biomechanics and trauma mechanisms involved make the cervical spine sometimes difficult to assess[1]. Careful evaluation of each region is necessary and errors can have devastating consequences for patients

The cause of missed cervical injuries has been suggested as being due to lack of an appropriate index of suspicion or inadequate testing[2] Astable injuryis one in which the vertebral components will not be displaced by normal movements and risk of further iatrogenic injury to cord is less, if the neural elements are undamaged there is little risk of them becoming damaged.[3] Estimated global SCI incidence is 40 to 80 new cases per million populations per year, based on quality country-level incidence studies of spinal cord injury from all causes.[4] The goal of any form of treatment is to obtain a painless, balanced stable spine with optimum neurological function and maximum spine mobility[5]. The goals of stabilization are to realign the spine, prevent further loss of neurological function, enhance neurological recoveryand restore biomechanical integrity to the spine[6]

Material and Methods

This is a quasi-experimental study carried out at NITOR, Dhaka, Bangladesh, conducted from January 2013 to December 2014. The sample size is 27. All the incomplete cervical injury patients treated by anterior decompression, stabilization by cervical plate & screws

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and fusion by autogenoustricortical bone graft in NITOR during the study period were included in the study.Data collection method was face to face interview.

A format was prepared as per protocol and it was filled with information from history, clinical examination, investigations, per-operative findings and postoperative follow- up. The data was collected by the researcher himself.Ethical clearance was obtained from the authority prior to commencement of the study. Keeping compliance with Helsinki Declaration of Research Activities Involving Human Subjects 1964

Operative techniques:

The patient was positioned supine with slightly extended neck under Gardner- Wells Tong traction putting roll of cotton sheet under the neck and shoulder blades. After skin preparation and draping, a horizontal incision was made at the appropriate level on the left side of the neck. The platysma muscle was usually split vertically for more cosmetic purpose.

The technique involved a thorough discectomy and removal of injured part followed by insertion of a tricortical autograft from illiac bone for fusion and the stabilization by plate under general endotracheal anesthesia

Extreme care and delicacy were to be exercised to avoid injury to the cord and nerve root by selecting appropriate screw size. Traction was released for better compression of graft. Finally a cervical collar was applied at operation site. Patient was returned to bed in the next morning and gradual active movement and rehabilitation started with a simple hard collar.

Follow-Up:

After surgery the patients started using wheel chair and walking aid or without support (if conditions permit) according to their clinical status and degree of fracture and transposition. After discharge each patient was followed up at OPD initially monthly-twice, then after three monthly for one year.

Work status[7]	
W1	Return to previous employment (heavy labor) or physically Demanding activities
W2	Able to return to previous employment (sedentary) or return to heavy labor with lifting restrictions
W3	Unable to return to previous employment but working full-time at a new job
W4	Unable to return to full-time work
W5	No work, completely disabled

On each visit the wound status, motion, presence of any infection, pain at the fracture site, work status or other complications were assessed. Radiographs were taken ateach visit to follow the fracture healing, position of screw & status of fusion. Neurological status was assessed by ASIA impairment scale system.

During each visit counseling of the patient was done about his further job, role of physiotherapy, psychological support and rehabilitation.Patient worn cervical collar for 3 months then discarded it. Patients were allowed to resume normal activities and employment at 3 months or later according to his job or when clinical examination and plain radiographic assessment revealed complete healing of all fractures and a stable fusion.

Classification of fusion grades according to Bridwell et al.1995[9]	
Fusiongrades	Grade Definition
I	Fused with remodeling and trabeculae
II	Graft intact , not fully remodeled and incorporated ,no luciencies
III	Graft intact with definite lucency at the top or the bottom of the graft
IV	Graft definitely not fused with graft resorption and collapse

Fusion type according to Vavruch et al.,2002[8]	
Fusion types	Type Definition
1A	Bridging bone anterior and through the disc space
1B	Bridging bone anterior but not through the disc space
2A	Bridging bone not anterior but through the disc space
2B	No bridging bone at all

Results

Follow up was done with clinical and radiological assessment for up to 4-12 months, mean follow up period was 7.6 months. The age range of patients was from 35-60 years, with mean age of (47.7± 9.1) years. Majority of the patients were male(78%) and most commonly affected people were farmers (44.44%), bearing load on the head was the most common cause

(45%), most involved level of spine was C5/C6 (66.66%). Distribution of patients according to findings of imaging on admission: subluxation/dislocation 18 (66.66%) was the most common cause. Then fracture-dislocation (11.11%), compression fracture (11.11%) & disc prolapse (11.11%). neurological status on the basis of ASIA grade. Highest number of patients (88.88%) were in ASIA grade D & lowest no of patients (11.11%) were in ASIA grade C , post -operative shift of ASIA grade was noted in 9(33.33%) patients, no shift of ASIA grade was noted in 18 (66.66%) patients, there was no (0%) down grade shift of ASIA grade. , shift of post-operative MRC grade was noted in 24(88.88%) patients, no shift of MRC grade was noted in 3(11.11%) patient, there was no (0%) down grade shift of MRC grade. Complications included neck pain (33%), dysphagia (22%), and donor site pain (22%) and there was no infection or implant loosening. Re-do surgery was not required. Bridewll fusion grade I was noted in patients 6(22.22%), grade II in 9(33.33%) and grade III in 12(44.44%) patients. Vavruch fusion type 1A was noted in 18(66.66%) patients, type 1B in 9(33.33%) patients. No patient is in fusion grade IV, fusion rate is 100%. According to Denis work scale highest number of patients were found in grade W-3, 12(44.44%), W-4 & W-2, 6(22.22%) and W-1, 3(11.11%) patients

Overall improvement was noted in 88.88% patients, result of bony fusion was highly satisfactory having 100% success rate. No death occurred in the series. Evaluation of final outcome revealed 78% satisfactory result and unsatisfactory (fair) in 22% patients.

DISCUSSION

The management of patients with subaxial cervical injuries lacks consensus, particularly in regard to the decision which surgical approach or combination of approaches to use and which approach yields the best clinical outcome in the distinct injury.[10].Though to operate or not to operate and when to operate and how to operate are still controversial issues. But there is considerably less controversy regarding the management of patient with incomplete spinal injury than for patient with a complete spinal injury[11]. Operative treatment for sub-axial spine injuries can be from anterior, posterior or combined 360 degree approach[12] Anterior cervical decompression, fusion and plating have gained popularity as the standard procedure. The anterior approach is less-traumatic and it provides the ability for decompression, reduction of dislocated facet joints, inter-body grafting with reconstruction and maintenance of lordosis[10]

Currently there is no National Spinal Cord Lesion Register in Bangladesh and a survey of the available literature has not revealed any previous report from this Country.[13]. The present study has been undertaken in NITOR from January 2013 to December 2014 to find the best option in the management of traumatic unstable cervical spinal injury with incomplete neurological lesion. A total 27 patients satisfying the inclusion and exclusion criteria were selected for this study.

In all the series, male representation is the majority. Male, being the major working force of the society are consistently exposed to the external environment, which probably accounts for this discrepancy

The large number of falls in Bangladesh is a result of crop harvesting which is an important part of our largely agricultural economy. We also found in Bangladesh that the second main cause of spinal cord injury resulted from carrying heavy weights on the head. These injuries at the C5/C6 level occur when a person trips and falls while carrying a heavy load on his or her head. This usually results in a ligamentous lesion which is probably of a "twisting" nature. The exact mechanics of these injuries merit further study. These accidents are more common in Bangladesh than elsewhere .It indicates that the people require more awareness about this habit of carrying load and climbing a tree to reduce chances of injury. But study in western countries showed that common cause of injury is RTA. Difference between these studies is again due to socio-economic status of the patient.

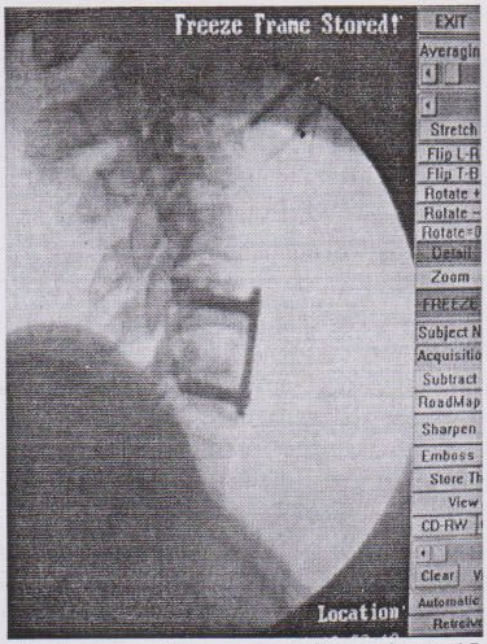
In this study highest number of patients were found in Denis work scale (DWS) grade W-3,12(44.44%), grade W-2 & W-4 had 6 (22%) in each group and only 3(11%) was in W-1. Koller et al. 2009 reported,out of 19 patients who were occupied at time of injury 16 had W1 according to the DWS (84.2%), 1 had W-3, and 2 had W4. Three patients (15.8%) were not able to resume previous full-time employment or unable to work, but 84% went back to the in previous work with a mean time out of work of 13.7 $\pm$ 9.7 weeks (range 3–38 weeks). Difference between these studies may be due to socio-economic status of the patients as most of the patients of this series are farmer and manual labour who were engaged in hard physical activity including weight lifting and carrying heavy weight on head.

In this study overall results were classified according to Modified Macnab criteria for characterizing outcome after surgery[14] as excellent, good, fair and poor. Majority of patients had satisfactory outcome 78% (good (56%)

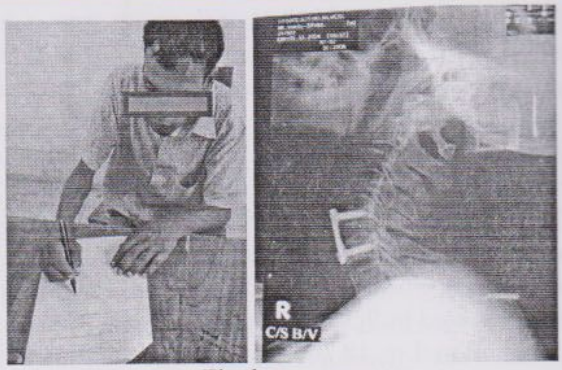
followed by excellent 22 %) and fair 22%. No patient deteriorated in the studies. In my study the number of excellent is less as most of my patients were heavy manual worker who could not return to their previous work or returned to previous work with some restrictions.

In conclusion,anterior decompression, stabilization by cervical plate and screw and fusion by tri-cortical autogenous bone graft from iliac bone is a safe, technically simple effective method with good neurological and radiological outcome.

Post-operative photograph



Just after operation view on image intensifier



Final outcome

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 15 Number 1

Psychiatric disorders among suicidal behavior patients attending mental health facilities: a retrospective cross-sectional study

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Abstract

Suicide is a leading cause of death worldwide. The precise effect of risk factors for the onset and persistence of suicidal behaviour were not well understood. Environmental or experiential factors also contribute to the onset and suicidal behaviours. There are no multinational population-based studies between psychiatric disorders and suicidal behavior.

Objective of the study was to find out psychiatric comorbidity profile and socio-demographic status of patients with suicidal behaviour over the life course and delineate the types of suicidal behavior. It was a retrospective cros-sectional study. All cases were selected from patients attending at NIMH, Dhaka, Comilla Medical College hospital and Private Hospitals in Comilla City from October 2014 to March 2016. A total 120 patient aged 9 to 40 years who fulfilled the enrolment criteria included in the study. The participants who were diagnosed as epilepsy and intellectual deficit excluded from this study. Respondents provided sociodemographic and diagnostic information, as well as an account of suicide-related thoughts and behaviours. Suicidality or suicidal behaviour was defined as suicide attempts and suicidal ideation in the total sample, and suicide plans and attempts among ideators. Following categories of mental disorders were considered: personality disorders, adjustment disorders, anxiety disorders, mood disorders, oppositional defiant disorder, conduct disorder, substance use disorders, composite disorders and others disorders. The association between suicidality and psychiatric comorbidity was examined. Frequency tables, summary tables and appropriate graphs were prepared to describe the population characteristics and study finding. A participation rate was found 77.5% female and 22.5% male. Of 120 suicidal behavior patients psychiatric disorders was 78 (65%. Among suicidal behavior patient's neurotic disorders was 15 (19%), psychotic disorders was 12 (15%), personality disorders was 30 (39%) and others disorder was 21 (27%). Among 78 psychiatric patients borderline personality disorder was 25.64%, adjustment disorders were 15.38%, mood disorders were 11.53%, psychotic disorder was 7.69%, multiple personality disorder and oppositional defiant disorder were 6.42%, hystrionic personality disorder and substance use disorder were 3.84%, antisocial personality disorder, conduct disorder and anxiety disorder were 2.57%, and miscleneous disorder was 11.53%. Among suicidal behavior in psychiatric patients suicidal ideation was 54, suicidal plan was 13, suicidal attempt was 45 , ideators only proceeded to plan was 17, ideation to attempt was 59, planned attempt was 8 and impulsive attempt was 51. Among suicidal behavior in total 120 participants suicidal ideation was 84, suicidal plan was 19, suicidal attempt was 56, ideators only proceeded to plan was 26, ideation to attempt was 76, planned attempt was 14 and impulsive attempt was 62. Most of the suicidal behavior participants were female (77.5%) and age group of <24 years (60%). Psychiatric disorders are important risk factors for the onset and persistence of suicidal behaviour, with this risk being the greatest in childhood, adolescence and early adult.

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Introduction

Suicide is the primary emergency for the mental health professional, with homicide and failure to diagnose an

underlying potentially fatal medical illness representing other. Suicide is also a major public health problem and impossible to predict precisely. Numerous clues can be seen, which are enumerated in this section. Suicide also needs to be considered in terms of the devastating legacy that it leaves for those who have survived a loved one's suicide, as well as the ramifications for the clinicians who cared for the decedents.[1] Etiology of suicide is still not well understood. Mental disorders are important risk factors for suicidal behaviour. Environmental or experiential factors also contribute to the onset and suicidal behaviours. There are no multinational population-based studies between mental disorders and suicidal behavior.[2, 3,4]

Suicide is derived from the Latin word for self-murder. It is a fatal act that represents the person's wish to die. There is a range, however, between thinking about suicide and acting it out. Some persons have ideas of suicide that they will never act on; some plan for days, weeks, or even years before acting; and others take their lives seemingly on impulse, without premeditation. Lost in the definition are intentional misclassifications of the cause of death, accidents of undetermined cause, and so-called chronic suicide for example, death through alcohol and other substance abuse and consciously poor adherence to medical regimens for addiction, obesity, and hypertension.[1]

Suicide death rates increased adolescent and decreased elderly rates for certain subpopulations during the last century.[5] This rate was remained constant; averaging about 12.5 per 100,000 through the 20th century and into the 21st. Suicide rate for those 15 to 24 years of age has increased two- to threefold. Suicide is currently ranked the 8th overall cause of death in the United States, after heart disease, cancer, cerebrovascular disease, chronic obstructive pulmonary disease, accidents, pneumonia, influenza, and diabetes mellitus.[6] Suicide rates in the United States are at the midpoint of the rates for industrialized countries as reported to the United Nations. The prime suicide site of the world is the Golden Gate Bridge in San Francisco, with more than 800 suicides committed there since the bridge opened in 1937.[5, 7]

Material and Methods

There was a retrospective cross-sectional study conducted in Depatrment of Psychiatry, Comilla Medical College, Comilla. All cases were selected from patients attending at NIMH, Dhaka, Comilla Medical College Hospital and Private Mental Health Facilities in Comilla City from October 2014 to September 2015. Duration of study was one year. Of 120 suicidal behavior patients who fulfilled the enrolment criteria were included in the study. The participant's age was 9 years and older living in households or in hostel accommodation. All racial and ethnic groups were represented.

The CIDI module on suicidality was used to assess the age of first onset, age of most recent episode, lifetime occurrence of suicidal ideation, suicide plans and suicide attempts. Suicidal ideation, suicide plans and suicide attempts were assessed with questions such as "Have you ever seriously thought about committing suicide? Have you ever made a plan for committing suicide?" and Have you ever attempted suicide?" respectively. Ideators only proceeded to answer questions about plans ("Have you ever made a plan for committing suicide?) and attempts ("Have you ever attempted suicide?"). To get a better understanding of the progression from ideation to attempt, the outcomes considered in this study were: suicide attempts in the total sample, suicide ideation in the total sample, suicide plans among ideators, suicide attempts among ideators with a plan (planned attempts) and suicide attempts among ideators in the absence of a plan (unplanned or impulsive attempts). Semi structural questionnaire and DSM-5 were were used for assessing mental disorders and collecting detailed information about the risk factors, psychiatric comorbodities, impairment, consequences sociodemographic and diagnostic information. Following categories of mental disorders were considered: personality disorders, adjustment disorders, anxiety disorders, mood disorders, oppositional defiant disorder, conduct disorder, substance use disorders, composite disorders and others disorders. All collected data were checked and verified thoroughly for consistency as well as for completeness. Finally appropriate statistical analysis was done to see the trends of the data. Frequency tables, summary tables and appropriate graphs were prepared to describe the population characteristics and study finding.

Results

Total 142 participants were approached for interview. Considering inclusion and exclusion criteria finally 120 patients were selected for the study. A participation rate was found 77.5% female and 22.5% male. Age range was 9-40 years.

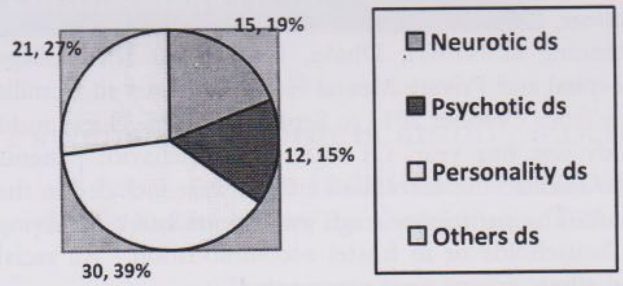

Figure-1: Broad category of psychiatric disorders among suicidal behavior patients (n=78)

Table I: Specific psychiatric disorders among suicidal behavior patients (n=78)

Psychiatric disorders	n (%)
Borderline personality disorder	20 (25.64%)
Hystrionic personality disorder	3 (3.85%)
Antisocial personality disorder	2 (2.57%)
Multiple personality disorder	5 (6.42%)
Mood disorders	9 (11.53%)
Adjustment disorders	12 (15.38%)
Oppositional defiant disorder	5 (6.42%)
Conduct disorder	2 (2.57%)
Anxiety disorder	2 (2.56%)
Psychotic disorder	6 (7.69%)
Substance use disorder	3 (3.84%)
Miscleneous disorder	9 (11.53%)

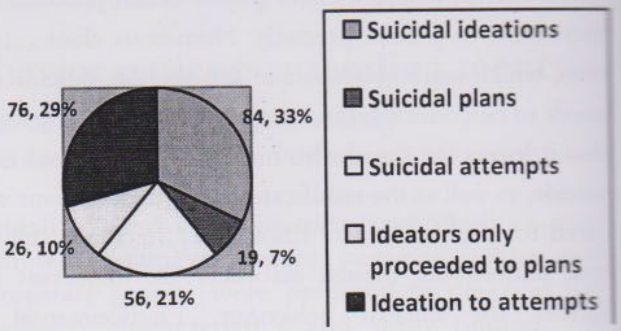

Figure-2: Broad categorical distribution of suicidal behavior

Table II: Categorical distribution of suicidal behavior among participants

Suicidal behavior		psychiatric patients	non-psychiatric patients
Suicidal ideation		54	30
Suicidal plans		13	6
Suicidal attempts		45	11
Ideators only proceeded to plans		17	9
Ideation to attempts		59	17
Nature of attempts	Planned	8	6
	Impulsive	51	11

Table III: Distribution of suicidal behavior among specific psychiatric disorders

Psychiatric disorders	Suicidal ideation	Suicidal plans	Suicidal attempt	Ideators only proceeded to plan	Ideation to attempt	Nature of attempts	
						Planned	Impulsive
Borderline personality ds.	15	1	12	5	20	1	19
Multiple personality ds.	4	2	1	3	5	1	4
Mood ds.	5	0	6	0	4	2	2
Adjustment ds.	9	4	6	4	7	0	7
Oppositional defiant ds.	4	0	4	1	5	0	5
Psychotic ds.	4	2	3	0	5	1	4

Table IV: Distribution of respondents by sociodemographic characteristics (n=120)

Characteristics	Respondents n (%)
Age (in years)	<18	24 (20%)
	18-24	48 (40%)
	>24-32	28 (23.33%)
	>32- 40	20 (16`67 %)
Age of first onset	<12	7 (5.83)
	12-<18	48 (40%)
	18-<24	35(29.17)
	24-30	23 (19.16)
	>30-40	7 (5.83)
Sex	Male	27 (22.5%)
	Female	93(77.5%)
Religion	Islam	104 (86.66%)
	Hindu	15 (12.5%)
	Buddis	1 (.87%)

characteristics (n=120)	Characteristics	Respondents n (%)
Educational status	Illiterate	16 (13`33%)
	Below PSC	8 (6`67%)
	Below SSC	37 (30`86%)
	SSC-HSC	30 (25%)
	Above HSC	29 (24`13%))
Occupation	Student	42 (35%)
	Service	8 (6`67%)
	Farmer	5 (4`17%)
	House wife	36 (30%)
	Business	5 (4`16%)
	Others	24 (20%)
Marital status	Unmarried	59 (49`16%)
	Married	47 (39`17%)
	Divorce	11 (9`17%)
	Seperated	3 (2`5%)
Famiy pattern	Single	72 (60%)
	Joint	48 (40%)
Habitat	Rural	54 (45%)
	Semiurban	15 (12`5%)
	Urban	51 (42`5%)
Socioeconomical status	Low class	52 (43`33%)
	Middle class	47 (39`17%)
	High class	21 (17`5%)
Psychiatric disorders	Present	78 (65%)

Discussion

Suicidal behavior is not a disease: rather it is the result of an adaptive difficulties, family discord, and interpersonal conflicts with peers and friends. Based on some research evidence as well as consensus, common associated psychiatric disorders included borderline personality disorders, adjustment disorders, mood disorders, anxiety disorders, oppositional defiant disorder, conduct disorder, substance use disorders and miscleneous disorders. It is important to understand and focus probable psychiatric disorders of suicidal behaviours participants. Reeviewing different literature on suicide, we tried to understand the distress of huge burden of psychiatric problem on persons with suicidal behaviours.[5,6] Most of the suicidal behavior patients were female (77.5%) and age group upto 24 years (60%). More than a half of the respondents with suicidal behaviour experienced at least one psychiatric disorder. Personality disorder, adjustment disorders, mood disorders, and disruptive behavior disorders had stronger associations with lifetime suicide attempts. Borderline personality disorder is the commonest psychiatric disorder associated with lifetime suicide attempts and ideation.[3] Adjustment disorders, disruptive behavior disorders, and anxiety disorder were identified as significant risk markers for lifetime suicide ideation, while borderline personality disorder and mood disorders were significantly correlated with suicidal attempts. Multiple personality disorders showed the highest prevalent of suicidal behavior both ideation and attempts. Borderline personality disorder was associated with a three fold higher risk of lifetime suicide attempts.[3] Among suicidal behavior in borderline personality disorder suicidal ideation was 15, suicidal plan was 1, suicidal attempt was 12 , ideators only proceeded to plan was 5, ideation to attempt was 20, planned attempt was 1 and impulsive attempt was 19. Among suicidal behavior in adjustment disorder suicidal ideation was 9, suicidal plan was 4, suicidal attempt was 6, ideators only proceeded to plan was 4, ideation to attempt was 7, and impulsive attempt was 7. Among suicidal behavior in mood disorder suicidal ideation was 5, suicidal attempt was 6, ideation to attempt was 4, planned attempt was 2 and impulsive attempt was 2. These findings also consistent partially with the previous study.[9]

The most prevalent psychiatric disorders endorsed borderline personality disorders followed by adjustment disorders, mood disorders, anxiety disorders, oppositional defiant disorder, conduct disorder, substance use disorders and miscleneous disorders. The most prevalent suicidal behavior experienced in those with a suicide attempt as well as in those with suicidal ideation. These findings were somewhat dissimilar to other studies due to strong family bonding, cohesive family system, and strong religious believes and cultural influences, and economical variable in our country. These possible explanations were accepted considering mentioned factors minor variation from previous study finding.[3]

The effect of psychotic disorders on suicidal tendencies varied over the life course. For example, personality disorders were significantly associated with suicide ideation and attempts during childhood and teen years, but not during young and later adulthood.[5] The estimated lifetime prevalence of suicidal behavior

patient's neurotic disorders was 19%, psychotic disorder was 15%, personality disorder was 39% and others disorder was 27%. After adjusting for mental illness adjustment disorders and anxiety disorder was a significant risk factor for suicidal ideation. These findings emphasise the need to focus particularly on suicide prevention strategies at youth. These findings were partially consistent with the previous studies.[6,7,8]. Childhood psychotic disorders emerged as a particularly robust risk factor for suicide attempts in younger participants. This was in keeping with other studies that psychotic disorders results in suicidal behaviour at a younger age. Disruptive behavior disorders emerged as risk factors for the emergence and persistence of suicidal behaviour, especially in adolescence. Single famiy pattern, divorce, marital separation and financial crisis had also been found to be associated with persistence of suicidality. These findings strengthen results of previous works carried out in other developing countries which showed psychiatric disorders to be a significant risk factor for suicidality.[10,11]

In conclusion, psychiatric disorders are important risk factors for the onset and persistence of suicidal behaviour, with this risk being the greatest in childhood, adolescence and early adult.

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ORIGINAL ARTICLE

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Results of Stabilization of subtalar and Talonavicular joints by K- wire in the surgical Management of Rigid variety of clubfoot

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Abstract

Clubfoot is the common congenital foot and ankle deformity in Bangladesh which often create socioeconomic problem. Most of the patients in our country need surgical treatment as they present late. The recurrence rate of clubfoot is very high mostly due to poor surgical correction in appropriate post-operative management and follow up. Stabilization of subtalar and talonavicular joints by K-wire during posteromdial release ensures reduction and maintenance of the surgical correction. This prospective interventional study was conducted from July 2007 to June 2009 at Dhaka Medical College Hospital. 24 clubfeet of 16 children were both clinically and radiologically evaluated following the posteromedial release with stabilization of subtalar and Talonavicular joint by K- wire. Only the rigid clubfoot between the age range from 6 months to 36 month with a mean age of 10.62 months were selected irrespective of sex. Regarding complications there were blister in 2 cases, pin dislodgements from the sole during plaster change 2 cases, Pin tract infection 1 case and late complication like stiffness and under correction in 2 cases. The follow up period was average 9.66 months. The result was poor in 8.33%, fair in 8.33%, good in 37.50% and excellent in 45.83% cases. The ultimate result was satisfactory (good 37.50% excellent 43.83%) in 83.33% and unsatisfactory (poor 8.33%, fair 8.33%) in 16.66% cases. So, one stage posteromedial release with stabilization of subtalar and talonavicular joints by K-were for rigid variety of clubfoot give. Satisfactory results in most of the cases.

[OMTAJ 2016; 15(1)]

Introduction

Congenital clubfoot or congenital talepes equinovarus (CTEV) is the commonest congenital deformity seen in orthopaedic practice.[1] The incidence and prevalence of CTEV deformities has yet to be determined in our country. But according to western literature it is about 1-2 in live births.[2] Clubfoot is a complex foot deformity that is readily apparent at birth. Before the era of modern surgery numerous machines were devised for the forcible correction of clubfoot and a variety of braces were worn.[3]

Today there is agreement among most Orthopaedists who treat congenital clubfoot in the newborn that the proper initial treatment still is gentle corrective manipulation of the foot and the skilled application of serial plaster casts to maintain the correction. If complete correction cannot be obtained and maintained, then surgical intervention is necessary.[4]

Controversy still exists as to the choice of operative procedures. The one-stage postero-medial soft tissue release procedure that was described by Turco is still favored by many.[4]

Most researchers agree that the fate of the surgically treated resistant clubfoot prior to Turco's preliminary report in 1971, included 'piecemeal' procedure and incomplete correction, resulting in multiple operation and far less that satisfactory results.[5]
Turco published a preliminary report in 1971 and later a follow-up report and 15 years experience in 1979 of his one-stage posteromedial release with internal fixation. He agreed with Scarpa (1818) that a congenital dislocation of the talocalcaneo-navicular joint in which the navicular and clacaneus are displaced medially around the talus is basic to clubfoot deformity.[5]

The original surgical technique has been modified to include stabilization of the subtalar joint in addition to the talonavicular joint.[6] By transfixing the subtalar and talonavicular joints the relationship between the navicular, calcaneus and talus remains constant as the foot is dorsiflexed. Two wire fransfixion is advantageous

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in a small foot with severe deformity or in a foot that had been operated on previously.[6]

Previously, when Turco performed this operation without stabilization of talonavicular and subtalar joints, there was a high incidence of wound problem and recurrent deformities.[6]

Recurrent deformity after surgical treatment of clubfoot is a major challenge for a developing country like Bangladesh. Brockman (1930) and Evans (1961) thought that a clubfoot did not "relapse" after treatment, but that in such cases the initial correction was inadequate. More over faulty postoperative management and follow-up is also responsible for recurrence.

Considering all these facts, the researcher has done a study as "Evaluation of the results of stabilization of talonavicular and subtalar joints by K-wire in the surgical management of rigid variety of clubfoot".

Material and Methods

This is a prospective interventional study done from July 2007 to June 2009 at Department of Orthopaedics & Traumatology, Dhaka Medical College Hospital. The study populations were the patients with idiopathic congenital clubfoot (CTEV) attending at the out patient department of Dhaka Medical College Hospital fullfiling the selection criteria. A total of 16 patients with 24 clubfoot, were selected consecutively from the study population.

Inclusion criteria:
1. Child having congenital rigid variety of clubfoot.
2. Age of child from 6 months to 3 yrs.

Exclusion criteria:
1. Age below 6 months & above 3 yrs.
2. Non rigid clubfoot.
3. Resistant rigid clubfoot.
4. Relapsed club for.

Surgical technique:
Under pneumatic tourniquet control, a single curvilinear skin incision was made over the posterior and medical aspects of the ankle and foot beginning postero medially over the musculotendinous junction of the tendo-achillis, progress distally behind 2 cm below the medical malleolus, and then curves forward along the medical aspect of the foot up to the base of the 1st metatarsal bone. The incision is deepened through the thick, fatty subcutaneous tissue to the investing fascia before a flap was elevated, thus ensuring preservation of the blood supply to the skin. The fascia is incised and the neuro-vascular bundle was identified and protected. The tendo-achillis was isolated and elongated by means of Z-plasty by detaching the medical part of its insertion. Then the tibialis posterior tendon was identified close to the posterior border of the tibia and the flexor digitorum longus and neuro-vascular bundle behind it. All these structures are uncovered and traced distally with division of the flexor retinaculum and the tendon sheath as far as the insertion of the tibialis posterior in to the navicular bone. The tibialis posterior tendon and flexor digitorum longus tendon were also lengthened with a z-plasty.

The distal segment of tibialis posterior was used as a guide to enter the medially subluxated talo-navicular joint. This joint is released dorsally, medially and inferiorly and only the portion of the broad insertion of the tibialis posterior to the navicular tuberosity was preserved.

The flexor hallucis longus tendon is indentified more deeply by incising a pad of fat and traced to the point at which it crosses the flexor digitorum longus tendon in the sole. Flexor hallucis longus tendon was used as a guide to reach the sub-talar joint. The flexor hallucis longus tendon is then retracted medially so it will be out of the way when the capsulotomy were done. The neurovascular bundle was also protected. The foot was dorsiflexed as much as possible and the posterior ankle joint was found as well as the postrior subtalar joint, both capsules were tranasected from medical to lateral. The interosseous ligament of subtalar joint was also divided.

Care was taken to preserve the deep portion of the deltoid ligament as well as the lateral colateral ligaments of the ankle joint. At this point the talus should be able to rotate back into the ankle mortice with complete correction of the equinus component of the deformity. We divided the flexor hallucis longus obliguely.

With the guide to the flexor digitorum longus tendon, the master knot of Henry was also divided. After the postero-medical portion of procedure has been accomplished a planter release was performed by cutting the origin of the abductor hallucis.

The planter appneurosis was divided by closed steindler procedure if necessary to correct the cavus deformity. After all the deforming components were found to be corrected the reduction was maintained by stabilization of talonavicular and subtalar joints by 2k-wires (2 mm). One inserted dorsum of the foot through the navicular to the reduced position of the head of the talus and second from the heel through the calcaneus into the talus. Then the tourniquet was removed, haemostasis done and the wound was closed in layers.

Post-operative management
After completion of operation, a well padded long-leg plaster cast was applied with 90^0 knee flexion and foot and ankle in a neutral position. The cast was splitted anteriorly. The foot was elevated by a small pillow and the circulation of the toes was checked frequently for first few hours.

Three weeks after the operations, the cast was changed and stitches were removed. At 6 week after the operation k-wire were removed and a new long leg cast was applied. Immobilization was continued for 3 months

with plaster change at 3 weeks interval. When the child could hold the foot in the corrected position a club foot shoe was advised to wear at day time and Denis browne splint at night up to the school going age. If the child could not hold the foot in the corrected position, we advised Denis-browne splint for full time (day and night) or at least 23 hours per day.

Results

In this present series the following results were obtained. 16 (Sixteen) patients with 24 clubfeat were selective for the study with a follow up of four to eighteen months. In this series 10 patients (62.50%) were in age group 6-10 months 3 patients (18.75%) were in age group 11-15 months and 3 patients (18.75%) were in age group 16-20 months.

Among 16 cases 11 patients (68.75%) were male and 5 patients (31.25%) were female.

Among 16 patients 8 patients (50%) had bilateral, 5 patients (31.25%) had rightfoot involvement and 3 patients (18.75%) had left foot involvement. Among the 16 cases 2 had other congenital anomalies. One patient (6.25%) had syndactyly of hand, one patient had cleft lip (6.25%). Among the 16 cases 3 patients (18.75%) had position family history.

In this series, 5 patients (31.25%) developed early complications and 2 (12.5%) developed late complications.

Table I: List of complications.

Complications	No. of patients	Percentage
A. **Early**		
Blister	2	12.50
Superficial pin site infection	1	6.25
Premature pin dislodgment	2	12.50
B. **Late**		
Stiffness	1	6.25
Under correction	1	6.25

Radiological evaluation summary:

Among the 24 feet, 16 feet (66.60%) achieved normal AP talo calcaneal angle, in lateral dorsiflexion view out of 24, 12 feet achieved normal talocalconeal angle (50%). Talocalconeal index of 18 feet (75%) achieved normal value out of 24 feet.

The functional outcome was evaluated by the J.B. Magone et. al. rating system. Out of 24 feet excellent in 11 feet (45.83%), good in 9 feet (37.5%) fair is 2 feet (8.33%) and poor in 2 feet (8.33%).

Table II: J.B. Magone et al. rating system for clubfoot.[9]

	Points
1. Hindfoot	
Nutral to 5^0 valgus	05
$>5^0$ Valgus	03
Varus	00
2. Forefoot	
Nutral to 5^0 adduction	03
$>5^0$ adduction	00
3. Equinus	
Dorsiflexion to 90^0	05
$<90^0$	00
4. Cavus	
Absent	05
Present	00
5. Supination	
Absent	03
Present	00
6. Ankle radiograph	
$>40^0$	25
$31\text{-}40^0$	20
$21\text{-}30^0$	15
11-20	08
<11	00
7. Flexion of great toe	
Present	05
Absent	00
8. Bimalleolar axis	
$75\text{-}85^0$	10
$70\text{-}74^0$	08
$65\text{-}69^0$	04
$<65^0$	02
9. Heel walking	
Present/not applicable	05
Absent	00
10. Toe walking	
Present/Not applicable	05
Absent	00
11. Pain	
Never	12
With heavy activity	08
With routine activity	06
With walking	03
12. Function	
Never limits	12
Limits heavy activity	08
Limits routine activity	06
Limits walking	03
13. Satisfaction	
Satisfied	05
Neither	03
Dissatisfied	00

Table III: Results:

Rating	Score
Excellent	90-100
Good	80-89
Fair	70-79
Poor	<70

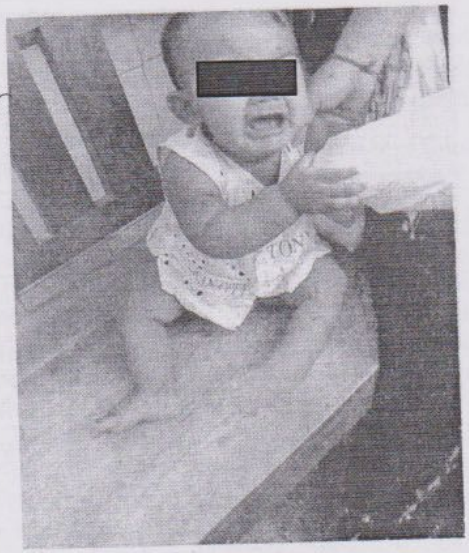

Fig. 1. Preoperative deformity of lt. foot.

Fig. 2. Pre-operative X-ray of lt. foot showing kite A.P talocalcaneal angle and lateral talocalcaneal angle forced dorsiflexion view.

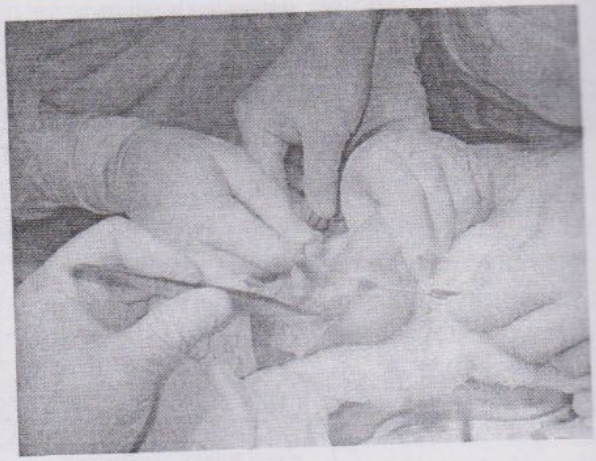

Fig. 3. Per-operative photograph of clubfoot surgery.

Fig.4. K-wire in situ.

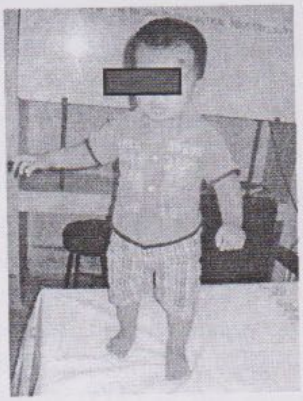

Fig. 5. Post operative photograph 9 months after operation.

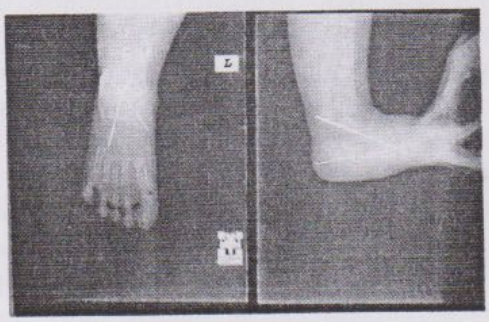

Fig. 6. Post-operative X-Ray of Lt. foot showing normal kite A.P talocalcaneal angle and lateral talocalcaneal angle in forced dorsiflexion view

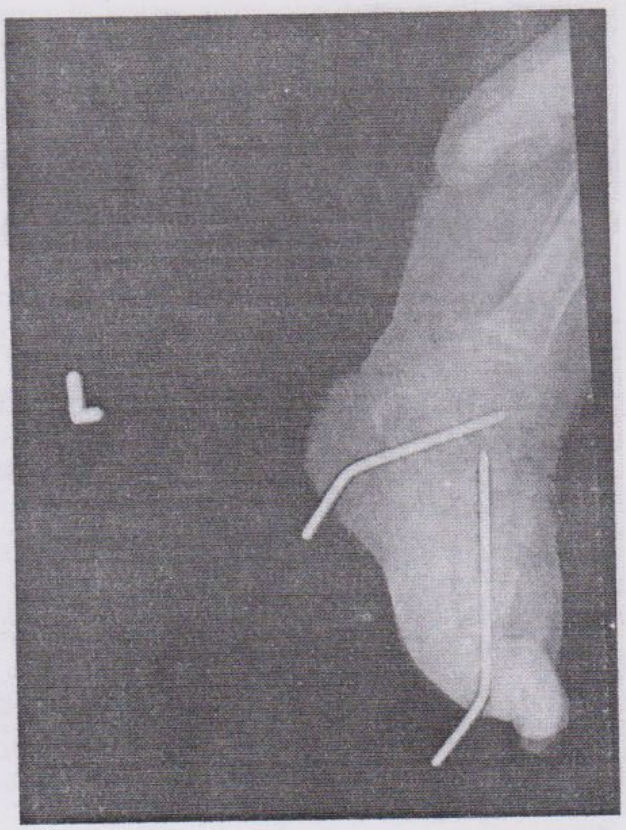

Fig. 7. Post-operative X-ray of lt. foot.

Discussion

In this series out of 16 patients 11 patients (68.75%) received preoperative plaster & gentle manual stretching. Most of the excellent and good result comes from the patient who received preoperative gentle manual stretching and serial corrective plaster. In the present series satisfactory result were obtained in 83.33% patient. (20 feet out of 24 feet) and unsatifactory results were obtained in 16.66% patients (4 feet out of 24 feet)

By J.B. Magone et al[9] scoring system the result was poor in 8.33%, fair in 8.33%, good in 37.50% and excellent in 45.83% cases the ultimate result was satisfactory (good 37.5% & excellent 45.85%) in 83.33% and unsatisfactory (poor 8.33% + fair 8.33%) in 16.66% cases. Finally at 95% confidence intervel (CI) of proportion, satisfactory outcome was 68.44% to 98.22%.

Here pre-operative and post-operative radiological evaluation was also used in the final functional outcome assessment. By using student's t-test calculated p value was <0.001, so, there was a highly significant ($p<0.001$) difference/improvement between pre and post operative radiological correction of clubfoot.

Turco[6] in a longterm follow up of his series found satisfactory results in 83.8 percent patients and unsatisfactory results in 16% patients. Mc Kay[7] in a 6 years following of 102 children found excellent to good result in 80% patients and unsatisfactory results in 20% patients. Alanis Balanaces LM[4] performed circumferntial soft tissue release with cincinnati in cision. A follow up of 28.5 months was made with satisfactory results is 85% and poor results in 15% cases. Brongham and Nicol corrected clubfoot deformity by cincinnoti in vision between April 1983 and may 1984 with 27.6 months follow-up satisfactory results were is 75% cases and unsatisfactory results were in 25% cases.

In the present study, satisfactory results were directly related to some factors namely age of the patients during operation, adequate preoperative corrective treatment and the magnitude of deformity at the time of operation. In this series age at the time of operation was 6 months to 20 months, overage age was 11 months.

The results were found 80% good or excellent at the age group of 6-10 months. Turco reported 84% good or excellent results in patients whose surgery was performed over the age of 1 year.

In this series the subtalar and talonavicular joints were stabilized by two percutaneous Kirschnar wire after complete correction of all the components of the deformity at the time of surgery and all had postoperative radiographic documentation of correction.

Internal fixation stabilizes the reduction and ensures maintenance of the surgical correction. The correction is maintained without cast pressure or hyperdorsiflexion, thus eliminating pressure and tension over the skin.

In this series the researcher followed J.B Magone et.al[9]. rating system for clubfoot to evaluate final functional outcome. The final result was as follows. Excellent 11 feet (49.83%) good 9 feet (37.50%) fair 2 feet (8.33%) and poor 2 feet (8.33%).

Here excellent and good result were taken as satisfactory (83.33%), fair and poor results as unsatisfactory (16.66%).

In conclusion, one stage posteromedial release with stabilization of subtalar and talonavicular joints by K-wire gives satisfactory results in most of the cases. Surgical correction is infact a part of total management of clubfoot. Follow-up and required measures up to skeleton maturity are also essential. This series was conducted only 16 patients with 24 clubfeet and mean follow-up period was nine months. So, further study with larger sample and longer follow-up period in multicenter setting will establish the procedure.

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 15 Number 1

Effect of combination use of diacerein-glucosamine plus Aceclofenac compared to Aceclofenac alone in knee osteoarthritis

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Abstract

Osteoarthritis (OA) is the most common type of degenerative joint disease which is a leading cause of chronic disability. Guidelines for the management of OA recommend disease and symptom modifying drug like diacerein for osteoarthritis in addition to anti-inflammatory drug. Glucosamine is a component of cartilage being used in combination with diacerein.This prospective comparative clinical study was conducted in the outpatient department of Orthopedics and Physical medicine of MAG Osmani Medical College Hospital, Sylhet during the period of July 2014 to June 1015, on 110 patients suffering from knee OA whose baseline pain score was 5 on Numeric Pain Rating Scale (NPRS), were divided into two groups; odd numbers in group A and even numbers in group B. The patients of group A were treated with combination of diacerein-glucosamine plus aceclofenac, while patients of group B were treated with aceclofenac alone, twice daily for 4 weeks. Effect on pain score was estimated by using "The Western Ontario and McMaster Universities (WOMAC)" OA index (item 1-24).WOMAC OA index consists of pain score, stiffness score and physical function disability score. WOMAC OA index was estimated on NPRS, which is a numeric version of Visual Analog Scale (VAS). Pain score, stiffness score and physical function disability score were estimated at base line, 14th, 21st and 28th day. Finally 48 patients of group A and 46 patients of group B were accounted as study subjects for statistical analysis.In course of treatment pain score, stiffness score, physical function disability score and total WOMAC score significantly decreased ($p<0.001$), recorded at 14th, 21st and 28th day compare to baseline score. When compared the effect of three drug combination: diacerein-glucosamine plus aceclofeanc (Group-A) with that of single drug: aceclofenac (Group-B), the former treated group showed marked increased effect ($p<0.001$). Three drug combinations of diacerein-glucosamine plus aceclofenac is more effective than aceclofenac administered alone in the treatment of knee OA

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Introduction

Osteoarthritis (OA) is characterized by focal loss of articular cartilage, subchondralosteosclerosis, osteophyte formation at the joint margin and remodelling of joint contour with enlargement of affected joint.[1]Currently, the World Health Organization (WHO) estimates that 9.6% of men and 18% of women have painful OA worldwide.[2] In Bangladesh the prevalence of knee pain is higher in urban rather than rural areas~DQGit is reported to be 10.20%.[3]OA of the knee increases advancement with age and is more common in women than in men. Local inflammation in the synovium and the cartilage may contribute to pain and at last joint damage occurs.[4] The primary goals of the management of patients with OA are control pain and to bring perfection in function and health-related quality of life, with avoidance of toxic Pharmacological effects.[5] The management of OA is broadly divided into non-pharmacological, pharmacological, and surgical treatments. As analgesic and anti-inflammatory

NSAIDs appears alternative of paracetamol, they can be associated with serious gastrointestinal (GI) complications and increase risk of cardiovascular and cerebrovascular events and also may accelerate cartilage degradation on long-term treatment[1] Now a day's researcher's attention focused on finding of a new drug that would prevent or retard the progression of degeneration of articular cartilage. Diacerein and Glucosamine are recommended by the European League Against Rheumatism guidelines 2003. "Diacerein" is suggested as a slow-acting, symptom and disease modifying agent in treatment of OA. Diacerein inhibits the production of interleukin-1 beta by human monocytes and the effects of the cytokine on chondrocytes, thus exerting chondroprotective effects on articular cartilage and reducing severity of cartilage, bone, and synovial membrane damage in OA.[7] It does not alter renal or platelet COX activity and is well tolerated by patients with prostaglandin dependent renal function.[8] In one study showed that celecoxib and diacerein are equally effective as aceclofenac. Glucosamine is an amino sugar and a prominent precursor in the biochemical synthesis of glycosylated proteins and lipids, including glycosaminoglycans (GAG) which is a component of cartilage. The diacerein and glucosamine involved in a large number of randomized controlled trial (RCT) and meta-analysis suggest that improve symptom and decrease structural progression in knee OA when compared to placebo.[9,10] As a chronic disease, OA requires continued management with several agents, with aim to provide synergistic benefit in term of symptom relief and safety in course of long term treatment. This study is aimed to evaluate the effect and adverse effect of combination use of diacerein-glucosamine plus aceclofenac in knee of osteoarthritis compare to single administration of aceclofenac in the treatment of knee OA.

Materials and Methods

A total 110 patients age range from 36 to 72 years with painful knee, pain full joint movement and joint stiffness complaining moderate pain [at least 5 on the NRS of 0 to 10 cm][7] attended the outpatient department (OPD) of Orthopedic surgery and Physical Medicine were examined and diagnosed as osteoarthritis and fulfilling the inclusion criteria were enrolled in this study. Patients with Coronary heart disease or hemorrhagic diasthesis, hypersensitivity to any of the studied medications, hepatic or renal impairment, active peptic ulceration bronchial asthma, rhinitis, urticaria, or other allergic manifestation were excluded from the study. Pregnant and lactating women and patient with secondary knee osteoarthritis and past history of knee surgery or trauma were also excluded. The aims and objectives of the study were explained to the patients in easily understandable local language and written informed consent was taken from each patient. The clinical histories of the patients were recorded. Each patient was examined thoroughly. All the findings, previous history, reports and investigations were analyzed. Inaddition, they were subjected to investigate the Hematological and biochemical investigations like Hemoglobin, WBC, Platelet, Serum Creatinine, Serum Bilirubin, and ALT were done before initiation and at the end of study. Clinical adverse events, if any, were recorded on each of the visits. Data were collected by direct interview using the questionnaire. Patients with osteoarthritis were randomly divided into two groups as odd numbers belonged to group A while even number in group B and each consisting 55 patients.

The patients of Group A were treated with fixed dose combination of Diacerein 50 mg and Glucosamine sulfate 750 mg (Tab.Jointec max) plus Aceclofenac 100 mg twice daily as tablet form, for 28 days. Patients of Group B were treated with Aceclofenac 100 mg twice daily as tablet form throughout the study period. Each patient was followed up at 14th day, 21st day & 28th day of treatment period. In each follow up efficacy was recorded by using NPRS (Numerical pain Rating Scale) on WOMAC (Western Ontario and McMaster University) osteoarthritis index.[11] Treatment-emergent adverse events and laboratory investigations were recorded for safety assessment. Pain, stiffness and functional disabilities on performance of activities of daily living of the two groups of patients were assessed using The WOMAC osteoarthritis index (0-24 items) which was estimated byNPRS. The NPRS for pain is a unidimensional measure of pain intensity in adults, a segmented numeric version of the visual analog scale (VAS) in which a respondent selects a whole number that best reflects the intensity of their pain. The common format is a horizontal bar or line.NPRS is a single 11-point numeric scale with 0 representing one pain extreme (e.g., "no pain") and 10 representing the other pain extreme (e.g., "pain as bad as you can imagine" and "worst pain imaginable").

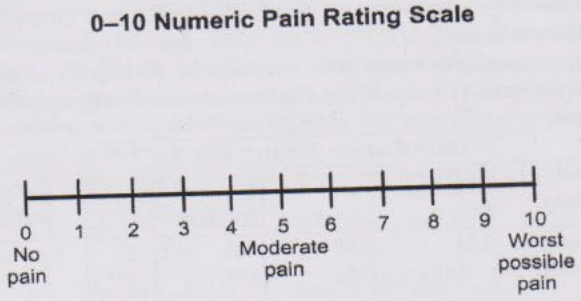

Figure 1 Numeric pain rating scale (NPRS)[12]

Data was processed and analyzed with the help of computer program SPSS (Statistical package for social sciences) 21.0 version.

Quantitative data was analyzed by mean and standard deviation and comparison were done between the groups by unpaired 't' test and within the groups by paired t-test. Repeated measure ANOVA was performed to analyze the repeated measure value. Qualitative data was analyzed by frequency and percentage and comparison were done between the groups by Chi-Square (χ^2) test, Fisher's exact test or Z test for proportion. A probability (p) value of < 0.05 was considered statistically significant.

Results

Total 110 patients were enrolled in this study. After randomization 7 patients from group-A and 9 patients from group-B who failed to complete follow up visit were excluded. So 48 patients of group-A (diacerein-glucosamine, plus aceclofenac treated group) and 46 patients of group-B (aceclofenac treated group) were analyzed in this study.Results regarding changes in pain score, stiffness, in physical function disability are shown in table I,II,III and IV.

The mean age of the patients in both groups was almost identical (56.06 ± 8.67 and 58.89 ± 9.07, p = 0.125). Our study suggests that OA is predominant in female (75%). The mean BMI of two treatment group also did not differ significantly (29.27 ± 1.82 and 29.94 ± 2.25, p = 0.116).

Table-I: Effect of diacerein-glucosamine plus aceclofenac (Group A) administration in combination or aceclofenac (Group B) alone on pain score (WOMAC items P1-P5) estimate before and 14th, 21st& 28th day after treatment of knee osteoarthritis

Study group	Pain score (Mean ± SD)				▲p value
	Baseline Day 0	At 14th day	At 21st day	At 28th day	
Group-A (n=48)	7.82 ± 0.73	3.90 ± 0.78	2.86 ± 0.81	2.22 ± 0.65	p<0.001
Group-B (n=46)	7.89 ± 1.13	5.24 ± 0.75	4.69 ± 0.85	4.70 ± 1.01	p<0.001
*p value	p=0.720	p<0.001	p<0.001	p<0.001	

*Unpaired t test and ▲repeated measure ANOVA was applied to analyze data.
▪WOMAC index items (1-24) were estimated by NPRS a numeric version of VAS.

Table-II: Changes in NPRS of stiffness score (WOMAC items S6-S7) (mean ± standard deviation) recorded before and 14th. 21st& 28th day after administration of diacerein-glucosamine plus aceclofenac (Group A) administration in combination or aceclofenac (Group B) alone in knee OA.

Study group	Stiffness score (VAS) (Mean± SD)				▲p value
	Baseline Day 0	At 14th day	At 21st day	At 28th day	
Group-A (n=48)	8.58 ± 1.06	5.96 ± 1.42	4.58 ± 1.51	3.58 ± 1.36	p<0.001
Group-B (n=46)	8.92 ± 0.95	7.40 ± 1.07	6.26 ± 1.19	5.50 ± 1.17	p<0.001
*p value	p=0.105	p<0.001	p<0.001	p<0.001	

*Unpaired t test and ▲repeated measure ANOVA was applied to analyze data.
▪WOMAC index items (1-24) were estimated by NPRS a numeric version of VAS.

Table–V: Percentage reduction of WOMAC score on NPRS score recorded in 14th, 21st& 28th day of administration of diacerein-glucosamine plus aceclofenac (Group A) in combination or aceclofenac (Group B) alone in the treatment of osteoarthritis of knee

Group	Percentage changes of WOMAC score (mean ± SD)			⅄p-value
	At 14th day	At 21st day	At 28th day	
Group-A (n=48)	-28.11 ± 6.85	-42.13 ± 6.38	-54.23 ± 6.42	p<0.001
Group-B (n=46)	-21.87 ± 4.11	-31.67 ± 5.26	-37.68 ± 8.71	p<0.001
*p- value	p<0.001	p<0.001	p<0.001	

' - ' means decrease compared to ' 0 ' week .⅄Repeated ANOVA and *unpaired t test

Adverse effects reported in this study were mild. The recorded adverse effects were altered urine color [15 (31.2%) vs 0 (0.0%); χ^2=17.104; p<0.001] and diarrhoea[6 (12.5%) vs 0 (0.0%); p=0.027] significantly more frequent in combined diacerein- glucosamine and aceclofenac treated group (Group A) than that of aceclofenac treated group (Group B); while nausea [4 (8.3%) vs 3 (6.5%); p=0.738], abdominal pain [5 (10.4%) vs 8 (17.4%); χ^2=0.959; p=0.329] and dependent oedema [1 (2.1%) vs 2 (4.3%); p=0.613] did not differ significantly between two treatment groups

Discussion

The present study was carried out to compare the effect and safety of combination use of diacerein-glucosamine plus aceclofenac with single drug aceclofenac, in treatment of knee OA. The result suggests that combination use of diacerein-glucosamine plus aceclofenac provide marked significant pain relief within two weeks of treatment.

This study revealed that the mean pain, stiffness and physical function disability score were decreased significantly from baseline value to end of treatment in combined diacerein-glucosamine plus aceclofenac treated group(p<0.001) and as were aceclofenac only treated group (p<0.001).But the reduction was marked in combined diacerein-glucosamine plus aceclofenac treated group consisting with the results observed by Loitongbam et al[13] who conducted comparative study between diacerein plus aceclofenac with aceclofenac alone on pain score. In their study Dalal et al [7] in a randomized controlled trial, used diacerein in combination with either celecoxib or aceclofenac.Furthermore Reginster et al [14] and Pavelka et al[15] studied effect of glycosamine on pain score. They studied WOMAC index on VAS and algo-functional indexes of Lequesne respectively. Korkmaz et al[16] observed no effect of glycosamine on osreoarthritis compared to placebo or diclofenac sodium in that order.

The present study showed that the change in total WOMAC score was more pronounced in three drug combination group. Patilet al[17] found that both aceclofenac and diclofenac were equally effective in reducing total WOMAC score (p<0.001) but the reduction was more marked in aceclofenac than that of diclofenac in OA knee (p<0.001). Gupta and Datta[18] also found that total WOMAC index in patients with OA knee were decreased in both combined diacerein and diclofenac plus diclofenac alone treated patients but there was no significant difference between two treatment groups in the 4 week (p=0.707) or at 8 weeks (p=0.203) of treatment.

Percent reduction in pain (p<0.001) and total WOMAC index (p<0.001) in combination of diacerein–glucosamine plus aceclofenac was more marked from starting to the end of the study. Whether Pavelka at al [19] observed identical change in diacerein only treated group after six months.

Diacerein and Glucosamine are recommended by the European League Against Rheumatism guidelines. "Diacerein" is suggested as a slow-acting, symptom and disease modifying agent in treatment of osteoarthritis.[7] It has a novel mode of action that diffe entiates it f om I s. iace ein inhi its the p od ction of inte le in-1 eta h man monoc tes and the effects of the c to ine on chond oc tes th s e e tin chond op otective effects on a tic la ca tila e and ed cin seve it of ca tila e one and s novial mem ane dama e in osteoa th itis.[7] There appears to be some inhibitory effects on leucocyte migration and activation, contributing to the weak anti-inflammatory activity. Diacerein does not block the synthesis of prostaglandins but may actually stimulate its synthesis, especially PGF-2 alpha, a prostaglandin with cytoprotective effect on the gastric mucosa.[10,7] It does not alter renal or platelet COX activity and is well tolerated by patients with prostaglandin dependent renal function.[8] Glucosamine is an amino sugar and a prominent precursor in the biochemical synthesis of glycosylated proteins and lipids, including glycosaminoglycans (GAG) which is a component of cartilage. It is

efficacious, safe, well-tolerated and is supplemented with NSAIDs.[9]

The tolerability profile in this study was generally consistent with the previous studies.[7,19] The adverse effects were mild and did not required any interruption of treatment.

In addition there were no clinically significant changes either in any of the haematological profile as an organ system in two groups during the study period. The majority of published data confined to comparative studies on diacerein with other NSAIDs. Diacerein is available in combination with glucosamine in our market as a fixed dose combination preparation. Therefore effect of diacerein on knee OA compared to either aceclofenac or other NSIADs was not feasible.

In conclusion, three drug combinations of diacerein-glucosamine plus aceclofenac is more effective than aceclofenac administered alone in the treatment of knee OA. Further randomized double blind study on large number of patients with variable doses is recommended.

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ORIGINAL ARTICLE

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Fast Food Preference and Pattern of Food Habits of Private Medical Students in Bangladesh

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Abstract

A cross-sectional study was carried out from December 2016 to February 2017 among medical students of two established private medical colleges of Bangladesh. A self-administered semi-structured questionnaire was used to collect information about age, sex, meal patterns, pocket money per month, fast food preference, fast food consumption per week, and knowledge of health complications. Prevalence of fast food consumption among private medical College students was 94% and about 32% medical students are consuming once a week. The important factors for the fast food preference were taste, easy accessibility and peer influence. Forty one percent of the respondents were skipped their breakfast and 46% mentioned that class pressure is the main cause for the skipping meal. 48% students were overweight and obese. Chi-square test was done for the analysis. P value <0.01 was considered as statistically significant association. For healthy life healthy food is necessary. It is suggested to limit the consumption of fast foods and soft drink, take three major meals daily and take balanced diet in every meal.

[OMTAJ 2016; 15(1)]

Introduction

Today the health of young people is critically linked to the health-related behaviours they choose to adopt [1]. Globalization and urbanisation have greatly affected one's eating habits and forced many people to consume fancy and high caloric fast foods, popular known as junk food[2]. The World Health Organization points out that 60% of the quality of an individual's health and life depends on his/her behaviour and lifestyle[1]. Increasing urbanization occurring in both developing and developed world is causing changes in the diet towards high energy-dense foods and sedentary lifestyle. Today fast food became an easy option for a busy family. Fast foodsarequick alternatives to home-cooked meals and lack in micro-nutrients such as vitamins, minerals and fibre and high in saturated fat, sugar and calories[3, 4]. Consumption of takeaway and fast food is becoming more popular among young people adolescents in developing countries[5]. The food consumption patterns and associated nutritional risks specific to medical students is a key concern[5]. Medical students are more prone to obesity due to their lifestyle with less physical activity, lack of sleep, stressful environment during their courses and examinations, disordered eating habits and their by are porn to obesity related health hazard [6] and also affect their psycho-social well being[7]. Eating too much fast food may leads to many incurable diseases like coronary heart diseases, type 2 diabetesmellitus, hypertension, stroke, obesity, colorectal cancer, prostate and breast cancer, osteoporosis, tooth decay etc[2, 4].A cross sectional study among private medical college students in Bangladesh represented that 27.16% of respondents were overweight which is higher than the national average[8]. Another study done on Grant Medical College Mumbai showed that many medical students have the habits of skipping meals especially breakfast which causes them less attentive and may because of poor academic performance[6].

The aim of the present study was to look into the preference, prevalence and pattern of fast food consumption among young medical students.

Materials and Methods

A cross-sectional study was carried out from December 2016 to February 2017 among the medical students of two established private medical colleges of Bangladesh: Tairunnessa Memorial Medical College situated in Gazipur and Aichi Medical College situated in Abdullahpur, Dhaka.The students within the ages of

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19 to 21 years were selected from those institutions. Only Bangladeshi medical students were included. All of the selected students were informed about the aim of the study and verbal consent was taken for their participation in the study. Interviews were conducted in the classroom or their college canteen when they enjoyed their class break. The permission to conduct study was obtained from the head of the respective institutions. A semi-structured questionnairewas used to collect data regarding age, sex, meal patterns, pocket money per month, fast food preference, fast food consumption per week, and knowledge of health complications. Height and Weight were recorded as per standard guidelines and BMI was calculated accordingly. In this study, based on the WHO BMI cut-offs level, a BMI<18.5 kg/m² was categories as under-weight, 18.5 – 24.9 kg/m² as the normal range, 25.0 – 29.9 kg/m² as overweight,30.0– 34.9 kg/m² as obese Class-l, 35.0 – 39.9 kg/m² as obese Class-ll and ≥40 kg/m² as obese Class-lll(9). The questionnaire was prepared in English.

Results

A total of 152 students of two private medical colleges in Bangladesh were shown interest and 150 students returned the complete questionnaires in the study. Age of the students were vary from 19- 21 years and mean age was 20.17±0.83. Out of 150 students 64.66% were females and 35.33% were males. 93.33% students like fast food and approximately 31.42% mentioned that they consumed fast food for once per week, 28.57% consumed fast food for twice in a week where3.57% reported to have fast food for 5 or 6 days per week. Male students (94.33%) were more habituated than Females (92.78%). Taste is the main cause of fast food consumption for (78.57%) students and 11.42% students reported that they take fast food due to its availability and peer influence (2.85%). In present study the students are preferred burger (35%) and second most choice is pizza (25.71%). 58% students had 3 major meal in a day. 46% students never escapeany major meal. Breakfast was skipped 66% students of total. The main reasons of skipping mealwere class pressure 46%, habit 26.66% and away from family 11.33% respectively. Approximately 89% students were concerned about the negative effects of fast food consumption. Most of the students reported they spent less than 5000 taka as their pocket money per month. Table II shows BMI of the respondents who consumed fast food. Out of 140 students 46.42% have normal weight, 37.85% were overweight and 9.28% were obese. The students who consumed fast food more than two days in a week had greater proportion of overweight or obesity than fewer consumers (table III) which is statistically significant.

Table I: Habits and patterns of food consumption of the respondents

Characteristics/food habits		Respondents (%)
Sex		
	Female	97 (64.66)
	Male	53 (35.33)
Fast food preference		
	Yes	140 (93.33)
	No	10 (6.66)
Fast food preference (n= 140)		
	Female	90 (92.78)
	Male	50 (94.33)
Fast food consumption (day/ week) (n=140)		
	1 day/ week	44 (31.42)
	2 days/ week	40 (28.57)
	3 days/ week	21 (15)
	4 days/ week	15(10.71)
	5 days/ week	5 (3.57)
	6 days/ week	5 (3.57)
	7 days/ week	10 (7.14)
Reasons of fast food consumptions (n=140)		
	Tasty	110 (78.57)
	Easily available	16 (11.42)
	Influenced by others	4 (2.85)
	Lack of other suitable option	7 (5)
	Pocket friendly	3 (2.14)
Type of fast food consumption (n=140)		
	Pizza	36 (25.71)
	Burger	49 (35)
	Samosa	25 (17.85)
	Chocolate	30 (21.42)
Soft drink consumption with fast food (n=140)		
	Yes	111 (79.28)
	No	31 (22.14)
Meal pattern per day (n=150)		
	1 meal	0
	2 meal	48 (32)
	3 meal	87 (58)
	More than 3 meal	15 (10)
Skipped meal		
	Breakfast	61(40.66)
	Lunch	4 (2.66)
	Dinner	16 (10.66)
	None	69 (46)
Causes behind skipping meal		
	Class pressure	69 (46)
	Habit	40 (26.66)
	Away from family	17(11.33)
	Others	24 (16)
Knowledge about hazards of fast food (n=150)		
	Yes	133 (88.66)
	No	17 (11.33)
Pocket money per month (n=150)		
	<5000	139 (92.66)
	5000 – 10,000	9 (6)
	>10,000	2 (1.33)

Table II: BMI of the respondents (n= 140)

Classification	BMI (kg/m²)	Respondents (%)
Underweight	<18.5	9 (6.42)
Normal range	18.5 – 24.9	65 (46.42)
Overweight	25 – 29.9	53 (37.85)
Obese l	30 – 34.9	13 (9.28)
Obese ll	35 – 39.9	0
Obese lll	>40	0

Table III. Association of fast food consumption with body mass index (n=140)

Freqyency of fast food consumption	Underweight/ normal	Overweight/ obese	Total
1 -2 days	73 (86.90%)	11 (13.10%)	84
3 – 7 days	20 (35.71%)	36 (64.29%)	35
Total	93	47	140
$X^2 = 30.4814$	significant at $p < 0.01$		

Discussion

Medical profession and university life are stressful and affects daily life and food choices[3]. Fast food is a type of mass-produced food that is prepared and served very quickly[4]. In recent years, junk food and cola consumption was high with predominance of overweight and physical inactivity[8]. Diet and lifestyle have a great influence on morbidity and mortality in life[9].The students who were taking snacks between breakfast and lunch were more likely to be overweight and obese than those who were not taking snacks between their meals[10]. This paper reports fast food consumption habits in young people attending two established private medical college students in Bangladesh. In Our study results showed that 93.33% respondents preferred fast food and 31.42% of them visited fast food outlets once a week. This higher frequency of fast food consumption once a week is similar to other study[3]. Male students are more habituated than female students which also found in study of Javalka at al.[3].Television and internet advertisement, brand reputation, taste, cost, hygiene and cholesterol level are the factors related to fast food preferences by the university students in Bangladesh[11]. Our study shown similarity with Bipasha that most favourite fast foods are burger, pizza, samusa and chocolates. Study done on Ghana Medical School showed that skipping breakfast causes fatigue and lack of concentration in medical students which also found in our study. Taking soft drink is unhealthy. However 79.28% students had soft drink with fast food though they are conscious about the hazards of consumption of fast food and soft drink. Same things shown in other studies where eating fast food as a regular habit might have increased over weight which leads to various cardiovascular disease, hypertension, type 2 DM.[2,8,12] In this study greater proportion of students were overweight (37.85%) and obese (9.28%) significantly more among most frequent usersof fast foods which was similar to the findings of other studies[4,6,9,12]. It is because students often choice fast food as a snakes for its taste. which is alarming for childhood obesity. Most of the students were well informed about the negative effects of fast food, but still they continued their affection without considering their health hazards.

In conclusion, as the future doctors medical students should adopt healthy dietary habit and lifestyle practise from the very beginning of their life. The study reports fast food preference and pattern of food habits among students of two private medical colleges of Bangladesh. The study showed that medical students have poor eating habits, like consumption of fast food, consumption of soft drink and skipping of meal. More than one third of the students were over-weight to obese. It is suggested to limit the consumption of fast foods and soft drinks, take three major meals daily, take balanced diet in every meal, and need more physical exercise. Specific health education programme, awareness about the major disease related to food habit and life style can improve the health of medical students. Food outlets in medical campus should be encouraged to provide healthy food for students.

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ORIGINAL ARTICLE

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Clinical profile in newly diagnosed patient with Graves' Disease: Bangladesh perspective

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Abstract

Graves' disease (GD) is one of the common thyroid disorders in Bangladesh. Clinical profile of newly detected Graves' disease may vary from region to region. This study was carried out to see the clinical profile of newly detected Graves'. This cross sectional study comprised of 100 newly diagnosed Graves' disease [age: 34.89±9.59 yrs, M±SD: sex (M: F): 41:59]. Detailed history as well as clinical profile and biochemical investigations [TSH, FT4, FT3, anti-thyroid antibodies, thyroid scan, radioactive iodine uptake (RAIU)] and Ultrasonography (USG) were done on individual basis. Data were collected in prescribed proforma after consent of the patients and processed using SPSS program (version-22.0). Highest frequency was found among subjects with 35-39 years (22%) followed by age ≥45 yrs. Palpitation (83%), tremor (79%), weight loss (85%), heat intolerance (86%), excessive sweating (82%), weakness (79%), thyromegaly (96%), and warm sweaty hand (87%) were most common. A good number of subject exerted increased appetite (50%), irritability (51%), eye ball swelling (46%), tachycardia (51%), and exaggerated reflex (47%) while about one third subjects have hyperdefecation (33%), thyroid bruit (31%), and proximal myopathy (30%). About 90% subjects manifest with toxicity.

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Introduction

Thyrotoxicosis is the state of thyroid hormone excess and is not synonymous with hyperthyroidism, which is the result of excessive thyroid function. The major etiologies of thyrotoxicosis are hyperthyroidism caused by Graves' disease, toxic multinodular goiter, and toxic adenomas.[1, 2] Graves' disease accounts for 60-80% cases of thyrotoxicosis.[1] Prevalence of Graves' disease varies with the degree of iodine sufficiency and it is the most common cause of thyrotoxicosis in iodine sufficient countries.[3] High dietary iodine intake is associated with an increased prevalence of GD.[1] There is a strong familial predisposition. About 15% of patient with GD have close relative with the same disorders.[4] It occurs more frequently in women than men[5] present at any age, with a peak incidence in 20-40-year age group.

Graves' disease is characterized by a variety of signs and symptoms including weight loss, heat intolerance, excessive sweating and palpitation, difficulty in sleeping, tremor, hyperdefecation, weakness, irritability, restlessness and menstrual irregularity, tachycardia, atrial fibrillation, thyromegaly, ophthalmopathy, resting tremor, hyperreflexia, and warm, moist and smooth skin.[4] Rare findings (in <1% of patients) include localized dermopathy (i.e. pretibial myxedema) and thyroid acropachy (i.e. clubbing).[6] Men with Graves' disease may have gynecomastia, reduced libido, and erectile dysfunction.[7] Women often have irregular menses. Weight loss is common, despite increased appetite and food intake.[8] Graves' disease is associated with a decreased quality of life.[9] Older patients more often present with weight loss or depression and referred to as apathetic hyperthyroidism.[10] Cardiovascular manifestations, especially atrial fibrillation, are common presenting symptoms in patients over 50 years of age.[11]

When hyperthyroidism is strongly suspected, diagnostic accuracy improves if serum TSH, FT_4 and FT3 are assessed at the time of the initial evaluation. Serum TSH levels are considerably more sensitive than direct thyroid hormone measurements for assessing thyroid hormone excess.[12]

In a patient with a symmetrically enlarged thyroid gland, recent onset of ophthalmopathy and moderate to severe hyperthyroidism, the diagnosis of GD is sufficient and further evaluation of hyperthyroidism causation is unnecessary. A radioactive iodine uptake (RAIU) is indicated when the diagnosis is in question (except during pregnancy) and distinguishes causes of thyrotoxicosis having elevated or normal uptake over the thyroid gland from those with near absent uptake. It is usually elevated in patients with GD and normal or high in toxic nodular goiter, unless there has been a

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recent exposure to iodine (e.g. radiocontrast). The pattern of thyroid scan in GD is diffuse unless there are coexistent nodules or fibrosis.[13]

A diagnosis of GD is made on the basis of clinical features of thyrotoxicosis (signs of thyrotoxicosis, diffuse enlargement of the thyroid gland, and exophthalmos and/or specific Ophthalmopathy), elevated thyroid hormones, suppressed thyrotropin (TSH) and thyroid 99m Technetium-pertechnetate scan evidence of diffuse homogeneous increased uptake in both lobes of the thyroid or increased RAIU.

Other causes of hyperthyroidism, such as iodine-induced thyrotoxicosis, subacute thyroiditis, silent thyroiditis and factitious thyrotoxicosis should be excluded before diagnosis of Graves' disease. Usually clinical, analytical and morphological procedures are employed to reach the diagnosis.

The majority of patients (60%) have either prolonged periods of thyrotoxicosis of fluctuating severity or periods of alternating relapse and remission. It is the minority who experience a single short-lived episode followed by prolonged remission and, in some cases, by the eventual onset of hypothyroidism.[14]

There are few studies in the field of GD in our country. Present study was conducted with the aim to observe the various clinical aspects of Graves' disease.

Material and Methods

This cross sectional study comprised of 100 newly diagnosed participants with Graves' disease attending at the department of endocrinology, BSMMU on the basis of history as well as clinical and biochemical findings. After full explanation about the purpose of the study, written informed consent was taken from all the eligible participants. Disease specific history was taken from each subject and underwent general, systemic, thyroid and eye examination. Investigations [TSH,FT4, FT3, anti-thyroid antibodies, thyroid scan, radioactive iodine uptake and ultrasonography(USG)] were done on individual basis. Each individual was interviewed by using structured questionnaires. Data were recorded in a prescribed proforma and processed by SPSS program (version 22).

Results

Present research studied clinical profile of 100 newly detected patients of Graves' disease, consecutively recruited from the department of endocrinology, BSMMU.

The age of the participant was 34.89±9.59 (yrs, M±SD) with the sex ratio 41:59(M: F).

Among of them highest frequency was observed between 35-39 years (22%) participants followed by age 45 and above (21%), 20-24years (17%), 25-29 years and 30-34 years (14%) each and 40-44 years (12%) and by occupation 43 were housewife, 10 students, 9 service holders, 13 businessmen, 3 farmers, 13 workers, 2 teachers and 7 were of miscellaneous occupation

Clinical signs and symptoms were studied among the subjects and higher frequencies were observed for palpitation (83%), tremor (79%), weight loss (85%), heat intolerance (86%), excessive sweating (82%), weakness (79%), thyromegaly (96%), and warm, sweaty hand (87%). A good number of subjects also exerted increase appetite (50%), irritability (51%), eye ball swelling (46%), tachycardia (51%), and exaggerated reflex (47%). About one third subjects were revealed to have hyperdefecation (33%), thyroid bruit (31%), and proximal myopathy (30%). However a small number of patients also showed weight gain (3%), menstrual irregularities (15%), high blood pressure (16%), clubbing (1%) and dermopathy (1%).

Table-I: Clinical features of newly diagnosed patients with Graves' disease (N=100)

Variable (s)	Value (%)
Palpitation	83%
Tremor	79%
Weight change	
Weight loss	85%
Weight gain	3%
No change	12%
Heat intolerance	86%
Excessive sweating	82%
Hyperdefecation	33%
Increase appetite	50%
Weakness	79%
Irritability	51%
Eyeball swelling	46%
Menstrual abnormalities (females=59)	
Regular	75%
Irregular	25%
Thyromegaly	96%
Grade 0	0%
Grade I	39%
Grade II	57%
Thyroid Bruit	31%
Tachycardia	51%
High Blood Pressure	16%
Warm sweaty hands	87%
Proximal myopathy	30%
Pretibial myxedema	1%
Clubbing	1%
Exaggerated reflexes	47%

Discussion

Graves' disease is one of the common thyroid problems prevailing in our community.[15, 16] This study was conducted in the department of Endocrinology, BSMMU, Dhaka, Bangladesh to observe the clinical profile of Graves' disease. This study included 100 newly diagnosed cases. As this is a tertiary hospital based study, findings may not represent the whole community.

It was observed that frequency of Graves' disease is more common between the ages of 35-39 years with females predominant. Regarding the clinical manifestations, higher frequencies were observed for palpitation, tremor, weight loss, heat intolerance, excessive sweating, weakness, thyroid enlargement and warm, sweaty hands. Similar to our findings others also observed higher frequency for this manifestations.[5, 6, 17, 18, 19, 20] None of these clinical manifestations can be regarded as cardinal/specific findings for GD. Some of the findings are relatively more important as manifestations of GD. Among them, eye ball swelling, thyroid bruit, proximal myopathy may be remarkably noted for GD which was found to be present among 30-50% of the subjects, contributing not much diagnostic help for the disease. Therefore, along with clinical merits, support of biochemical findings as well as clinical history and finally holistic assessment of the patient is required for diagnosis of the disease. About one third of women in present study exerted menstrual irregularities. Reported observation by others is similar to present study.[8] Enlargement of thyroid is very common in GD[19, 20] which was also observed in the present study in 96% of subjects. As mentioned above, ophthalmopathy is a relatively specific and important manifestation for GD.[4]

In conclusion the present pilot study was carried out in a tertiary level hospital and observed in newly diagnosed patients with GD present with palpitation, tremor, weight loss, sweating, heat intolerance, weakness, thyromegaly and warm, sweaty hands all of which are common manifestations with higher frequency and about 90% subjects manifest with toxicity.

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INFORMATION FOR THE CONTRIBUTORS

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Abbreviations

Except for units of measurements, abbreviations are discouraged. The first time an abbreviation appears, it should be preceded by the words for which is stands.

Drug name

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