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Original Articles

Case Report

Obituary

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Diabetes Prevention Program Research Group.

Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. Hypertension. 2002;40(5): 679-86 No author given:

21st century heart solution may have a sting in the tail. BMJ. 2002;325(7357):184

Volume with supplement:

Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42 Suppl 2:S93-9.

Issue with supplement:

Glauser TA. Integrating clinical trial data into clinical practice. Neurology. 2002;58(12 Suppl 7):S6-12.

Article published electronically ahead of the print version: Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. Blood. 2002 Nov 15; 100(10):3828-31. Epub 2002 Jul 5.

2. Books and Other Monograph Personal author(s):

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

3. Other Published Material MaterialNewspaper article:

Tynan T. Medical improvements lower homicide rate: study sees drop in assault rate. The Washington Post. 2002 Aug 12; Sect. A:2 (col. 4).

Dictionary and similar references:

Dorland's illustrated medical dictionary. 29th ed. Philadelphia: W.B. Saunders; 2000. Filamin; p. 675.

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Original Article

Effect of Extra-corporeal Shock-wave Therapy in the Management of Chronic Plantar Fasciitis

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ABSTRACT

Plantar fasciitis is a progressive degenerative condition of the plantar fascia which is reported to be one of the most common causes of lower heel pain in adults. Extracorporeal Shock Wave Therapy is being used for the management of plantar fasciitis now a day. The aim of the study was to find out the effects of Extracorporeal Shock-wave therapy in patients with chronic plantar fasciitis. A randomized clinical trial was conducted from May to October 2015, on 60 patients aged more than 18 years with plantar fasciitis attending in the department of Physical Medicine and Rehabilitation (PMR) in the Dhaka Medical College Hospital (DMCH) to observe the effectiveness of Extracorporeal shock-wave therapy (ESWT) in the treatment of plantar fasciitis and its therapeutic outcomes.60 patients were allocated randomly into intervention group (Group A) and control group (Group B). Data were composed through face to face interview using a questionnaire based on 1.Visual analogue scale, 2.Modified Roles and Maudsley score, and 3.100-point Scoring System for Plantar Fasciitis. But after 8 weeks, score was found lower in Group A than Group B (p<0.05).The usual total pain score was higher in 100-point Scoring System for Plantar Fasciitis (p<0.001) after 8 weeks of treatment as well average function score (0.001) in Group A. Patient satisfaction was also found higher in Group A by using Modified Roles and Maudsley score. Extracorporeal shock-wave therapy showed effective, so it can be suggested for the patients.

Keywords: *Plantar fasciitis, extracorporeal shock-wave therapy (ESWT)*

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INTRODUCTION

Plantar fasciitis (PF) is a progressive degenerative disorder of the plantar fascia subsequent from recurrent trauma at its beginning on the calcaneus. Plantar fasciitis is the commonest cause of inferior heel pain in adults. Other names for plantar fasciitis include painful heel syndrome, heel spur syndrome.[1]

The word "fasciitis" means inflammation is an inherent component of this condition. However, recent research suggests that some presentations of Plantar fasciitis manifest non-inflammatory, degenerative processes and should more be termed "plantar fasciosis".[2] Plantar fasciitis is synonymous with inflammation of the plantar fascia. In fact, the suffix "-ītis" essentially implies an inflammatory disease. Plantar fasciitis is widely described in the literature as having a multifactorial and widely disputed etiologyThe term Plantar fasciitis is used to describe a painful heel with inflammation of the plantar fascia at its origin. Plantar fasciitis is one of the common cause of heel pain, affecting 10% or more of the general population.[4] It may be due to strain to the origin of the plantar fascia or to biomechanical abnormalities of the foot.[5] Though a heel spur may present, but up to 27% of patients were without symptoms.[6] It mentions a clinical condition of pain in the plantar aspect of the heel, characteristically worse on

arising in the morning and after periods of prolonged sitting. The etiology of plantar fasciitis is not clear and probably multifactorial. Some rheumatologic disease like sero-negative spondyloarthopathy also may develop plantar fasciitis.

However, management advocated for plantar fasciitis have included rest, ice, stretches, non-steroidal anti-inflammatory drugs.[7], corticosteroid injection[8], iontophorosis, orthotics,[9] Tuli heel cups[10],night splints[11] ,heat, ultrasound[12], below the knee non weight bearing casts[5] , and short leg walking casts[13]. A very few number of patients undergo surgery. Extra corporeal shock wave therapy is well established for the treatment of urological condition. It was introduced in the 1980s for the treatment of insertion tendinopathies[14].ESWT is an application procedure where shock waves are passed through the skin to the painful part of the foot, by means of a special device. Extracorporeal means external to the body. The shock-waves are machine-driven sound waves; they are audible, low energy sound waves, which work by increasing blood stream to the injured area. This accelerates the body's healing process .It usually requires a course of three to four treatment, one to two weeks apart.

Extracorporeal shock-wave therapy for musculoskeletal conditions is assumed to offer extended analgesia and aids the healing process. It has been suggested as management for chronic plantar fasciitis.[15]Patients with chronic plantar fasciitis will be more efficiently treated by ESWT, so recommend ESWT to be used for patients who are not improving after 3 months of conservative measures.[16]It is safe and effective and has produced a very good rate of success in relief of pain and functional status.[17]

The aim of this study is to assess further the clinical efficiency of high energy shock wave therapy for the treatment of chronic plantar fasciitis throughout a twelve therapeutic session.

MATERIALS AND METHODS

A Randomized clinical trial (RCT) was accompanied in the Physical Medicine and Rehabilitation (PMR) Department, Dhaka Medical College Hospital, Dhaka, Bangladesh to establish the effect of Extra-corporeal Shock-wave Therapy in the management of chronic plantar fasciitis. One was a intervention group which is treated with Extracorporeal shock wave therapy (ESWT) along with NSAIDs, Exercises, orthotic as heel cushion/ shoe modification like slight high heel with heel cushion while control group did not receive Extracorporeal shock-wave therapy (ESWT). Intervention group and control group were done by lottery method and single blinding method was applied.

Patients attending in the Physical Medicine & Rehabilitation department, Dhaka Medical College Hospital, who were suffering from plantar fasciitis and more than 18 years of age, were the study population.

Diagnostic criteria of Plantar Fasciitis

- Aching, piercing in sole of foot.
- Foot pain that occurs immediately steps out of bed or get to feet after persistent periods of sitting.
- Pain that may decline subsequently patients have been on feet for a though, only to reappearance later in the day.
- Abrupt heel pain that builds steadily
- Foot pain that has carry on for more than a few days
- Limping

Inclusion criteria

- Age limit more than 18 years
- Unilateral single-site plantar medial heel pain
- Symptoms greater than 3 months
- Participation in a prearranged stretching package within the last 3 months
- Tenderness on confined pressure above the medial calcaneal tuberosity with passive dorsiflexion of the foot
- Visual Analogue Scale (VAS) score more than 5 (0- to 10-cm scale) for pain throughout the first few minutes of walking in the morning
- Modified Roles and Maudsley Score of 3 (FAIR) or 4 (poor)
- Readiness to relinquish any other concomitant therapies for the duration of the study

Exclusion criteria

- Previous surgery, conservative or physical therapy management within 3 months
- Pesplanus, pescavus or any other foot deformity
- Corticosteroid injection within few days
- Documented autoimmune or systemic disease
- Coagulation abnormalities
- Peripheral vascular disease
- Diabetes
- Local tumor
- Any previous trauma/fracture
- Infections

Sixty patients with chronic plantar fasciitis who satisfy the selection criteria were taken as sample. They were distributed into two groups (Group-A and Group-B). Each group comprises of 30 patients. Sampling technique was Simple random sampling by lottery. At first suitable participants were nominated and then separated into two groups; Group A and Group B.

Group A: ESWT+ NSAID+ Exercise+ Orthotics

Group B: NSAID+ Exercise+ Orthotics

a) ESWT: Patient was treated with shock-wave therapy three times weekly for four weeks of a total 12 sessions. The top of the applicator was placed directly to the proximal aspect of plantar fascia. Direction was 90degree to the joint. Gel is used for granting penetration. Shock-wave treatment was administered for 10 minutes per session at an 800 shocks with frequency of 4Hz, an intensity of 2-3 Bars.

b) NSAIDs: Tab. Etoricoxib 90 mg at night orally for two weeks was prescribed with coverage of Cap. Omeprazole 20mg twice daily. Same commercial preparation was used.

c) Exercise: Plantar fascia stretching at a rate of 10 repetitions twice daily was prescribed and demonstrated to all patients.

d) Orthotics: Heel cushions/ Medial arch support.

Data were collected through face to face interview. Before the interview, the detail of the study was explained to each eligible participant.

Demographic variable:

a. Age b. Sex c. Educational status d. Socio-economic condition

Three scales were used in this study

(1) Visual analogue scale (1-10)

(2) Modified Roles and Maudsley score

(3) 100-point Scoring System for Plantar Fasciitis

Data processing and exploration

Data processing and exploration was done by using Statistical Packing for the Social Sciences (SPSS) software Version 16.At first questionnaire was checked for completeness after completion of data collection. Data were entered into computer using SPSS 16. Then data were checked thoroughly after frequency run and necessary cleaning and editing done. An analysis plan was developed as per specific objectives of the study. Distribution was checked for normality and log transformation was done if any variable had data that was not normally distributed.

At the beginning of analysis, expressive analysis was done. Means and standard deviations were calculated for continuous variables when frequencies and percentages were calculated for categorical variables. Student's t-test was performed to assess the mean differences. Statistical significance was defined as $p<0.05$ and $p<0.01$ was defined as highly significant. Data were presented by tables and graphs.

RESULT

This Randomized Controlled Trial was conducted among 60 persons with chronic plantar fasciitis of both sexes. The 60 patients were further distributed arbitrarily into two groups; Group A and Group B. Patients in Group A were treated with Extracorporeal shock-wave therapy (ESWT) along with NSAIDs, Exercises, orthotic as heel cushion and Group B were managed with shoe modification like slight high heel with heel cushion. Data were analyzed with SPSS software using appropriate statistical methods and were presented in this chapter in tables and graphs. The finding were divided into several sections and organized as follows;

Background characteristics

VAS scores of both groups at 0 week, 2nd week, 4th week, 8th week.

Modified Roles and Mausdley scores of both groups at 0 week, 2nd week, 4th week,8th week.

100- Point scoring system for plantar fasciitis (pain score, function score and total score) of both groups at 0 week, 2nd week, 4th week, 8th week.

Background characteristics

Background information was collected from the participants. It included participant's age, sex, educational status and socio-economic status. These characteristics were displayed in tables and figures.

Age

Table 1 shows average age of the patients was 48.13 years with standard deviation of ±9.88 years. Minimum age of the participants was 32 years where the maximum was 67 years. The mean age of Group A was 47.27 years (±9.19) while it was a little bit higher in Group B (49.00±10.67).

Table 1 Age distribution in two groups

Age in year	Mean	±SD	Minimum	Maximum
Group-A	47.27	9.19	32	62
Group-B	49.00	10.67	32	67
Total	48.13	9.88	32	67

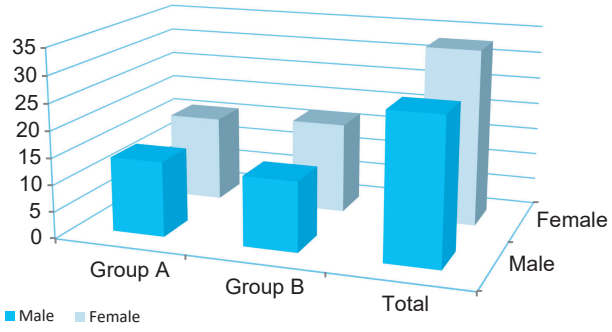

Fig.-1: *Sex distribution in groups*

Figure 1 shows among the participants, female were 55% (33) and the rest 45% (27) were male. Among 30 participants of Group A, 14 were male and 16 were female. Among equal number of participants in Group B, 13 were male and 17 were female.

Educational status

Educational status of the participants was divided into four categories: the participants who were illiterate or can sign only or did not pass primary school was categorized as "below primary", the participants who completed primary education but did not pass SSC were categorized as "primary to SSC" and the participants who passed SSC or HSC was categorized as "SSC to HSC" and above them were leveled as "graduate and above".

Table II shows all participants, among them 31.6% had completed SSC or HSC, 30% participants completed their graduation or above. In group A, 16.7% participants were below primary level of education.

Table II : Educational status of participants of both groups

Educational status	Below primary	Primary to SSC	SSC to HSC	Graduate and above
Group A	4 (13.3%)	8 (26.7%)	8 (26.7%)	10 (33.3%)
Group B	6 (20.0%)	5 (16.7%)	11 (36.6%)	8 (26.7%)
Total	10 (16.7%)	13 (21.7%)	19 (31.6%)	18 (30.0%)

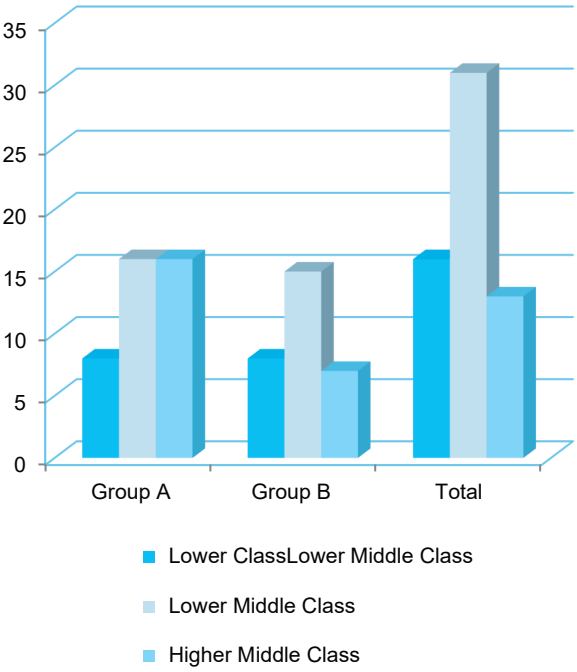

Fig 2 : Socio-economic status of the participants

Socio-economic status

Figure 2 shows socio-economic status of the participants was divided into lower socio-economic, lower-middle, higher-middle and higher class on the basis of their monthly family income. Among the participants, belonged to lower middle socio-economic class (average income 12,000 taka) 31 (51.6%), higher middle class (average monthly income 20,000 taka) participants were 13 (21.7%). There were no participant in higher class (monthly income >20,000 taka) while 16 (26.7%) in lower class (average monthly income were <12,000 taka). The proportion remained almost unchanged when they were divided into Group A and Group B.

Visual Analogue Scale (VAS) scores

Visual Analogue Scale (VAS) scores of both intervention group (Group A) and control group (Group B) were recorded at various intervals. Patients were advised to point their score on a Visual analogue scale and the score was recorded. VAS scores were recorded at beginning of the study (0 week), after 2 week, after 4 week and after 8 week. After that, student's t-test was performed to measure the mean difference among two groups at different time interval.

Table III shows Visual Analogue Scale (VAS) scores that were recorded at the beginning of the study for both of the groups. The mean VAS scores were almost equal for the both groups (Group A- 7.47±0.63; Group B-7.67±0.80). At the end of second week, VAS scores was dignified again and till then scores remained close for both groups (Group A-7.20±0.76; Group B- 7.40±0.62). This technique was repeated at the end of fourth week and then mean score was set up lower in Group A (5.40±0.72) than that of Group B (6.33±0.61). Scores were recorded for the last time at the end of eight week. The mean score remained lower in Group A (4.07±0.94) than in Group B (5.20±0.66). The differences found statistically significant (p value >0.05) at fourth and eighth week.

Table III Visual Analogue Scores of both groups

	Group	Mean ±SD	P value
VAS (0 week)	Group A	7.47 0.629	NS
	Group B	7.67 0.802	
VAS (2 week)	Group A	7.20 0.761	NS
	Group B	7.40 0.621	
VAS (4 week)	Group A	5.40 0.724	<0.05
	Group B	6.33 0.606	
VAS (8 week)	Group A	4.07 0.944	<0.01
	Group B	5.20 0.664	

VAS= Visual Analogue Scale

Modified Roles and Maudsley Score

Modified criteria of Roles and Maudsley score was developed on the basis of patient compliance about a treatment. There are four grading in this scale; score 1= Excellent, score 2= Good, score 3= Fair, score 4= Poor.

Table IV (a) shows at the beginning of the study, 26 patients experienced poor with pain and 4 felt fair in Group A, while it was 24 and 6 respectively in Group. After 2 weeks, 15 patient experienced fair and 1 patient experienced good in Group A, while 13 patients felt fair and no patient felt good in Group B. At the end of treatment, 8 patients felt excellent and 17 patients felt good in Group A. No patient felt poor in Group A after completion of treatment. After completion of treatment, no patient felt excellent while three patients felt poor in Group B.

Table IV (b) shows after 2 weeks of treatment, the Group A had mean Modified Roles and Maudsley (MRM) score 3.43±0.57 while the score was 3.57±0.50 in Group B. MRM score was lower (more compliance) after 4 weeks of treatment in Group A (2.57±0.51) than in Group B (3.23±0.61). The situation remained unchanged after 8 week (1.90±0.67 in Group A and 2.67±0.43 in Group B). All of the differences were statistically significant.

Table IV (a) MRM score of both groups

	Group	Poor	Fair	Good	Excellent
0 week	Group A	26 (87.7%)	4 (13.3%)	0 (0.0%)	0 (0.0%)
	Group B	24 (80.0%)	6 (20.0%)	0 (0.0%)	0 (0.0%)
2nd week	Group A	14 (46.7%)	15(50.0%)	1 (3.3%)	0 (0.0%)
	Group B	17 (56.6%)	13 (43.3%)	0 (0.0%)	0 (0.0%)
4th week	Group A	0(0.0%)	16 (53.3%)	14 (46.7%)	0 (0.0%)
	Group B	12 (40.0%)	16(53.3%)	2 (6.7%)	0 (0.0%)
8th week	Group A	0 (0.0%)	5 (16.7 %)	17 (56.7%)	8 (26.7%)
	Group B	3 (10.0%)	20 (66.7%)	7 (23.3%)	0 (0.0%)

Table IV (b) MRM score of both groups

	Group	Mean	±SD	P value
MRMS(2 week)	Group A	3.43	0.568	<0.05
	Group B	3.57	0.504	
MRMS(4 week)	Group A	2.57	0.507	<0.01*
	Group B	3.23	0.606	
VAS (8 week)	Group A	1.90	0.662	<0.01*
	Group B	2.67	0.434	

MRMS= Modified Roles and Maudsley Score, *= Highly Significant (HS)

100 –Point Scoring System for plantar fasciitis score

"100 –Point Scoring System for plantar fasciitis", measures pain in two domains; 70-points for pain score and 30-point for function score. Both pain score and function score were measured and compared.

Pain score

Table V shows pain scores were almost equal for both groups at 0 week (Group A-19.93±7.03; Group B-20.20±6.18) and end of 2nd week (Group A-20.20±6.53; Group B-20.67±6.78). At the end of 4th week, Group A scored higher (27.27±6.78) than Group B (24.67±6.33). But the above differences were not statistically significant. After 8th week Group A had better pain score (36.87±8.31) than Group B (33.40±8.01) and the difference was statistically significant.

Function score

Table VI shows function scores were also almost equal for both groups at 0 week (Group A-13.60±0.89; Group B-13.80±1.06) and end of 2nd week (Group A-14.00 ±1.39; Group B-14.33±1.32). after 4th week, Group A scored a little higher (18.87±2.73) than Group B (16.93±1.98). None the above differences was statistically significant. After 8th week Group A achieved better function score (21.47±2.97) than Group B (19.13±2.97) and the difference found statistically significant (p<0.05).

Table V : 100 –Point Scoring System for plantar fasciitis (pain score) of both groups

	Group	Mean	±SD	P value
100-PSS(pain score); 0 week	Group A	19.93	7.032	NS
	Group B	20.20	6.183	
100-PSS(pain score); 2nd week	Group A	20.20	6.531	NS
	Group B	20.67	6.774	
100-PSS(pain score); 4th week	Group A	27.27	6.782	NS
	Group B	24.67	6.332	
100-PSS(pain score); 8th week	Group A	36.87	8.312	<0.05
	Group B	33.40	8.013	

Table VI : 100 –Point Scoring System for plantar fasciitis (function score) of both groups

	Group	Mean	±SD	P value
100-PSS(function score); 0 week	Group A	13.60	0.894	NS
	Group B	13.80	1.064	
100-PSS(function score); 2nd week	Group A	14.00	1.390	NS
	Group B	14.33	1.322	
100-PSS(function score); 4th week	Group A	18.87	2.726	NS
	Group B	16.93	1.982	
100-PSS(function score); 8th week	Group A	21.47	2.968	<0.05
	Group B	19.13	2.968	

Total score for 100- Point Scoring System for plantar fasciitis

Table VII shows total scores were also almost equal for both groups (Group A-33.5±7.83; Group B-34.00±6.93) at week and by the end of 2nd week (Group A-34.20±7.62; Group B-34.00±7.76), and those were not statistically important as well. After 4th week, Group A had a higher (46.13±8.34) than Group B (41.60±7.52). This difference was statistically significant (p<0.05). After 8th week of management, Group A attained better score (58.33±10.46) than Group B (52.53±8.74) and this difference was found statistically significant (p<0.01).

Table VII: Total score for 100- Point Scoring System for plantar fasciitis

Group		Mean	±SD	P value
100-PSS (0 week)	Group A	33.53	7.825	NS
	Group B	34.00	6.928	
100-PSS (2nd week)	Group A	34.20	7.622	NS
	Group B	34.00	7.764	
100-PSS (4th week)	Group A	46.13	8.337	<0.05
	Group B	41.60	7.518	
100-PSS (8th week)	Group A	58.33	10.456	<0.01
	Group B	52.53	8.740	

DISCUSSION

Plantar fasciitis is a most common presenting disorder of foot in which symptoms become chronic and functionally incapacitating. It occurs in similar proportions in all culture, interferes with equality of life and work performances. It is common reason for medical consultations. Along with other treatment, recently, ESWT has been advised for treatment of this condition. A randomized clinical study was accompanied on 60 patients with plantar fasciitis attending in the physical medicine and rehabilitation department in the Dhaka Medical College Hospital to assess the efficacy of Extracorporeal Shock-wave therapy (ESWT) in the treatment of plantar fasciitis and its therapeutic outcome. The patients were randomly divided into two groups by lottery; Group-A and Group-B. In Group-A, Extracorporeal shock-wave therapy (ESWT) along with NSAIDs, Exercises, orthotic as heel cushion/ shoe modification like slight high heel with heel cushion and Group-B NSAIDs, Exercises, orthotics as heel cushion/ shoe modification will be given for a period of 8 weeks.

Visual Analogue Scale (VAS) scores of both intervention group (Group A) and control group (Group B) were recorded at various intervals. VAS scores were recorded at the beginning of the study for both of the groups. The mean VAS scores were almost equal for the both groups (Group A-7.47±0.63; Group B-7.67±0.80). After then, at the end of second week, VAS scores were measured again and till then scores remain close for both groups (Group A-7.20±0.76; Group B-7.40±0.62). This procedure was repeated after fourth week and then the mean score was found lower in Group A (5.40±0.72) than that of Group B (6.33±0.61). Scores were recorded for the last time at the end of 8th week. The mean score remained lower in group A (4.07±0.94) than in Group B (5.20±0.66). The mean difference were found statistically significant (p value > 0.05) at fourth and eighth week.

Similar study was conducted by Krishnan et al., in 2012 in Delhi, India among 25 patients. The mean pretreatment VAS for the entire group was 9.2±0.7. Four weeks after treatment the VAS decreased to 3.4±1.9. This difference was statistically significant (p<0.05). VAS scores were improved in both of the studies though improvement was greater in the study of Krishnan et al.

On the other hand, at the beginning of the study, 26 (87.7%) patients experienced poor with pain and 4 (13.3%) felt fair in Group A, while it was 24 (80.0%) and & (20.0%) respectively in Group B. After 2 weeks, 15(50.0%) patient experienced fair and 1 patient experienced good in Group A, while 13 (43.3%) patient felt fair and no patient felt good in Group B. At the end of treatment, 8(26.7%) patients felt excellent and 17(56.7%) patients felt in Group A. No patient felt poor in Group A after treatment completed. After completion of treatment, no patient felt excellent while three patients felt poor in Group B. In the study of Krishnan et al., 2012 four weeks post treatment, 18(72%) heels were rated as `1` (excellent), 4 (16%) as `2` (good), and 1(4%) as `3`(fair) and `4` (poor or unchanged).Though excellent were more in Krishnan et al's study, the scenario in both study was similar.

Another study was conducted by Chen et al., in Taiwan in1999 on similar topic by using 100-point scoring system among 74 patients. The average total pain scores were 29.3±14.6 pretreatment and 49.2±13.9 post treatment (p<0.001). The average function scores were 15.2±4.6 pretreatment and 21.6±6.0 post treatment (p<0.001).

On the other hand this study also revealed similar result. The average total pain score were 19.93±7.03 pretreatment

and 38.87±8.31 post treatment (p, 0.001). The average function scores were 13.60±0.89 pretreatment and 21.47±2.97 post treatment (p<0.001).This study was found consistent with most of the other studies.

CONCLUSIONS

This study found the effect of Extra-corporeal Shock-wave Therapy in the treatment of chronic plantar fasciitis when treated together with other treatment choices. The patients treated with Extra-corporeal shock-wave therapy along with other options had better presentation than those who did not receive extracorporeal shock-wave therapy. The effect was better after 4th week and it was clear after 8 week of extracorporeal shock-wave therapy. There was no significant difference between two groups after two weeks of treatment. So it may be recommended that extracorporeal shock-wave therapy might be rewarding after 4 weeks of treatment. Extracorporeal shock-wave therapy showed better compliance, and can be suggested by the physicians.

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Original Article

Early Signs of Autism and It's Relation with Gestational Factors: An Urban Based Study in Bangladesh

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Abstract

A cross-sectional study was conducted to observe the prevalence autism spectrum disorders (ASD) and its correlation with gestational factors in country population between January and December of 2016. The study population was nursery school child aged 3-5 years whose parents were willing to participate in the study. In this study, the children are excluded whom already being identified as any forms of autism spectrum disorders. Convenient sampling technique was followed to select the samples from 47 schools of Uttara, Ashulia and Nikunjo area of Dhaka City Corporation and Tongi area of Gazipur City Corporation under Dhaka Division, Bangladesh. A total of 1000 children were recruited in the study. The research instrument was a semi-structured questionnaire based on Early Screening of Autistic Traits (ESAT) tool. Based on the diagnosis of the cases, parents were invited to another interview to fill out questionnaire related to some parental and gestational factors to assess the relationship with autism. The study found early signs of autism in 2.6% cases (26 in 1000), by using Early Screening of Autistic Traits (ESAT) questionnaire. Among the children having early signs of autism, history of normal birth weight was found more in term pregnancy (62.5%) than its preterm counterpart (60.0%). Growth parameter was higher in normal birth weight (68.8%) than low birth weight (60.0%). Similarly, growth parameter was also higher in children that are from 3rd gravida (75.0%) than that of 2nd gravida (66.7%) and 1st gravida (61.5%). Birth weight was also higher in >2 years birth spacing (60.0%) than that of <2 years (50.0%). Complication was more in home delivery (50.0%) than institutional delivery (20.8%). Birth injury happened more in home delivery than institutional delivery. Similarly, complication during delivery was higher in >2 years birth spacing (30.0%) than that of <2 years (0%), However, the difference was not significant statistically in any of the comparisons (P>0.05). Hence, no causal relation was found between autism and gestational factors.

Keywords: *Autism spectrum disorder, early signs of autism, prevalence, gestational factors*

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INTRODUCTION

Autism spectrum disorders (ASD) are a diverse group of conditions. Commonly seen in the beginning in infancy and toddler years, those developmental disorders are characterized by lac of social interaction and communication, constricted and dreary interests and behaviours.[1] Characteristics of autism may be detected in early childhood, but autism is often not diagnosed until much later.[2] Although several studies have hypothesized and showed that some of the parental, postpartum or obstetric conditions are associated with autism,[2-4] the problematic effects, or causations and overall conclusions of those studies were found often inconsistent.[5] In this regard, research into prenatal factors were focused on usually parental factors, like age, comorbidity, medications, while perinatal research were focused on

usually possible trauma during the birth process with its complications like Caesarean section, breech presentation, fetal distress, postpartum hemorrhage and prolonged labour, incidence of multiple gestations, pregnancy with co-morbidities and complications, preterm and/post-term birth etc. Similarly, newborn research concentrated on neonatal distress, including low birth weight and neonatal complications.[6-9] However, in our country, there is no such research reports available to date; hence we lack evidence. During the last 10 years, autism has appeared as a major public health issue around the globe.[1] Though the degree of impairment and consequences might differ among the patients, ASD is a lifelong condition. Immense support is required to overcome the conditions and social situations.[1] It is common in ASD condition that children are deprived from the proper routine education.[1] Therefore, studies related to epidemiology and underlying factors are important especially on the relation of pre-, peri- and neonatal risk factors on ASD from an ethnically and socially diverse country like Bangladesh. Considering those points, we did this study to see the relationship between gestational factors/exposures and autism in children in an urban area.

MATERIALS AND METHODS

This study was cross-sectional and conducted in the span of January to December of 2016. The population of study was school going children aged 3-5 years whose parents were willing to participate in this study. We excluded children who were already diagnosed as having autism spectrum disorder. However, a convenient sampling technique was followed to select the samples from 47 schools of Uttara, Ashulia, Nikunjo areas of Dhaka City Corporation and Tongi area of Gazipur City Corporation under Dhaka Division, Bangladesh. A total of 1000 children aged 3-5 years, who fulfilled the selection criteria, were recruited in the study. The instrument was pre-tested among 10 children in Azampur Govt. Primary School at Uttara Area under Dhaka City Corporation for clarity, accuracy, lucidity and find out the validity of the questions. Minor modifications were considered in the final interview schedule. The research instrument contained a semi-structured screening questionnaire, based on Early Screening of Autistic Traits (ESAT) questionnaire tool to determine early signs of autism.[10] Early Screening of Autistic Traits (ESAT) is a primary screening checklist with 19 items that was designed for infants 0-36 month(s) old. It is based on prominent early signs and symptoms of autism spectrum disorders (ASD), and designed to be completed by parents/caregivers during children's health visits. Failure on three or more items indicates the need for further evaluation.[10] Based on the diagnosis of the cases, parents were invited to another interview to fill out questionnaire related to some parental factors and gestational factors which could be helpful to assess their relationship with autism.

Proportions of early sign of autism were determined by frequency and percentage. Other data ware also shown in tables with frequency and percentage. In order to see the association of gestational factors and autism in those children, Chi-square (χ^2) test was done. All the tests were two tailed; $P<0.05$ was considered statistically significant. Data analysis was done using SPSS (Statistical Package for Social Science) version 16.0 software. This research was approved by the Institutional Ethical Committee of National Institute of Preventive and Social Medicine (NIPSOM), Dhaka, Bangladesh.

RESULTS

Table-I shows a prevalence of early signs of autism in 2.6% cases (26 in 1000). Children having deficits or failure on three or more items were detected as having early signs of autism. 4(0.4%) had deficiency to show interest in different objects, 4(0.4%) could not express their feeling as deserved by the situation, 2(0.2%) could not react to normal sensory stimulation, 7(0.7%) did not cry or call, while left alone. Stereotype repetitive body movements were observed in 6(0.6%), 1(0.1%) could not bring objects as directed, 8(0.8) failed to show interest on others, 6(0.6%) did not like to be cuddled, 5(0.5%) never smiled to others, and 4(0.4%) did not like to play with others. Besides, 1(0.1%) failed to react to spoken language, 3(0.3%) failed to speak conjoining 2/3 words together, 1(0.1%) failed to gaze at something shown or pointed to. Finally, 4(0.4%) children were found who could not ever pretend like making a cup of tea using a toy cup & teapot from the toys.

Table I: Early signs of autism as screened by using ESAT tool (n=1000)

Variables	Yes (Percentage)	No (Percentage)
Interested in different object	996 (99.6)	4 (0.4)
expresses feeling (crying/smiling) on expected/appropriate time	996 (99.6)	4 (0.4)
React normal way to sensory stimulation	998 (99.8)	2 (0.2)
If child is left alone, does it start crying/ calling?	993 (99.3)	7 (0.7)
Without stereotype repetitive movement (banging head/ rocking body)	994 (99.4)	6 (0.6)
Own accord, bring objects over you	999 (99.9)	1 (0.1)
Showing interest to other children or adults	992 (99.2)	8 (0.8)
Child likes to be cuddled	994 (99.4)	6 (0.6)
child ever smiled at you or others	995 (99.5)	5 (0.5)
Child likes to play with others	996 (99.6)	4 (0.4)
React to spoken language to for instance (by looking/ listening/ smiling/ babbling)	999 (99.9)	1 (0.1)
Child can speak a few words or utter various words	997 (99.7)	3 (0.3)
Child can follow your gaze to see what you are pointing to	999 (99.9)	1 (0.1)
Can the child ever pretend, make a cup of tea using a toy cup & teapot?	996 (99.6)	4 (0.4)
Early signs of autism present (as done by using ESAT tool)	**26 (2.6)**	**974 (97.4)**

Table-II shows that gestational age was term 16(61.5%), rest was preterm 10(38.5%). Normal birth weight 16(61.5%), low birth weight 10(38.5%). Birth injury was present in 2(7.75%). H/O milestone of growth 17(65.4%). 1 gravida 13(50.0%) and 2(7.7%) respondents had birth spacing (comprising previous issue) was less than 2 years and 10(38.5%) respondents birth spacing was greater than 2 years. Mode of delivery were, Caesarean section 20(76.9%), followed by normal vaginal delivery 5(19.2%) and Forceps' delivery 1(3.8%). No complication during delivery 20(76.9%) and 6(23.1%) respondents were complication during delivery.

Table II: Gestational factors at a glance (n=26)

Variables	Frequency	Percentage
Gestational age		
Preterm	10	38.5
Term	16	61.5
Weight at birth		
Low birth weight	10	38.5
Normal birth weight	16	61.5
Birth trauma /injury		
No	24	92.3
Yes	2	7.7
H/O milestone of growth		
No	9	34.6
Yes	17	65.4

Variables	Frequency	Percentage
Gravida		
1st	13	50.0
2nd	9	34.6
3rd	4	15.4
Birth spacing comprising previous		
<2 years	2	7.7
>2 years	10	38.5
Mode of delivery		
Normal vaginal delivery	5	19.2
Caesarean section	20	76.9
Forceps' delivery	1	3.8
Complication during delivery		
No	20	76.9
Yes	6	23.1

Table-III shows that normal birth weight was in term pregnancy 62.5% preterm group 60.0%. However, the result was found statistically not significant (P>0.05).

Table III: Gestational age and weight at birth

Gestational age	Weight at birth		χ^2	P value
	Low Birth Weight	Normal Birth Weight		
Preterm	4(40.0%)	6(60.0%)	.016	>0.05
Term	6(37.5%)	10(62.5%)		
Total	10(38.5%)	16(61.5%)		

Table-IV shows that, parameters of growth were higher in normal birth weight (68.8%) than that of low birth weight (60.0%), the result found statistically not significant though (P>0.05).

Table IV: Weight at birth and milestone of growth

Weight at birth	Milestone of growth		χ^2	P value
	No	Yes		
Low birth weight	4(40.0%)	6(60.0%)	.208	>0.05
Normal birth weight	5(31.2%)	11(68.8%)		
Total	9(34.6%)	17(65.4%)		

Table-V shows that, parameters of growth were higher in the 3rd gravida (75.0%) than that of the 2nd gravida (66.7%) and the 1st gravida (61.5%). However, the result was not found statistically significant (P>0.05).

Table V: Gravida of the respondents and milestone of growth

Gravida	Milestones of growth		χ^2	P value
	No	Yes		
1st	5(38.5%)	8(61.5%)	.255	>0.05
2nd	3(33.3%)	6(66.7%)		
3rd	1(25.0%)	3(75.0%)		
Total	9(34.6%)	17(65.4%)		

Table-VI shows that, birth weight was higher in >2 year birth spacing (60.0%) than that of <2 year birth spacing group (50.0%), the result was not statistically significant though (P>0.05).

Table VI: Birth spacing of respondents and birth weight

Birth Spacing	Birth Weight		χ^2	P value
	Low	Normal		
<2yrs	1(50.0%)	1(50.0%)	.069	>0.05
>2yrs	4(40.0%)	6(60.0%)		
Total	5(41.7%)	7(58.3%)		

Table-VII shows that, complication during delivery was higher in home delivery (50.0%) than institutional delivery (20.8%), though the difference was not statistically significant (P>0.05).

Table VII: Mode of delivery of the respondents and complications

Mode of delivery	Complication during delivery		χ^2	P value
	No	Yes	.885	>0.05
Home Delivery	1(50.0%)	1(50.0%)		
Institutional Delivery	19(79.2%)	5(20.8%)		
Total	20(76.9%)	6(23.1%)		

Table-VIII shows that, birth injury was higher in home delivery (50.0%) than institutional delivery (4.2%), though the difference was not statistically significant (P>0.05).

Table VIII: Mode of delivery of respondents and birth injury

Mode of delivery	Birth injury		χ^2	P value
	No	Yes		
Home Delivery	1(50.0%)	1(50.0%)		
Institutional Delivery	23(95.8%)	1(4.2%)	5.462	>0.05
Total	24(92.3%)	2(7.7%)		

Table-IX shows that, complications during delivery was higher in >2 year birth spacing (30%), while no complication was in <2 year birth spacing (0%). However, the result was found statistically not significant (P>0.05).

Table IX: Birth spacing of the respondents and delivery complications

Birth Spacing	Complication during delivery		χ^2	P value
	No	Yes	.800	>0.05
<2yrs	2(100%)	0(0%)		
>2yrs	7(70.0%)	3(30.0%)		
Total	9(75.0%)	3(25.0%)		

DISCUSSION

The study estimated that the prevalence of ASD was 2.6% (n=1000) and it is in agreement with other population-based study, such as 2.64% in South Korea[11], Japan[12] and China[13]. In contrast, a study done in our neighbouring country, India, on its diverse populations reported the ASD prevalence was 1.4% among children aged 6-9 years.[14] It is estimated that worldwide about one in 160 children has the ASD.[15] However, it has shown increasing trends in the western world.[16-17] In this study, ASD cases were determined in the overall sample, which were in mainstream school population, previously undiagnosed and untreated.

Earliest in 1956, that is just only a few years after ASD was first described, Pasamanick and colleagues tried to report the link between complications during pregnancy and autism.[18] Since then, plenty of interpretations have been portrayed and studies trying to identify risk factors of autism; but those hardly clarify the relation between autism and adverse exposures during the pre-, peri- and infant periods. Nonetheless, increasing evidence also suggests a role of genetic factors in the origins of autism.[19,20] Still it remains unclear whether "certain complications at birth are causal, play a secondary role in shaping clinical expression in individuals with genetic vulnerability, or represent some of the shared causal factors" in the development of ASD.[19]

In this study, there was no significant association between gestational age and weight at birth (P>0.05). However, Schendel et al. reported that birth weight <2.5 kg and preterm birth at <37 weeks gestation were associated with 2-fold increase risk of autism, as studied on a Danish population.[21] We did not find any relationship between gravida and autism (P>0.05); however, Curran et al. reported an increased risk of autism with higher number of gravida, in Swedish population.[22] Unlike ours, they also confirmed that children born by elective Caesarean section were 21% more likely to be diagnosed as having ASD.[22] Many of the earlier studies that examined pre-, and perinatal risk factors in autism[2-4,23-25] could not report significant differences, due to smaller sample size[26], as we assume research on such a sensitive issue impacts willful participation in a disability-averse society. Similar happened to ours. The present study was limited to cross-sectional design that signifies that the association found in this study does not necessarily mean to establish any causal relationship. Moreover, probability sampling technique could not be employed to recruit the study unit; our samples were selected conveniently due to time and budget constraints. As a result, there might be a selection bias. Last but not the least, most of the information about gestational factors was collected with a questionnaire based on the memory of the respondents, which may be liable to a recall bias.

CONCLUSIONS

This study finds that the prevalence of autism spectrum disorder is 2.6% in urban population of Bangladesh. However, no causal relationship was found between autism and gestational factors in children in our study. This was a small-scale cross-sectional study conducted in a few schools in urban region within a limited time frame and constrained budget. Further studies are recommended by using large, population-based epidemiological samples to explore associations between perinatal variables and the risk of autism all over Bangladesh.

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Original Article

Co-Morbidities and Family History Among Methamphetamine Users

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Abstract

The abuse of methamphetamine, locally known as Yaba locally, has increased in Bangladesh recently. The study was designed to determine the proportion of co-morbidities, in terms of physical, psychiatric and other substances, and family history of substance use and other psychiatric disorders among methamphetamine abusers in Bangladesh.This was a cross-sectional study. Data were collected from the available medical documents of a private hospital dedicated for the management of substance abusers in Dhaka, Bangladesh. Information of the individuals admitted in the hospital during 1 January, 2014 to 31 December, 2015 due to substance related disorders having history of using methamphetamine within one month of hospitalization were enrolled in the study. Completed data of 115 individuals were taken and data analysis was performed using Statistical Package for Social Sciences (SPSS) version 24.Most (91.3%) of the respondents were male. Mean age of the respondents was 24.6 (±5.8) years. Half of the respondents (50.4%) belonged to the age group 21-30 years. Most (89.6%) of them resided in urban area and was Muslim (94.8%). Majority (52.2%) was unmarried. Regarding education status, majority (34.8%) completed graduation. About one-third (33.9%) were currently unemployed. All the methamphetamine users had used other substances. Among the other co-morbid substances, nicotine was the substance used by most (94.8%) respondents, followed by cannabinoids (56.5%) and opiates (38.3%). Among the respondents about one-third (33.9%) had current physical co-morbidities. Co-morbid psychiatric disorders were present among 29.6% of the respondents. Among the respondents, more than one-fourth (27.8%) had family history of substance use, 20.9% had family history of other psychiatric illnesses. All the methamphetamine users had used other substances. A substantial proportion of methamphetamine users had physical and other psychiatric comorbidities and family history of substance and other psychiatric disorders. This essential issue should be considered in the management strategy of methamphetamine use.

Keywords: *Bangladesh, co-morbidity, family history, methamphetamine, substance, yaba*

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INTRODUCTION

Substance use disorders have become a major public health problem in Bangladesh. Curiosity about substances, peer pressure, seeking enjoyment and availability of drugs are among the important causes of substance dependence in Bangladesh. Frequent use of drugs causes educational dropout, unemployment, financial crisis, family disharmony, marital discord and many other social disadvantages. Substance abusers became an additional burden to the family and society.

There are much variations in the estimate of substance abusers in the studies conducted in Bangladesh due to the difference of study place and data collection technique. While national survey on mental health revealed that 0.63% of the adult population (18 years and above) in Bangladesh had been suffering from substance related and addictive disorders, study conducted in outpatient department of National Institute of Mental Health (NIMH), Dhaka revealed that 7.66% of the respondents were suffering from substance related disorder. A study among patients attending general practice showed that 2.88% were suffering from substance use disorders while study conducted in a private clinic in Dhaka city showed that 29.6% of the patients were suffering from substance related disorders.

Though studies conducted in the ending years of last century reported opiates group as the primary drug of substance[1], recent studies indicate that methamphetamine use has been increased in Bangladesh.[2] The reports by print and electronic media showing the recent trend of substance use, drug trafficking and

seizure of substances by law enforcement agencies in Bangladesh also support the notion. Locally methamphetamine is used in the name of "Yaba" which is a mixture of methamphetamine and caffeine. There has been an increase in seizure of Yaba and other methamphetamine-containing substances since 2008, with more than 1.3 million pills seized in 2011 and 20.1 million pills seized in 2015.

There is only one government drug de-addiction centre with facilities for inpatient treatment in Dhaka, the capital city of Bangladesh. Some substance abusers of the city can get inpatient treatment from National Institute of Mental Health. Other health-care facilities for management of substance abuse belong to private sector. Patients of these private hospitals can be reliable source of the information regarding the current pattern of substance abuse, variation in the availability of these substances and alteration in profile of the substance abusers, so as to enable the formulation of management strategies. With this view, the present study was designed to assess the socio-demographic profile and co-morbidities related to the use of methamphetamine among individuals admitted in a private hospital dedicated for the substance abusers in Dhaka.

MATERIALS AND METHODS

This was a cross-sectional study. Data were collected from the available medical documents of a private hospital for the management of substance use. The hospital was situated in Dhaka, the capital city of Bangladesh. It was dedicated for the management of individuals with substance use for about 20 years. Both outpatient and inpatient services were available there. There was a team of psychiatrists, clinical psychologists, peer counsellor and physicians in that hospital. With the permission of the authority of the hospital, data of all the individuals admitted in the hospital during 1 January, 2014 to 31 December, 2015 due to substance related disorders were checked by the researchers. Information of the individuals who had history of using substances containing methamphetamine within one month of hospitalization were enrolled in the study. Total 205 individuals with substance related disorders were admitted in the hospital during that period. Of them, 130 (63.4%) had history of methamphetamine abuse. Information of the admitted individuals were taken from the individuals and their legal guardians and diagnoses were confirmed by the consultant psychiatrists of the hospital. Information were written in the medical documents by the on-duty physicians of the hospital. There were lack of information and incompleteness in some documents. Completed data of 115 individuals were taken and data analysis was performed using Statistical Package for Social Sciences (SPSS) version 24. All the ethical issues were addressed and confidentiality was maintained throughout the study.

RESULTS

Table **I** shows the most (91.3%) of the respondents were male. Mean age of the respondents was 24.6 (±5.8) years. The youngest respondent was of 16 years, the oldest 55 years. Half of the respondents (50.4%) belonged to the age group 21-30 years, followed by 31-40 years' group (26.2%). Most (89.6%) of them resided in urban area and was Muslim (94.8%). Regarding education status, majority (34.8%) completed graduation. About one third (33.9%) were currently unemployed. More than half (52.2%) were unmarried.

Table I: Socio-demographic characteristics of the respondents (n=115)

Socio-demographic characteristics	Frequency	Percentage
Gender		
Male	105	91.3
Female	10	8.7
Age (in years)		
≤ 20	20	17.4
21-30	58	50.4
31-40	30	26.2
41-50	5	4.3
> 50	2	1.7
Residence		
Urban	103	89.6
Semi-urban	12	10.4
Religion		
Islam	109	94.8
Hinduism	4	3.5
Others	2	1.7
Education		
Primary	7	6.1
Secondary	18	15.6
Higher Secondary	39	33.9
Graduation	40	34.8
Post-graduation	11	9.6
Current occupation		
Unemployed	39	33.9
Student	20	17.4
Home-maker	5	4.3
Businessman	32	27.9
Service-holder	9	7.8
Others	10	8.7
Marital status		
Unmarried	60	52.2
Married	36	31.3
Widow/Widower	2	1.7
Separated	6	5.2
Divorced	11	9.6

Table **II** shows the all the amphetamine users had used other substances. Among the other substances, nicotine was the substance used by most (94.8%) respondents, followed by cannabinoids (56.5%) and opiates (38.3%).

Table II: Use of other substances among methamphetamine users (n = 115)

Substances	Frequency*	Percentage
Nicotine	109	94.8
Cannabinoids	65	56.5
Opiates	44	38.3
Alcohol	33	28.7
Benzodiazepines	17	14.8
Others	10	8.7

* Multiple responses

Table **III** Shows the majority (42.6%) of the respondents started to take methamphetamine between 16-20 years of age

Table III: Age of starting methamphetamine use (n = 115)

Age of starting (in years)	Frequency	Percentage
≤15	19	16.5
16-20	49	42.6
21-25	32	27.8
26-30	11	9.6
>30	4	3.5

Table IV shows the Among the respondents 33.9% had some kinds of acute or chronic physical co-morbidities, of which urinary tract infection, bronchial asthma and dyslipidemia were common

Table IV: Physical co-morbidities among the respondents (n=115)

Physical co-morbidities	Frequency	Percentage
Absent	76	66.1
Present	39	33.9
Types of physical problems*		
Urinary tract infection	9	7.8
Bronchial asthma	8	6.9
Dyslipidemia	8	6.9
Dermatological problems	7	6.1
Dental problems	7	6.1
Neurological problems	5	4.3
Diabetes mellitus	5	4.3
Hypertension	5	4.3
Gynaecological problems	3	2.6
Hypothyroidism	3	2.6
Others	3	2.6

***multiple response**

Table V shows the co-morbid psychiatric disorders were present among 29.6% of the respondents, of which personality disorders was the commonest

Table V: Psychiatric (other than substance related disorders) co-morbidities among the respondents (n= 115)

Psychiatric co-morbidities		
Absent	81	70.4
Present	34	29.6
Types of psychiatric problems*		
Personality disorders	20	17.4
Anxiety disorders	9	7.8
Depressive disorders	7	6.1
Bipolar and related disorders	5	4.3
Obsessive compulsive and related disorders	5	4.3
Schizophrenia spectrum and other psychotic disorders	4	3.5
Others	5	4.3

***multiple response**

Table VI shows that 69.6% of the respondents were admitted to the hospital against their will.

Table VI: Type of current admission (n = 115)

Type of admission	Frequency	Percentage
Voluntary	35	30.4
Involuntary	80	69.6

Table VII shows that 33.9% respondents had no previous history of admission it was the first hospitalization for the treatment of substance use. Others (66.1%) had previous history of hospitalized treatment.

Table VII: History of previous admission (n= 115)

Previous Admission	Frequency	Percentage
No previous admission	39	33.9
1-2 times	35	30.4
3-4 times	18	15.7
5-6 times	13	11.3
>6 times	10	8.7

Table VIII Shows the family history substance use among respondents 27.8% had family history of substance use other than nicotine and caffeine, 20.9% had family history of other psychiatric illnesses.

Table VIII: Family history of substance use and other psychiatric illnesses (n = 115)

Family history	Frequency	Percentage
Family history of substance use (other than nicotine and caffeine)		
Absent	83	72.2
Present	32	27.8
Family history of other psychiatric illnesses		
Absent	91	79.1
Present	24	20.9

DISCUSSION

The completed data of 115 subjects with methamphetamine use revealed that most (91.3%) of them were male. The earlier studies conducted in Dhaka city in the last decade of the last century also found the male predominance in this regard[7,8] but comparing to many of those studies rate of female users are higher in the current study. In a more recent study conducted in a private drug de-addiction centre reported 9.5% female among the inpatients with substance use disorder.[1] In another recent study found that 8.4% of hospitalized opiate abusers were female.[9] It may be assumed that more females are abusing substances than two-three decades ago. The findings may also be due to the fact that the study was conducted among the hospitalized substance abusers.

Mean age of the subjects was 24.6 (±5.8) years. The youngest was of 16 years, the oldest 55 years. Half of the subjects (50.4%) belonged to the age group 21-30 years, followed by 31-40 years' group (26.2%). The previous studies conducted among the substance abusers in Bangladesh and India also found more abusers in a relatively younger age group.[1,8]

Most (89.6%) of the subjects resided in urban area. As the study place was in the capital city, majority were expected to be from urban background. Regarding religion, most (94.8%) of the respondents were Muslim as Bangladesh is a Muslim-dominant country with 90.4% Muslim people.

More than half (52.2%) of the subjects were unmarried. It may be because more than two-thirds (67.8%) of the respondents were below 30 years of age. Among the subjects, 9.6% was divorced and 5.2% was separated but it was not conclusive whether separations or divorces were reasons or consequences of methamphetamine use. Regarding educational status, majority (34.8%) completed graduation. Alam et al. (1999) found that majority (58.5%) of his study sample belonged to secondary and higher secondary level.[8] In current study, the education status may be a reflection of the higher socioeconomic status of the sample, which was also the fact of other recent studies in private de-addiction clinic.[1,9] Nevertheless, about one-fifth (21.7%) of the respondents was below higher secondary level. It was not also conclusive whether the dropout is a consequence of the methamphetamine use.

One-third (33.9%) of the subjects were currently unemployed. The unemployment rate is lower than the findings of the study by Alam et al. (1999) and Hossain et al. (2005).[8] In our study, businessmen were found in a significant proportion (27.9%) which corresponds to the other studies conducted in private clinics.[1,9]

All the methamphetamine users also used other substances. It may indicate that methamphetamine users were interested in experimenting more types of substances or there was easy availability. In our study, among the other co-morbid substances, nicotine was used by most (94.8%) individuals. The rate was more than double of the finding by Alam et al. (1999) and slightly lower than the finding of other study among opiate abusers.[9] All the substance abusers were found to have abused tobacco in a study by Hossain et al. (2005). Cannabinoids (56.5%) and opiates (38.3%) were the other common co-morbid substances in our study. In a study among hospitalized substance abusers, the most common substance group was opiates followed by cannabinoids.[1]

Regarding the age of onset of methamphetamine use, 16-20 years was the starting age group for majority (42.6%), followed by 21-25 years age group (27.8%). The similar age group was found as the age of onset for majority of the respondents of the other studies regarding substance abuse in Bangladesh.[1] In an Iranian study, age of onset of methamphetamine use was 20.3 ± 3.3 years. A considerable proportion (16.5%) of our subjects started to use methamphetamine before or at the age of 15 years.

Individuals with substance use disorders are known to have a high prevalence of co-morbid medical and psychiatric

conditions that often complicate clinical care. Chronic methamphetamine use results in a variety of medical consequences, including cardiovascular disease, pulmonary problems, neurological problems, and dental disease. In our study, about one-third (33.9%) of the subjects had current physical co-morbidities, of which urinary tract infection, bronchial asthma and dyslipidemia were common.

Psychiatric symptoms have been well-documented in methamphetamine abusers. Anxiety, depression, insomnia, and psychosis are among the most commonly reported symptoms. In our study, more than one-fourth (29.6%) of the respondents had co-morbid psychiatric conditions. Personality disorders was the commonest diagnosis, followed by anxiety disorders and depressive disorders. An American study revealed that a significant proportion of methamphetamine abusers had co-morbid primary psychotic, mood and anxiety disorders. In a Bangladeshi study among male patients with major depressive disorder, 8.3% of the respondents had lifetime history of methamphetamine abuse. In another study among substance abuser male juvenile offenders in Bangladesh, 77.4% had psychiatric disorders. In case of female juvenile offenders, 10% of the respondents with psychiatric disorder had history of substance abuse. In current study, physical and psychiatric disorders were confirmed from the medical and related documents of the hospitalized patients who were assessed by the consultant psychiatrist for psychiatric problems and concerned medical specialist for the physical problems.

More than two-thirds (69.6%) of the respondents were admitted to the hospital against their will. It may indicate that methamphetamine users were not motivated to take treatment. For about one third (33.9%) respondents, it was the first hospitalization for the treatment of substance use. Others (66.1%) had previous history of hospitalized treatment. It reconfirms the relapsing nature of substance related disorders and is consistent with the findings of Hossain et al. (2005) where 63.6% of the respondents were treated for 2-5 times.

Genetic factors are strongly implicated in substance use disorders. Substance use in general is largely dependent on availability and social environment but the genes contribute to the propensity to develop harmful use and dependence. In current study, among the respondents, more than one-fourth (27.8%) had family history of substance use other than nicotine and caffeine, 20.9% had family history of other psychiatric illnesses. Similar findings were revealed in a study among opiate abusers.[9]

The study was conducted in a selected urban private hospital dedicated for the substance users. So, the study population is not representative of the whole community. Data of all the admitted individuals with methamphetamine related disorders during a specified period were included, no sampling was done. As most of the information was collected from the medical and related documents, there was no scope to check for the reliability of all the information.

CONCLUSIONS

This study provides information about sociodemography, co-morbidities and family history of substance and other psychiatric illnesses related to methamphetamine use. All were poly-substance users with a number of respondents with cannabinoids use. A significant proportion of methamphetamine users had physical and psychiatric co-morbidities. Family history of substance and other psychiatric illnesses was present in a considerable proportion of the subjects. The study findings would help in management and prevention strategy of methamphetamine use in Bangladesh.

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Original Article

Association of *Helicobacter Pylori* and Portal Hypertensive Gastropathy in Patients with Cirrhosis of Liver

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Abstract

Portal hypertensive gastropathy (PHG) is a common endoscopic finding in patients of cirrhosis of liver. The cause and pathogenesis of PHG in cirrhotic patients is poorly understood. Some studies showed, association of Helicobacter pylori (H. Pylori) with portal hypertensive gastropathy in cirrhosis of liver, but the evidence is not robust. The aim of this study was to assess the association of H. pylori infection and PHG in patients with cirrhosis of liver. This case control study was conducted in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from April 2016 to August 2018. A total of 230 patients with cirrhosis of liver were included in this study. There were 115 cirrhotic patients with PHG as cases and 115 cirrhotic patients without PHG as controls. Upper gastrointestinal Endoscopy and 13C Urea Breath Test (UBT) was done in both cases and controls. In this study, out of 230 cases, 147 (63.91%) found to have H. pylori infection. Among cirrhotic patients with PHG case, 77 (66.95%) was positive in UBT. Out of these 77 UBT positive cases, 55 had mild PHG whereas 22 cases had severe form of PHG. Among 38 cases of cirrhosis with PHG who had negative UBT, 23 had mild PHG and 15 cases had severe form of PHG. The risk of positive urea breath test was not statistically significant in cirrhotic patients with PHG in comparison with cirrhotic patients without PHG (P=0.337, OR 1.303, 95% CI 0.759-2.235). In this study, statistically significant association was not found between H. Pylori and PHG in cirrhotic patients.

Keywords: Cirrhosis of liver, *helicobacter pylori (H. Pylori),* portal hypertensive gastropathy (PHG)

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INTRODUCTION

Portal hypertension is a common condition in cirrhosis of liver. When hepatic venous pressure gradient (HVPG) >5mmHg is called portal hypertension.[1] Cirrhosis of liver, non-cirrhotic portal fibrosis and extra hepatic portal vein obstruction are common causes of portal hypertension. Gastrointestinal haemorrhage, hepatic encephalopathy, hepato-renal syndrome, ascites are common complications of portal hypertension.[2] Liver cirrhosis and portal hypertensive gastropathy patients are very prone to develop acute or chronic GI bleeding.[3,4] Prevalance of portal hypertensive gastropathy in cirrhotic patients is approximately 9-80%.[5,6,7,8] Portal hypertensive gastropathy causes change in the mucosa of the stomach in patients with portal hypertention. The most common cause of this is cirrhosis of liver. Mucosal changes occur in PHG including friability of mucosa and the presence of erratic blood vessels.[9]

PHG is common both in cirrhotic and non-cirrhotic portal hypertension. The endoscopic findings of PHG is mosaic-like pattern of gastric mucosa.[10] Whole of the stomach can be involved in portal hypertensive gastropathy (PHG). Not only mucosal changes but also the severity mosaic pattern and red spots increase bleeding risk.[11,12]

Numerous mechanisms are involved in the development of PHG. High gastrin level causes huge amount of acid secretion and altered blood flow, reduced prostaglandin secretion and the presence of *H. pylori* infection.[13,14,15,16] In PHG gastric mucosal ability to regenerate has lost.[17] Another study showed increased susceptibility of portal

hypertensive gastropathy by bile acid and *H. pylori* infection [18].

H. pylori is a gram negative organism is found in gastric mucosa or between the epithelial and mucous layer of stomach. In developing country the prevalence of *H.pylori* is higher than the developed countries[17].The prevalence and association of *H.pylori* in cirrhosis of liver is under debate[18,19,20]. *H. pylori* infection is one of the most common cause of peptic ulcer disease. In cirrhosis of liver *H.pylori* may have a role in developing PHG[21,22].

Sensitivity and specificity of serological test to diagnose *H.pylori* is very low. Other than *H.pylori* , no bacteria is found to be involved in the development of PHG[24].

PHG does not provide a favorable environment for colonization by *H. pylori*, suggesting no contribution of the bacteria in the pathogenesis of PHG[25].

Urea breath test (UBT) which is widely used to diagnose *H.pylori* infection.UBT relies on bacterial hydrolysis of orally administered urea tagged with a carbon isotope ^{13}C. Hydrolysis of urea generates ammonia and tagged CO2 which can be detected in breath samples. The specificity of UBT is 95% and sensivity is about 80-95%[26] .Association of *H. pylori* with PHG is still now a debating issue. The mucosal lesion of stomach and several extra-gastric conditions are associated with *H.pylori* infection. Unexplained vitamin B12 deficiency, Idiopathic thrombocytopenic purpura (ITP) and Iron deficiency anaemia (IDA) is associated with *H.pylori* infection[28]. If *H. pylori* is associated with portal hyperensive gastropathy eradication of *H. pylori* may be beneficial in the management of PHG, if *H. p.* To the best of our knowledge, in Bangladesh no such study has been carried out. So this study was carried out to find out the association of *H. pylori* infection with PHG in patients with cirrhosis of liver.

MATERIAL AND METHODS

This case control study was conducted in the Department of Gastroenterology, BSMMU, Dhaka, Bangladesh during the period of April 2016 to August 2018. A total of 230 patients with cirrhosis of were included in this study. There were 115 cirrhotic patients with PHG as cases and 115 cirrhotic patients without PHG as controls. Patients with age < 18 years, peptic ulcer disease found in upper gastrointestinal endoscopy, patients with intake of proton pump inhibitors, bismuth compounds, antibiotics (within 2 weeks), *H. pylori* eradication within past 2 month, patients on NSAIDs or history of gastric surgery were excluded from the study.

DATA COLLECTION

At first, stable cirrhotic patients were selected for study as per inclusion and exclusion criteria. After proper counseling an informed written consent was taken from every participant. Information about demographic and clinical profile and laboratory parameters was collected on the predesigned data sheet. Detailed clinical history including history of jaundice, drug abuse, alcohol intake, blood transfusion, haematemesis, melaena etc was elicited from the participants. General physical and systemic examination was done for presence of ascites, splenomegaly and other peripheral signs of liver cirrhosis such as jaundice, palmar erythema, spider naevi, alopecia, gynaecomastia, testicular atrophy etc. Complete blood count, liver function tests including serum bilirubin, aminotransferase (ALT, AST) enzymes level ANA, 24 hours' urinary copper, prothrombin time, serum albumin, viral markers (HBsAg, Anti-HCV), renal function test and imaging by abdominal ultrasound was done.

Endoscopy of upper gastrointestinal tract was performed in a single endoscopy unit using a video endoscope (OLYMPUS GIF-H190) at gastroenterology department of BSMMU to identify the presence of portal hypertensive gastropathy, assess its severity and also oesophageal or fundal varices. Upper GI endoscopy was done by single endoscopist to avoid interovserber variability. The severity of PHG was graded according to McCormack's classification and the severity of liver cirrhosis was assessed by using Child-pugh classification.

^{13}C UBT was performed to identify *H. pylori* infection at gastroenterology department of BSMMU in accordance with the manufacturer's recommendations (HCBT-01, Headway ^{13}C Urea Breath Analyzer, China). UBT was done after an abstinence of proton pump inhibitor, antibiotics, bismuth compounds for two weeks and fasting for 6 hours on the day of procedure.

STATISTICAL ANALYSIS

After collection of data, all data were checked and cleaned. After cleaning, the data were entered into computer and statistical analysis of the results being obtained using Statistical Packages for Social Sciences (SPSS). Numerical variables were expressed as mean and standard deviation, whereas categorical variables were expressed in percentage. Numerical variables were compared using student's t test

and categorical variables were analyzed by Chi-square test. The risk was expressed in odd's ratio with 95% confidence interval (CI). P value of less than 0.05 was considered statistically significant.

ETHICAL CONSIDERATION

Before starting this study, the research protocol was submitted to the institutional review board of BSMMU, Dhaka and IRB clearance was taken. All participants were informed about the objectives, methodology and purpose of the study in easily understandable way. Informed written consents were obtained from all participants without any influences prior to sample collection.

RESULTS

This case control study was conducted in the Department of Gastroenterology, BSMMU, Dhaka, Bangladesh during the period of April 2016 to August 2018. A total of 230 patients with cirrhosis were included in this study. There were 115 cirrhotic patients with PHG as cases and 115 cirrhotic patients without PHG as controls.

Table I shows the age distribution of the study patients according age-group in patients of cirrhosis with or without PHG. Most of the patients were of age more than 40 years in both groups. The mean age was 54.37 years for cases and 52.03 years for controls. The age difference among the cases and controls was not significant.

Table I: Distribution of the patients according to age in two groups

Age (years)	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
21 – 30	2 (1.7)	4 (3.5)	0.109ns
31 – 40	12 (10.4)	20 (17.4)	
41 – 50	31 (27.0)	31 (27.0)	
51 – 60	37 (32.2)	32 (27.8)	
>60	33 (28.7)	28 (24.3)	
Mean±SD	54.37 ± 10.97	52.03 ± 11.05	

Ns=not significant

Unpaired t test was done to measure the level of significance

Table II shows the gender distribution of cases ad controls. There were 88 (76.5%) male and 27 (23.5%) female patients of cirrhosis with PHG and 83(72.2%) of male and 32 (27.8%) of female cirrhotic patients of cirrhosis without PHG. There was no significant gender difference in cases and controls.

Table II: Distribution of the patients according to gender in two groups

Gender	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
Male	88 (76.5)	83 (72.2)	0.450ns
Female	27 (23.5)	32 (27.8)	

ns= not significant

Chi-square test was done for the level of significance.

Table III shows the distribution of study patients according to clinical features. The cases and controls show no significant differences in presentation of clinical features.

Table III: Distribution of the patients according to clinical features in two groups

Clinical feature	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
Jaundice	30 (26.1)	19 (16.5)	0.096ns
Ascites	94 (81.7)	83 (72.2)	0.085ns
Leg oedema	73 (63.5)	61 (53.0)	0.109ns
Anaemia	73 (63.5)	63 (54.8)	0.180ns
Leukonychia	10 (8.7)	7 (6.1)	0.450ns
Spider	18 (15.7)	17 (14.8)	1.000ns
Splenomegaly	62 (53.9)	51 (44.3)	0.147ns

ns= not significant

Chi-square test was done to measure the level of significance

Table IV shows the laboratory parameters in cases and controls. The patients of cases and controls had no significant difference in the laboratory finding.

Table IV: Investigation findings of the patients in two groups

Investigations	Cases (n=115) [mean±SD]	Controls (n=115) [mean±SD]	p value
Hb (g/dl)	10.77 ± 1.40	11.08 ± 1.14	0.066ns
ESR (mm in 1st hour)	49.64 ± 16.75	45.89 ± 17.55	0.098ns
TC (No/mm3)	6196.35 ± 2164.04	6648.69 ± 1819.77	0.088ns
Platelet count (per mm3)	131426.09 ± 95576.63	151464.91 ± 56544.94	0.055ns
Serum creatinine (mg/dl)	1.05 ± 0.27	1.00 ± 0.27	0.225ns
Na+ (meq/L)	132.62 ± 4.30	133.56 ± 4.61	0.109ns
K+ (meq/L)	3.91 ± 0.44	4.02 ± 0.40	0.057ns
ALT (U/L)	38.98 ± 21.28	36.74 ± 12.48	0.331ns
AST (U/L)	49.96 ± 26.33	48.28 ± 21.77	0.600ns
S. Bilirubin (mg/dl)	1.75 ± 1.08	1.48 ± 1.10	0.063ns
S. Albumin (g/L)	25.11 ± 5.07	26.13 ± 3.46	0.075ns
Prothrombin time			
Control	11.90 ± 0.16	11.88 ± 0.12	0.252ns
Patient	17.32 ± 3.31	16.71 ± 2.61	0.119ns
INR	1.46 ± 0.29	1.41 ± 0.25	0.189ns

ns=not significant

Unpaired t test was done to measure the level of significance

Table V shows the case and control patients of cirrhosis with different etiology. There were 63 (54.7%) patients in cases and 60 (52.1%) patients in controls with CHBV infection. Chronic hepatitis C virus infection was found in 11 (9.6%) of patients in cases and 14 (12.2%) of patients in controls as a cause of cirrhosis. There was no etiological difference among the cases and controls.

Table V: Distribution of the patients according to etiology in two groups (n=230)

Etiology	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
HBsAg	48 (41.7)	43 (37.4)	0.500ns
HbsAg-Anti-HBc	15 (13.0)	17 (14.7)	0.849ns
Anti HCV	11 (9.6)	14 (12.2)	0.525ns

ns=not significant

Chi-square test was done to measure the level of significance

Table VI shows the distribution of cases and controls according to Child-Pugh score. Most of the patients of cases and controls were of Child-Pugh class B and Child-Pugh class C. There were no significant difference in the Child-Pugh class of cases and controls.

Table VI: Distribution of the patients according to Child pugh score in two groups

Child Pugh Class	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
A	12 (10.4)	20 (17.5)	0.074ns
B	48 (41.7)	55 (48.2)	
C	55 (47.8)	39 (34.2)	

ns= not significant

Chi-square test was done to measure the level of significance

Table VII shows the distribution of cases according to grade of PHG. There were78(67.8%) of patients with mild PHG whereas 37(32.2%) of patients had severe PHG.

Table VII: Distribution of cases according to grade of PHG (n=115)

PHG	Frequency (n)	Percentage (%)
Mild	78	67.8
Severe	37	32.2

Table VIII shows distribution of patients according to the test result of UBT. There were 77 (67.0%) patients of case and 70 (60.9%) patients of control with positive UBT. There were 38 (33.0%) patients of case and 45 (39.1%) patients of control had negative UBT. There was no statistically significant difference in test result among the cases and controls with OR 1.303 at 95% CI, 0.759-2.235. Patients with PHG did not have significant increase risk of H.pylori infection.

Table VIII: Distribution of the patients according to ^{13}C Urea Breath Test in two groups

^{13}C Urea Breath Test	Cases (n=115) n (%)	Controls (n=115) n (%)	p value	OR (95% CI)
Positive	77 (67.0)	70 (60.9)	0.337ns	1.303 (0.759-2.235)
Negative	38 (33.0)	45 (39.1)		

ns= not significant

Chi-square test was done to measure the level of significance

Table IX shows the distribution and association of *H. pylori* with severity of PHG. Out of 77 *H. pylori* positive patients with PHG, 55 patients had mild PHG whereas 22 patients had severe form of PHG. There were 38 patients with PHG had negative UBT out of which 23 had mild PHG and 15 patients had severe form of PHG. There was no significant association among the patients of *H. pylori* infection and severity of PHG (p= 0.290).

Table IX: Association of *H. pylori* with severity of PHG (n=115)

PHG	H. pylori		p value
	Positive (n=77) n (%)	Negative (n=38) n (%)	
Mild(78)	55 (70.5)	23 (29.5)	0.290ns
Severe(37)	22 (59.5)	15 (40.5)	

ns= not significant

Chi-square test was done to measure the level of significance

DISCUSSION

This case control observational study was conducted in the Department of Gastroenterology, BSMMU. The objective of the study was to find out the association of *H. Pylori* infection with PHG in the patients of cirrhosis of liver. We included 115 patients as cases (cirrhosis of liver with PHG) and 115 patients as controls (cirrhosis of liver without PHG) for this study who attended inpatient and outpatient department of Gastroenterology, BSMMU during the study period.

In the present study, the mean age of patients was 54.37 ± 10.97 years in cases and 52.03 ± 11.05 years in controls with majority of patients were from fourth to sixth decade of life with no significant difference of age (p=0.109). A study was conducted in India in 2014 to see the association of H. pylori with PHG and the mean age of cases was 54.80±10 years and mean age of controls was 52.09 ± 10.3 years which was almost similar to this study[24]. The gender distribution of the cases and controls in our study were well-matched with no significant difference (p=0.450).

Regarding clinical feature, jaundice was present in 26.1% cases and in 16.5% controls. 81.7% patients in case group had ascites whereas 72.2% patients in control group presented with ascites. Aforementioned study showed ascites in 71.4% cases and in 58.6% controls[24]. Anaemia was more common in cases (63.5%) than controls (54.8%) which may reflect bleeding from PHG in case group but not reached statistical significance (p=0.180). Splenomegaly, a cardinal feature of portal hypertension, was present in 53.9% cases and in 44.3% controls.

In our study we found that chronic HBV was the most common etiology of cirrhosis of liver (41.7% in case group and 37.4% in control group) followed by chronic HCV (9.6% in case group and 12.2% in control group). Whereas HBV in 21.4% cases and in 25% controls, alcohol in 48.6% cases and in 52% controls were in previous study. HBV was the most common cause of cirrhosis in our study which may be due to higher prevalence of HBV in our country.

We quantified the severity of liver disease using the Child Pugh classification. In case group twelve patients (10.04%) had liver cirrhosis with Child class A, 48 (41.7%) Child class B and 55 (47.8%) Child class C whereas the frequency in control group was 20%, 55% and 39% respectively. Our study showed no significant difference between cases and controls regarding Child-Pugh classes, with most of the patients from Child-Pugh B and Child-Pugh C (p=0.074).

In our study, out of 230 patients with cirrhosis, 147 patients were *H. pylori* positive with overall proportion of *H. pylori* infection was 63.91%, which was comparable to another study done by Abbas *et al.*[29] who found a prevalence of *H. pylori* was 62.1% and Safwat *et al*[30]. who found prevalence of *H. pylori* was 60%.

The concern of our study was to find out the association of H. pylori with portal hypertensive gastropathy in cirrhosis of liver. In our study, we had positive UBT in 77 (67.0%) patients of cirrhosis with PHG and 70 (60.9%) patients of cirrhosis without PHG. Thirty-eight patients with PHG had negative UBT out of which 23 had mild PHG and 15 patients had severe form of PHG. There was no significant association of *H. pylori* with presence of PHG in cirrhotic patients (p= 0.337 with OR 1.303 at 95% CI: 0.759-2.235). Hammad *et al.*[31] conducted a similar study in Egypt and reported *H. pylori* infection among 70% cases and 63.3% controls and insignificant association of *H. pylori* with PHG.

The severity of PHG was mild in 55 *H. pylori* positive patients and 23 *H. Pylori* negative patients whereas severe PHG was present in 22 *H. pylori* positive and 15 *H. Pylori* negative patients. The severity of PHG and *H. Pylori* infection had no significant association in cirrhotic patients. These findings were similar as studied by Bahnacy *et al* [32]. *H. pylori* positivity decreased when the severity of PHG increased. As there is severe hemorrhagic congestion and oedema of the gastric mucosa in PHG, so it may not provide a favourable environment for the colonization of *H. pylori*. In contrast Sathar *et al.*[24] and Safwat *et al.* [30] had noticed a significant association between *H. pylori* and severity of PHG ($p< 0.001$). They had suggested that *H. pylori* colonization of the stomach of cirrhotic patients likely to be contributory to the pathogenesis of PHG.

CONCLUSIONS

No significant association was found between *H. pylori* infection and PHG in cirrhotic patients in this study. The data also showed that, severity of PHG was not associated with *H. pylori* infection. Further prospective studies with a large number of samples are required to see the association of *H. pylori* with PHG.

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Original Article

Comparison of Serum Zinc and Copper Level in Psoriatic and Non-Psoriatic Individual

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Abstract

Psoriasis is a common chronic inflammatory disease of skin and multiple organs of body. The exact etiology of psoriasis is not yet certain. It is assumed that trace elements may have some role in pathogenesis of psoriasis. They can act as co-enzymes for metabolism and can act as antioxidants against free radicals. Therefore they can participate in epidermal proliferation and inflammatory process of psoriasis. This study aimed to evaluate the relation between psoriasis and trace elements namely zinc and copper. This study was conducted on 40 diagnosed cases of psoriasis and 40 non psoriatic individuals in the department of Dermatology and Venereology in Bangabandhu Sheikh Mujib Medical University, Dhaka. Biochemical analyses of serum copper and zinc were analyzed and compared statistically with cases and healthy controls. Serum zinc level was significantly lower and serum copper level was significantly higher in patient with psoriasis compared to control (p= < 0.001). Individuals with moderate to severe psoriasis had significantly lower zinc levels and significantly higher copper levels than patients with mild psoriasis, according to Psoriasis area and Severity Index Score (p= < 0.05). Correction of serum zinc and copper level could be beneficial for psoriasis patients.

Keywords: P*soriasis, serum zinc, serum copper, PASI score*

INTRODUCTION

Psoriasis is a multifactorial disease in which certain environmental factors interact with people who have a genetic predisposition to develop immune dysregulation and inappropriate keratinization.[1] The common characteristics of psoriasis is symmetrically involved erythematous plaques with thick silvery scale. Typical nail changes and joint involvement are also the diagnostic features of psoriasis. There is no specific antigenic factors has been found as causative agents in pathogenesis of this disease.[2] There are very limited data available on role of zinc and copper in pathogenesis of psoriasis.[3]

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Oxidative stress is one of the important etiological factor that may initiate psoriasis. Antioxidant systems have been found to be significantly impaired in the blood and lesions of psoriatic patients.[4] An deficient antioxidant system has been linked to elevated levels of reactive oxygen species (ROS) in the pathophysiology of this disease. Deficiency of trace metals like zinc and copper can cause oxidative stress. Trace elements regulate enzymatic activity of keratinocytes and an imbalance in trace elements causes changes in enzymatically dependent keratinization.[5]

In human body zinc is the second most common trace element after iron. Structure stability is assured by zinc protein binding in some enzymes, such as Copper and Zinc superoxide dismutase and catalytic activity is provided by the active copper site.[6]

Copper (Cu) is linked to several metalloproteins. Superoxide dismutase, a copper-containing metalloenzyme, protects against free radical damage. SODs are copper and zinc containing enzymes that convert super oxide radical to peroxide which can be removed subsequently by catalase and other antioxidant defenses. Ceruloplasmin, a plasma protein, binds to copper ions and protects cells from oxidative damage caused by free copper ions, which produce hydroxyl radicals.[6]

There is no comprehensive study of trace elements estimation in Psoriasis in Bangladesh. In the present study, serum zinc & copper levels were analyzed & their relationship with the severity of psoriasis was assessed.

MATERIALS AND METHODS

From July 2018 to June 2019, a cross sectional study was conducted at the department of Dermatology & Venereology, Bangabandhu Sheikh Mujib medical University, Dhaka. For this study 40 diagnosed case of psoriasis age range 18 to 70 years were selected as cases & 40 non psoriatic individuals were selected as controls from the outpatient department of BSMMU, Dhaka. Patients

who had other skin disorders, cardiac & metabolic problems, liver and renal diseases, pregnant and lactating mother were excluded from this study.

After the study subjects were selected, the study's goals, objectives, risks, benefits were explained to the patients. After taking the informed written consent the participants' personal & medical histories were recorded thoroughly.

Under all aseptic precaution 5 ml blood sample was collected from study subjects. Serum zinc & copper was assessed by colorimetric method in Stat Fax 3300 semi-autoanalyzer. The severity of the disease was assessed by a dermatologist on the basis of psoriasis area and severity index (PASI) score.

Reference value of serum zinc concentration is 80-120 µg/dl & serum copper is 70-140 µg/dl.[6] Participants who had zinc level < 80 µg/dl were considered as zinc deficient patients & who had copper level > 140 were considered as patients with high copper level. Depending on PASI score the cases are divided in two groups. Patients with PASI score < 10 (mild psoriasis) were considered as group I and patients with PASI score > 10 (moderate to severe psoriasis) were considered as group II.

All data were collected, preserved and analyzed statistically by using IBM SPSS (version 20). The level of significance for quantitative data was determined using an independent student's t test. The level of significance of qualitative data was expressed as frequency and percentage and analyzed by chi-square test.

RESULTS

Table-I showed that 50% of the cases were male and 50% were female, whereas 47.5% of controls were male and rests were female. Age, weight, height, BMI & family history of study subjects were indifferent statistically.

Table I: Demographic profile of study group (n=80)

Variables		Case (n=40) Mean ± SD	Control (n=40) Mean ± SD	p- value
Gender	• Male	20 (50%)	19 (47.5%)	
	• Female	20 (50%)	21 (52.5%)	
Age of the respondent		38.6 ± 10.6	40.4 ± 10.4	
Duration of psoriasis (in year)		3.8 ± 1.8	-	> 0.05^{ns}
Weight of the respondent (in Kg)		58.1 ± 7.1	58.3 ± 5.8	
Height of the respondent (in cm)		163 ± 3.8	164.3 ± 3.3	
BMI of the respondent (kg/sqm)		21.8 ± 2.2	21.6 ± 1.9	
Family history of psoriasis	• Present	7	2	
	• Absent	33	38	

Data was expressed as mean ± SD and comparison between groups was done by Student's t test. Qualitative data was analyzed by Chi-square test to compare among the groups. n= number of subjects, p-value < 0.05 is significant, ns= not significant.

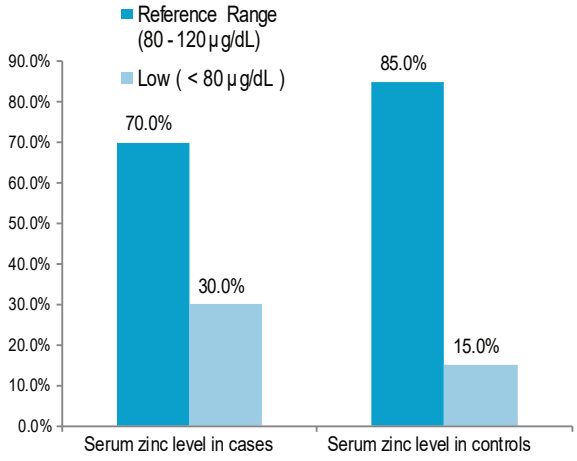

Fig -1: Among the total participants 30.0% and 15.0% had zinc deficiency in cases and controls respectively as shown in

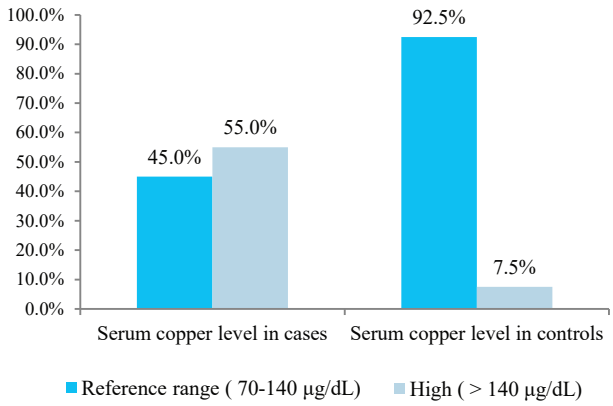

Fig.-2: Among the total participants 55.0% and 7.5% had high level of copper in cases and controls respectively as shown in

Table –II shows the mean values of zinc & copper in both cases & controls. Mean value of serum zinc in psoriasis is significantly low (66.9 ± 12.4 µg/dL) compared to controls, which was significant ($p < 0.001$). Mean value of serum copper in psoriasis is significantly high (142.9 ± 29.5 µg/dL) compared to controls, which was also significant ($p < 0.001$). Table –II also showed that serum zinc is significantly lower & serum copper is significantly higher in patients of group-II compared to group-I.

Table-II: Comparison of serum zinc & copper level in study population (n=80) and their relationship with PASI Score in cases (n=40)

Variable		Serum Zinc (µg/dL)	Serum Copper (µg/dL)	p- value
Study Subjects	Case	66.9 ± 12.4	142.9 ± 29.5	< 0.001
	Control	85.7 ± 11.9	121.2 ± 18.2	
Group according to PASI Score	Group: I (PASI Score < 10)	70.9 ± 13.1	130.7 ± 25.7	< 0.05
	Group :II (PASI Score > 10)	63.1 ± 10.6	155.1 ± 28.4	

Data was expressed as mean ± SD and comparison between groups was done by Student's t test. n= number of subjects, p-value < 0.05 is significant, ns= not significant.

DISCUSSION

Zinc (Zn) is an essential trace metal for synthesis of protein, activity of various enzymes and removal of free radicals from our body.[7,8] Zn also helps in the formation of structural proteins during the keratinization process.[9] In our study we found that serum zinc level was significantly lower in patients with psoriasis compared to controls. This result is consistent with the study of other researchers.[3,10-12] In contrast to our findings, Butnaru et al.[13] found that serum Zn levels were higher in psoriasis patients. However, some researchers did not find any significant changes in serum Zn levels in patients with psoriasis compared with healthy controls.[8,14,15]

Zn is a constituent of DNA and RNA polymerases enzymes. These enzymes are needed for protein synthesis in the affected skin. Low level of zinc in psoriasis may found due to decrease serum protein or albumin which may occur as a consequence of the removal of a large quantity of scales from the body surface.[11]

In our study we also found that serum zinc level was significantly low in patients with moderate to severe psoriasis than in patients with mild psoriasis. Keratinocyte exfoliation increases in people with severe psoriasis, perhaps leading to more severe skin lesions. Immune dysfunction and decrease antioxidant activity are also found in patients having low serum zinc level and these patients are more vulnerable to viruses and bacterial infections which can lead to abnormal skin changes and trigger psoriasis. So oral Zn supplementation could be used as a psoriasis adjuvant therapy.[16]

In this study, serum copper levels in psoriasis patients were found higher than in controls. This result is consistent with the study of other researchers.[3,8,11,17] Some researchers found low levels of copper in their investigations, which contradicts our findings.[10,18] We also found that serum copper was significantly higher in patients with moderate to severe psoriasis than in patients with mild psoriasis which is in accordance to other studies.[19,20] These inconsistent results may arise from different study designs. Serum Cu is primarily bound to ceruloplasmin which is a multifunctional enzyme that helps to keep Cu levels normal in serum.[8,11] Ceruloplasmin has recently been discovered to be an acute inflammatory response protein that may scavenge free radicals.[21,22] As psoriasis is a chronic inflammatory skin disease that has a higher level of oxidative stress so ceruloplasmin activity is increased.[11] The levels of ceruloplasmin and serum Cu are positively correlated.[21] So, high serum Cu levels might be found in psoriasis patients due to elevated ceruloplasmin levels. Our study only included a small number of population and more research with larger number of patients is needed to prove the involvement of trace elements in the pathogenesis of psoriasis.

CONCLUSIONS

According to the findings of this study patients with psoriasis have a lower serum zinc level & greater serum copper level compared to control. Serum copper and zinc levels are correlated to the Psoriasis Area Severity Index which can be used as a marker for determining disease severity. Correction of trace element imbalances may improve in psoriasis treatment and outcome.

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Original Article

Severity of Pain According to Visual Analog Scale in Adhesive Capsulitis of Shoulder in Diabetic Patients

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Abstract

The aim of the present study was to assess the severity of pain according to visual analog scale in adhesive capsulitis patients with DM. A descriptive, cross sectional study was conducted from January to June 2019 among 200 patients attending at Physical Medicine and Rehabilitation Department, Bangabandhu Sheikh Mujib Medical University after obtaining requisite consent from the patients. Data were collected through the assessment of patients in the Outpatient Department. The collected data were analyzed by using SPSS (version 20.1) to assess the severity of pain according to visual analog scale in adhesive capsulitis patients. The study was approved by the institutional ethical committee of BSMMU. Mean age of patients with adhesive capsulitis was 54.85±9.35 years among them more than one third (35%) was 51-55 years of age group. Among the patients 61% was female and 39% was male. Among the patients 54(27%) had adhesive capsulitis, and 146(73%) did not have. Nearly two third female patients (65%) suffered from adhesive capsulitis of shoulder than male patients (35%). The hight number of adhesive capsulitis patients suffering from moderate type of pain and visual analogue score is 4-6, where one third of them suffer from severe type (VAS score 7-10). Overall frequency of adhesive capsulitis of the shoulder among diabetic individuals attending in physical medicine and rehabilitation department of a tertiary care hospital was 27%. Most of the adhesive capsulitis patients suffering from moderate type of pain which visual analogue score is 4-6.

Keywords: *Adhesive capsulitis, diabetes mellitus, visual analogue score.*

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INTRODUCTION

Adhesive capsulitis is a well-defined disorder characterized by progressive pain and stiffness of the shoulder which usually resolves spontaneously after about 18 months.[1] The patients typically present with progressive painful restriction in range of movement of the glenohumeral joint without any preceding trauma. They exhibit a capsular pattern of restriction with external rotation being the most restricted followed by abduction in the plane of the scapula and then flexion.[2] Diabetes mellitus is a chronic metabolic condition characterized by persistent hyperglycemia with resultant morbidity and mortality related primarily to its associated micro vascular and macro vascular complications.[3] There is a well-documented relationship between adhesive capsulitis and diabetes mellitus. 10.8% diabetics and 2.3 % non-diabetics were found to have peri-arthrosis of the shoulder, a statistically significant difference between the two groups of patients (P<0.005).[4] There was three consecutive stages: pain, stiffness, and recovery. The stiffness stage was usually related to the duration of the recovery stage. The total duration was longer than is generally supposed (an average total of 30.1 months in contrast to about 18 months as often postulated). Generally speaking, the longer the stiffness stage is, the longer is the recovery stage.[5] Visual Analogue Scales (VAS) provides a simple technique for measuring subjective experience. They have been established as valid and reliable in a range of clinical and research applications, although there is also evidence of increased error and decreased sensitivity when used with some subject groups. The pain VAS is a continuous scale comprised of a horizontal (HVAS) or vertical (VVAS) line, usually 10 centimeters (100 mm) in length, anchored by 2 verbal descriptors, one for each symptom extreme. Instructions, time period for reporting, and verbal descriptor anchors

have varied widely in the literature depending on intended use of the scale. For pain intensity, the scale is most commonly anchored by no pain (score of 0) and pain as bad as it could be or worst imaginable pain (score of 100 [100-mm scale]. To avoid clustering of scores around a preferred numeric value, numbers or verbal descriptors at intermediate points are not recommended.

MATERIALS AND METHOD

A descriptive, cross sectional study was conducted from January 2019 to June 2019 among 200 diabetic patients attending at Physical Medicine and Rehabilitation Department, Bangabandhu Sheikh Mujib Medical University after obtaining requisite consent from the patients. Purposive sampling was adopted for collecting data. The study was approved by the institutional ethical committee. The assessment of patients was held directly in the Outpatient Department. Diagnosis of adhesive capsulitis is clinical. Pain occurs insidiously in deltoid region with shoulder stiffness. Pain at the end of external rotation. Restriction of the movement on both active and passive testing. No abnormal X-Ray findings in the shoulder joint. These characteristic of shoulder pain at onset to three months duration were included. The relevant information was entered into the predesigned proforma to estimate the severity of pain according to visual analog scale in adhesive capsulitis patients with DM. The collected data were entered into the computer and analyzed by using SPSS (version 20.1)

RESULT

Table I Shows that Mean age of patients with adhesive capsulitis was 54.85±9.35 years. In 200 patient's 35% was 51-55 years, 31% was 56-60years, 22% was 46-50 years and 12% was 40-45 years. Among 200 patients with 61% was female and 39% was male.

Table 1: Demographic characteristics of the study population (n=200)

Parameters		Number	Percentage
Age of the patients			
	40-45 years	24	12
	46-50 years	44	22
	51-55 years	70	35
	56-60 years	62	31
Total		200	100
Sex			
	Male	78	39
	Female	122	61
	Total	200	100

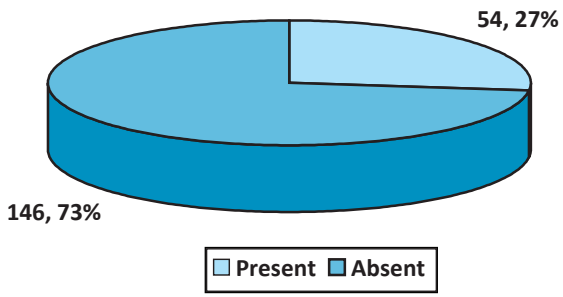

Figure 1: D*istribution of patients according to frequency of Adhesive Capsulitis (n=54)*

Figure 1 A total of 200 patients with diabetes were included in the final analysis. Among the DM patients 54(27%) had adhesive capsulitis, and 146(73%) did not have adhesive capsulitis.

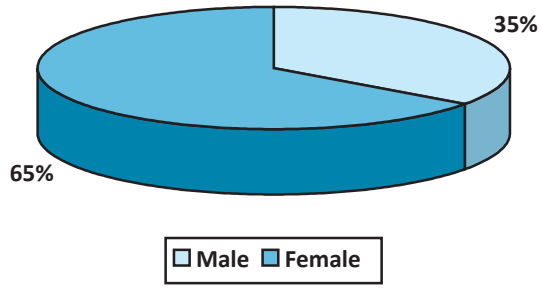

Figure 2: *Pie chart showing presence of adhesive capsulitis among male and female diabetic patient (n=54).*

Figure 2 Female patients (65%) suffered from more adhesive capsulitis and male patients (35%).

Table II Shows that among the diabetic patients with adhesive capsulitis, 22 (41%) had VAS score 4-6 (moderate pain), 14 patients (26%) had VAS score 1-3 (mild pain), 18 patients (33%) had VAS score 7-10 (severe pain).

Table 2: Severity of pain according to Visual Analog Scale (n=54)

Visual analogue score	No. of patients	Percentage
0 (No pain)	0	0
1-3 (Mild pain)	14	26
4-6 (moderate pain)	22	41
7-10 (severe pain)	18	33

DISCUSSION

Adhesive capsulitis is a distinctive clinical entity, usually occurring in the fifth and sixth decades. It may be associated with trauma or with various illnesses, but most cases are idiopathic. The evidence for disease relationships is uncovering, with the possible exception of diabetes mellitus. A total number of 200 patients with diabetes were include in the final analysis. Among the patients 54(27%) had adhesive capsulitis, and 146(73%) did not have adhesive capsulitis. So, prevalence of Adhesive Capsulitis was 27%. A study was conducted by Khan et al. in a tertiary care hospital of Bangladesh upon 300 diabetic and 300 non-diabetic individuals. There, frequency of Adhesive Capsulitis in diabetic group was 20% and in non-diabetic group it was 5.66%.[6] According to that study our frequency result is higher. Probably because, a lot of diabetic patients with Adhesive Capsulitis come from BIRDEM General Hospital, which is a diabetic hospital and very near to BSMMU. Mean age of patients with adhesive capsulitis was 54.85±9.35 years. Among 200 patients, majority 35% was between 50-55 years, 31% was 56-60 years, 22% was 46-50 years, 12% was 40-45 years. In a case report in Bangladesh by Uddin et al. reported that mean age of the patients was 53 years which is similar to our study.[7] Other observer found maximum patients 39% were between the age group of 51-60 which is also similar to our study.[8] Among 200 patients with 61% was female and 39% was male. In a study by Ahmed et al. reported among 325 patients 52.3% were male and 47.7 % were female which is not similar to us.[9] In another study by Khan et al. 31.67% patients were male and 68.33% were female which is similar to our study.[10] Among the patients with adhesive capsulitis most of the patient 16(29.62%) had VAS score 5-6, 14(25.92%) had VAS score 7-8, 12(22.22%) had VAS score 3-4, 8(14.81%) had VAS score 1-2, and 4(7.4%) have VAS score 9-10. In a study among 50 patients 32% had severe pain, 52% had moderate pain, and 16% had mild pain.[11] Which is also similar to this study. Adhesive capsulitis is a chronic disabling condition associated with pain, which require long-term management in the form of physiotherapy and repeated injections. Unfortunately, the treatment is more prolonged in DM patients, and surgery may be required if the condition is not treated early.[12]

CONCLUSION

Study finds that more than one fourth (27%) diabetic patients suffer from adhesive capsulitis of the shoulder. The disease affects predominantly females in sixth decade of age. Most of the adhesive capsulitis patients suffering from moderate type of pain which visual analogue score is 4-6. Further large scale study can be done for longer period to measure the pain score in different stages of adhesive capsulitis.

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Conflict of interests: None

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Original Article

Patterns of Post-endoscopic Retrograde Cholangiopancreatography (ERCP) Complications

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Abstract

In the treatment of common bile duct stones and palliative decompression of malignant strictures, endoscopic retrograde cholangiopancreatography (ERCP) is the gold standard. However, there are still concerns about procedure-related complications and patient discomfort. The aim of the study is to evaluate the pattern of post ERCP complications. This prospective observational study was conducted at the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from February to October 2017. A total of one hundred patients who were eligible for ERCP were included in this study but five patients were excluded due to cannulation failure. Clinical examination , biochemical, and radiological investigation were performed before and after ERCP to assess the complication that occurred. The majority of patients in this study were at and below the age of 50 years, with a mean age of 49.74 ± 14.07 years and the age range was between 18 to 80 years. Majority of the subjects were male (54.7%), and male to female ratio was 1.21:1. The highest number of patients were diagnosed as choledocholithiasis (58.9%) followed by proximal cholangiocarcinoma (13.7%), Ca-gallbladder with biliary infiltration (8.4%), Distal cholangiocarcinoma (6.3%), Chronic calcific pancreatitis and Periampullary carcinoma each (3.2%), Suspected SOD & Chronic pancreatitis each (2.1%) and Worm in CBD and benign biliary stricture each (1.1%). In this study, the overall post-ERCP complication was 12.6%, with pancreatitis accounting for 9.4%, bleeding accounting for 2.1%, and cholangitis accounting for 2.1%. From the study, it can be concluded that pancreatitis is the most frequent Post-ERCP complication.

Keywords: *ERCP,c holangitis, obstructive jaundice, pancreatitis.*

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) was first introduced by the surgeon, McCune and co-workers[1] as a diagnostic tool for evaluating diseases of the biliary tract and pancreas. Eventually, it became a therapeutic modality. Although the ERCP procedure has progressed technically, it is still associated with potentially serious complications[2] and patient's discomfort.[3] Endoscopic retrograde cholangiopancreatography (ERCP) is widely used for the treatment of a variety of pancreatico-biliary diseases. However, it is a high risk procedure that can result in complications such as acute pancreatitis, bleeding, cholangitis, cholecystitis, and perforation.[4] The most common and serious complication of ERCP is Pancreatitis (PEP). According to recent research, the incidence of post- ERCP pancreatitis ranges between 2 and 5%.[4-6] However, in severe cases, it is associated with a high morbidity and mortality.[6,7] By identifying high-risk populations, it is possible to reduce the occurrence and severity of post-ERCP pancreatitis. Several studies have revealed number of risk factors for post-ERCP pancreatitis.

Cholangitis is a difficult-to-diagnose complication of ERCP. It can be an indication as well as a complication. PEP occurs immediately after an ERCP, but cholangitis can occur as a fulminant, uncontrolled sepsis within the first hours of an ERCP, or it can occur days or even weeks later. It can be difficult to detect mild cholangitis in a patient

with multiple medical conditions. Cholangitis is primarily caused by a failure or incomplete drainage.[7,8]

Bleeding after an ERCP is another common complication. The majority of bleeding is oozing from the precut sphincterotomy site, with no or minor clinical consequences. Arterial bleeding that stops on its own can be difficult to detect because it resembles a temporary pause caused by a vessel spasm.[10]

In Bangladesh, there are very few ERCP-related studies. Accordingly, we sought to identify patterns of post-ERCP problems.

METHODS

This prospective observational study was conducted in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period of February 2017 to October 2017. A total of 100 patients eligible for ERCP in Department of Gastroenterology, BSMMU were enrolled in this study but five of them were excluded due to cannulation failure. Prior to data collection both verbal and written consent was taken from the patients. Data were collected using a preformed data collection sheet (questionnaire).

Anticoagulant and antiplatelet medications were all stopped 72 hours before the procedure. Prior to ERCP, a prophylactic dose of third generation cephalosporine was routinely administered. To prevent sphincter of Oddi spasm, hyosine-N-butyl bromide was also given intravenously at the comencement of ERCP. The procedure was carried out under fluoroscopic supervision. The procedure was carried out with patients under conscious sedation to help them relax and stay comfortable, or under general anaesthesia, depending on the anaesthesiologist's individual assessment of the patients. Midazolam and pethidine was used for sedation and analgesia respectively. Propofol was used as an anaesthetic agent during ERCP in the presence of an anaesthesiologist. Patients were placed on an x-ray table in the prone position while a duodenoscope was inserted down the esophagus, through the stomach, and into the duodenum. The papilla of Vater was identified. For contrast injection, a catheter was advanced past the sphincter of Oddi into the common bile duct (CBD). The pancreatic duct was cannulated selectively based on the ERCP indications and endoscopic or radiologic findings. The conventional sphincterotome was used to perform sphincterotomy selectively. Therapeutic procedures were carried out in accordance with the appropriate indication. Stone extraction was used to treat choledocholithiasis. Worm extraction was used to treat worms in the common bile duct. Biliary stenting was used as a palliative therapy in patients with malignant biliary obstruction. The consultant gastroenterologist checked on all patients after the procedure and again the next morning. Patients were closely monitored for ERCP complications such as sedation-related complications, pancreatitis, cholangitis, bleeding, and perforation.

RESULTS

Out of the 100 eligible patients for ERCP, 5 were excluded due to cannulation failure. Thus, n=95.

Table I shows mean age of the patients was 49.74 ± 14.07 years within the range of 18 – 80 years. Males (54.7%) were predominant than female (45.3%).

Table I: Demographic profile of the study subjects (n=95)

	Number of patients (n)	Percentage (%)
Age (groups)		
≤40	26	27.4
41 - 50	30	31.6
51 - 60	20	21.1
>60	19	20.0
Mean ± SD	49.74 ± 14.07	
Gender		
Male	52	54.7
Female	43	45.3

Table II shows patients of choledocholithiasis (58.9%) followed by proximal cholangiocarcinoma (13.7%), Ca gallbladder with biliary infiltration (8.4%), Distal cholangiocarcinoma (6.3%), Chronic calcific pancreatitis & Periampullary carcinoma each (3.2%), Suspected SOD & Chronic pancreatitis each (2.1%) and Worm in CBD & Biliary stricture each (1.1%).

Table II: Distribution of study subjects according to indication of ERCP (n=95)

Indications	Number of patients (n)	Percentage (%)
Choledocholithiasis	56	58.9
Proximal cholangiocarcinoma	13	13.7
Ca gallbladder with biliary infiltration	8	8.4
Distal cholangiocarcinoma	6	6.3
Periampullary carcinoma	3	3.2
Chronic calcific pancreatitis	3	3.2
Chronic pancreatitis	2	2.1
Suspected SOD	2	2.1
Biliary stricture	1	1.1
Worm in CBD	1	1.1

Table III shows stone extraction was done in 51.6% patients, stenting in common bile duct in 40% patients and only papillotomy done in 7.4% patients and removal of worm in 1.1% patients.

Table III : Distribution of study subjects according to therapeutic procedure performed (n=95)

Therapeutic procedures	Number of patients (n)	Percentage (%)
Stone extraction	49	51.6
Stenting in common bile duct	38	40
Only papillotomy done	7	7.4
Removal of worm	1	1.1

Table IV shows pancreatitis was observed in 9.47% patients, bleeding in 2.1% patients and cholangitis in 1.1% patients.

Table IV: Distribution of study subjects according to complications (n=95)

Complication	Number of patients (n)	Percentage (%)
Pancreatitis	9	9.5
Bleeding	2	2.1
Chaolangitis	1	1.1
Total	12	12.6

DISCUSSION

ERCP is one of the most technically demanding and high-risk procedures performed by gastrointestinal endoscopists (Adler et al.,2015, Colton and Curran, 2009). It requires significant focused training and experience to maximise success and minimise poor outcomes (Colton, 2002, Testoni et al., 2010).

In this study maximum patients were below the age of 50 years with a mean age of 49.74 ± 14.07 years (age range of 18 – 80 years). More than half of the patients were above 70 years old.[11] Males (54.7%) were predominant than female (45.3%) and male female ratio was 1.21:1.

The most common diagnosis was choledocholithiasis (58.9%), followed by proximal cholangiocarcinoma (13.7%), gallbladder carcinoma with biliary infiltration (8.4%), distal cholangiocarcinoma (6.3%), chronic calcific pancreatitis and periampullary carcinoma (3.2%), suspected SOD and chronic pancreatitis (2.1%), and worm in CBD and biliary strict (1.1 %).

Therapeutic procedure of the study subjects, stone extraction done in 49 patients (51.6%), stenting in common bile duct in 38 patients (40%), only paillotomy done in 7 patients (7.4%) and removal of worm in 1 patient (1.1%).

The overall complication rate in this study was 12.6% which is comparabe to other Bangladeshi studies.Islam et al.[2] revealed 9.01% complications in their study conducted in BSMMU. Complications occurred in 11.6% cases in the study of Glomsaker et al.[11]. Complication rate in other studies were 11.2%[13] and 4.9%[4]. The incidence of PEP in a meta-analysis of 21 prospective studies was approximately 3.5% - 18%. [15,6]

Pancreatitis was seen in 9.4% patients, bleeding in 2.1% patients and cholangitis in 1.1% patients in this study. One of the most common complications in post-ERCP is pancreatitis. Islam et al.[12] found pancreatitis 5.15% and Glomsaker et al.[11] found 3.1%. Cholangitis was observed 3.6% in the study of Glomsaker et al.[11]. The post-ERCP cholangitis rate was 1% or less.[17] In this study, cholangitis was less due to adequate per and post procedure control of infection. Kapral et al.[8] found bleeding in 4.2% cases and Glomsaker et al.[11] found bleeding in 2.4% cases.

CONCLUSIONS

According to the findings of this study, pancreatitis is the most common complication of ERCP. Overall, 12.6% of

patients experience complications, with pancreatitis accounting for 9.4%, bleeding accounting for 2.1%, and cholangitis accounting for 2.1%.

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Original Article

Cardiovascular Risk Factors amongst the Patient Living with HIV Attending at Anti-Retroviral Therapy Center of Bangladesh

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Abstract

Human immunodeficiency Virus (HIV) seropositive individual is at risk of developing disease of cardiovascular system (CVD). There are scarce of research work regarding this field in Bangladesh. Considering scarcity, this study was conducted at anti-retroviral therapy (ART) center of Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh to find out the frequency of the CVD and their common risk factors in HIV seropositive patients from March 2017 to September 2019. Different CVD risk factors were assessed in this study. The demographic data were assessed and World Health Organization STEPS questionnaire were used to collect demographic data. The 10-year CVD risk was calculated by using the Framingham coronary risk score (FRS). Mean age of study population was 38, SD= 9.8. Among them sixty-five (65%) were men and thirty-five (35%) were women. About one third were overweight followed by 5% were obese. High cholesterolemia, high triglyceridemia, high low-density lipoprotein (LDL) and low high-density lipoprotein (HDL) were found in 23%, 58%, 14%. and 63% of the HIV patent, respectively. Hypertension was present in 19% and diabetes in 15% of the patients. In Framingham risk score, 19% of the participants had intermediate to high risk of cardiovascular disease within 10 years. The cardiovascular risk factors were common in HIV patients attending ART center of BSMMU, where base line 10-years CVD risk was low. People living with HIV appear to be an imminent risk to develop CVD.

Keywords: *HIV, anti-retroviral therapy, 10-year cardiovascular disease risk.*

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INTRODUCTION

The common cardiovascular events are associated with HIV infection. In HIV seropositive patient, atherosclerosis and cardiovascular disease are developed by several mechanism like vascular endothelial dysfunction, abnormal coagulation process and systemic inflammatory response.[1] It is found in different studies that cardiovascular risk factors like smoking, dyslipidemia, hypertension and central obesity were prevalent in the HIV sero-positive patients.[2,3] So, cardiovascular disease risk and cardiovascular risk factors in people living with HIV needs to be studied. The data are scarce regarding cardiovascular diseases and risk factors in HIV populations in Bangladesh. So, this study would be helpful for both the clinician and the patients in making a rational approach in management of overlapping HIV infection with cardiovascular diseases and this report may contribute to the monitoring of the cardiovascular disease prevention and control policy among HIV infected patient in our country. This study may be helpful in reduction of the sufferings and burden of cardiovascular diseases in HIV patients.

MATERIALS AND METHODS

This was a cross-sectional observational study done from March 2017 to September 2019 in the ART Center of Bangabandhu Sheikh Mujib Medical University. The socio-demographic characteristics were evaluated by

interviewing face to face using WHO STEPS questionnaire. Anthropometric measurements were performed following standard procedures. The venous blood samples were drawn and fasting blood glucose, HbA1c and fasting lipid profile were measured in department of Biochemistry, BSMMU.

The participant was considered as diabetic who were already diabetic or fulfilled the criteria having HbA1c ≥ 6.5% or fasting plasma glucose level ≥7 mmol/L. The US National Cholesterol Education Program (NCEP) III guidelines was used to define dyslipidemia. All the participant had provided written informed consent before enrollment. Ethical approval was obtained from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University. After collection of the data analysis was performed by SPSS Version 22.

RESULTS

Table I shows a total of 100 participants were enrolled between March 2017 to September 2019 in the ART Center of Bangabandhu Sheikh Mujib Medical University. The age range of the participants were 18-64 years. Mean age was 38.05 ±9.85 years. Female participants were 35 (35%) and male participants were 65 (65%) in number and male: female ratio was 1.8:1. Among the male participant 48 resided in rural area where as 29 of female participant were living in the rural area. Male were educated above higher secondary level more in number than the female (27 vs 6) but there was a little difference in illiteracy level/primary level(38 v29). All the female participant were married and divorced rate was higher in them (10 vs 0). Regarding the transmission route heterosexuality is the predominant both in the male and female (59 vs 35) followed by MSM in case of male in our study. The commonest opportunistic infection was Tuberculosis and only one patient was found to be have CMV retinitis. Except one patient among the male and 100% of the female patient were receiving HAART. PPI use was more common in the male participant (14 vs 1) (Table-1). Fifteen participants (15%) were underweight, thirty three participants (33%) were overweight, five participants (5%) were obese but forty seven participants (47%) were normal in weight at presentation (Figure-1). Very small amount (5%) of the participants were physically active as per World Health Organization (WHO).

Table 1 Study population socio demographic characteristics(N=100)

Characteristic	Male	Female
Sex of the participants	65/100	35/100
Age (Range of years)	18-65 (years)	25-64 (years)
Type of community		
Rural	48 /65	30/35
Urban	17/65	5/35
Level of education		
Illiterate/Primary	38/65	29/35
Secondary or Above	27/65	06/35
Occupation		
Employed	48/65	3/35
Unemployed	17/65	32/35
Marital status		
Never married	8/65	0/35
Married	57/65	25/35
Divorced/Widow	0/65	10/35
Route of transmission		
Heterosexual	59/65	35/35
MSM	06/65	0/35
Blood borne	0/65	1/35
Injectable syringe/Unknown	0	0
Opportunistic infection		
Pulmonary TB	05/65	02/35
Extrapulmonary TB	03/65	0/35
CMV retinitis	0/65	1/35
HAART		
On HAART	64/65	35/35
Current PI use	14/65	1/35

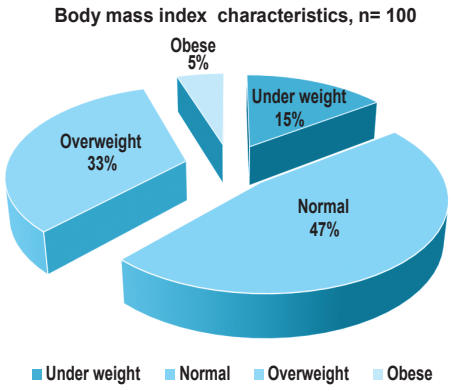

Figure 1: *Body mass index characteristics of study participants.*

Figure 1 shows that 47% participants had normal body weight. 33% participant were overweight, 15% were underweight and 5% were obese

Table II shows the framingham risk scores, 81% patient was in low-risk group, 16% were in intermediate risk group followed by 3% were in high-risk group population

Table II: Shows the Framingham risk scores of HIV infected peoples (N=100)

FRS	All	Male	Female
Low risk (<10% cardiovascular disease risk)	81 (81%)	49 (75.4%)	32 (91.4%)
Intermediate risk (10%-20% cardiovascular disease risk)	16 (16%)	13 (20%)	3 (8.5%)
High risk (>20% cardiovascular disease risk)	3 (3%)	3 (4.6%)	0 (0%)

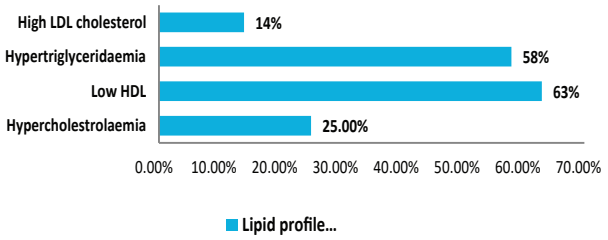

Figure 2: Lipid profile characteristics of study participants.

Figure 2: shows the lipid profile characteristics of study participants frequency of hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL were present among 25%, 58%, 14% and 63% of the participants respectively

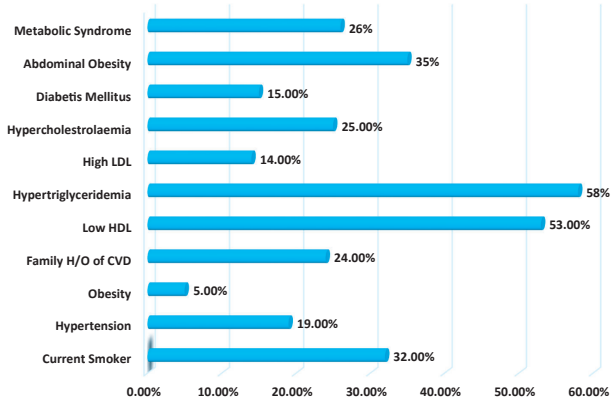

Figure 3: Cardiovascular risk factors characteristics of study participants.

Figue-3 shows overall frequency of Hypertension was 19%, Diabetes was 15 %, Hypercholesterolaemia 25%, High LDL was 14%, Hypertiglyceraldemia was 58%, Low HDL was 53%, family history of CVD was present in 24%, Obesity was 5%. Among the male participant 32% participant were current smoker

Almost all the patients (99%) received ART among them 15% were treated protease inhibitors (PI) like lopinavir. The median duration of ART was 3 years.

DISCUSSION

This is probably the pioneer study in Bangladesh about the CVD and its risk factors in HIV patients. The WHO STEPS questionnaire was utilized to assess dietary habit, physical activity, tobacco use and alcohol consumptions.

In the study population, male to female ratio was 1.8:1 with males comprising 65% of cases. Male predominance was also observed in several studies.[4,5] Age range of our study population was 18 years to 65 years and median age was 35. Higher prevalence seen as this is sexually active and reproductive age. Similarly, higher prevalence in this age group was observed in previous studies conducted in Bangladesh.[4] About 67% of HIV patient completed up to primary level education. These findings were similar the study conducted in India.[5] It is possible that educated people are more motivated and exposed to prevention programs.

Majority of participants were married (82%), eight (8%) participants were unmarried and ten (10%) were widows. High number of married persons having HIV/AIDS was also reported in other Indian studies.[5] Almost all widows gave history of death of their spouses due to HIV/AIDS. In this study, most common possible route of transmission was heterosexual (92%). This is due to probably homosexuality is not common in Bangladesh.[6]

Majority of participants cited fever, weight loss and diarrhea as symptoms within 6 months of HIV diagnosis. Tuberculosis was the commonest opportunistic infection found in 10% patients in this study. This is near similar to studies done in ICDDRB, Bangladesh[4] but lower from the other South Asian[7] study done in 2006 which reported tuberculosis in 62% patients of their study populations.

That study was conducted a decade before, when wide spread use of ART was not possible. Now the good availability and wide spread use of ART could be the reason of this decrease in opportunistic TB infection in HIV seropositive patients, despite the high prevalence of tuberculosis in the Bangladesh.

Ninety-nine participants (99%) were receiving ART of which fifteen (15%) were receiving protease inhibitors (PI) in the form of boosted lopinavir-based therapy. The median duration of ART exposure was 3 years. Only five (5%) of the participants were involved in physical activity consistent with WHO recommendations and only 2 study participant's dietary habits were in compliance with WHO recommendation. According to the participant response low intake was due to their low financial condition. Other study had shown less consumption of fruits and vegetable is associated with increase in CVD rsik.[8,9] A high rate of unemployment (49%) was observed in this study, as 91% of female were housewife and 26.15% male had no jobs. This high unemployment rate and stigma related to HIV infection, may cause high levels of stress to HIV seropositive patients.

Thirty-nine participants (39%) reported to have ever smoked, of which thirty-two (32%) were current smokers, all of them being men. 25% of participants used tobacco with betel leaf. Only 5 participants occasionally use alcohol, all of them being men. These behavioral risks are similar to Indian studies.[10]

About 5% were obese and metabolic syndrome was present in 26% in our study. These findings are similar to other study findings conducted in Asia.[11] The female was more obese than male in our study and the reason behind this may be physical inactivity.

Among metabolic risk factors, hypertension was observed in nineteen (19 %) participants. Diabetes mellitus in males and females were 15% similar to studies in Malaysia (12). In this study, Hypercholesterolemia was present in 25% of the participants which is similar to the results from other studies. Hypertriglycedaemia and low HDL was the predominant lipid abnormalities found in this study which was consistent with other studies.[13] High level of TG and low HDL may be associated with low intake of fruits and vegetables.[14]

To detect the cardiovascular disease risk, Framingham risk score was used because was a proven tool to assess CVD risk in non-HIV patients [15] and it can also provide an early prediction of presence of carotid atherosclerosis.[16] Framingham risk score showed 81% of participants had low cardiovascular disease risk. Only 19% had intermediate to high risk based upon Framingham risk score, which is par compared with rates observed among individuals with HIV in South Korea (29%) (17), Western countries (19.6%-21.1%) (18) where sedentary life style were also high.

Limitations of this study include that this study was conducted at only one ART center. Therefore, the study findings may not be generalizable to people receiving HIV care from other centers. The cross-sectional design limits our understanding of causal links between risk factors and the development of cardiovascular diseases.

CONCLUSIONS

Cardiovascular diseases among people living with HIV appear to be an imminent risk group. The 10-year cardiovascular disease risk was low. Risk factors for CVD were common and significantly related to individual living with HIV. Stepping up of preventive services including screening services should be considered.

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Case Report

An Eleven Months Old Infant with Very Early Onset Inflammatory Bowel Diseases (IBD): A Rare Case Report

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Abstract

Inflammatory bowel disease (IBD) in pediatric cases has been seen rapidly increasing in number over the last decade. Now a days four types of pediatric IBD has been identified: less than ten years of age - early onset IBD, less than six years of age - very early onset IBD, less than two years of age- infantile IBD and less than twenty eight days of age - neonatal onset IBD. Young children presented with more aggressive clinical features and severity is more than the older children and adults. Early onset disease presenting in children may have a monogenic basis. Infantile IBD or neonatal IBD having the high rates to affect the first-degree relatives and there is very high chance to develop resistance against immunosuppressive treatment. Very early onset IBD (VEO-IBD) most commonly presenting per rectal bleeding with or without mucous stools, isolated colonic disease, perianal involvement, skin lesions, whereas early onset IBD (EO-IBD) commonly presented with abdominal pain and weight loss. A thorough history, physical examination, biochemical markers, endoscopic evaluation with macroscop and microscopic findings are the only way to reach the diagnosis. The treatment of VEO-IBD is the same as that given to the adolescents and adults with IBD (eg, anti-inflammatory agents, immunomodulators, biologics, antibiotics, and surgical approaches). Here, we report a rare case of very early onset IBD of a 11 months old male infant, who presented with the complaints of blood and mucus mixed loose watery stool for 10 days, having similar episodes for last five months. He was mildly pale, and had thrombocytosis with raised C reactive protein (CRP), features of colitis in stool routine microscopic test. The diagnosis was confirmed by colonoscopy and histopathology study, which showed features of Crohn's colitis. He was treated by anti-inflammatory drugs (steroid and mesalazine) with a significant improvement in a short time.

Keywords: *Pediatric inflammatory bowel disease, monogenic VEO-IBD, very early onset IBD*

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For correspondence

INTRODUCTION

Inflammatory bowel disease (IBD) in children constitutes about 25% of all patients of IBD.[1] "very early-onset IBD" (VEO-IBD) means key symptoms of IBD or is diagnosed before six years of age. Compared with children whose IBD develops later in life, those with VEO IBD and particularly those with infantile IBD are more likely to have single gene defects that alter immunity or epithelial barrier function may disturb, and often have a more severe disease course[2,3]. The common disorders are interleukin-10 (IL-10) signaling defects, atypical severe combined immuno-deficiency (SCID), common variable immunodeficiency, chronic granulomatous disease and other neutrophil defects, hyperimmunoglobulin M syndrome, Wiskott-Aldrich syndrome, agammaglo- bulinemia, familial hemophagocytic lymphohistiocytosis, and IPEX (immune dysregulation, polyendocrinopathy, enteropathy, X-linked) or other autoimmune related enteropathy.[4]

Near about, 50 genetic variants have been associated with IBD and these disorders are collectively called as monogenic IBDs.[5]

Clinical features that give suspicion for monogenic IBD include:[6]

- Early age of onset (eg, younger than six years, particularly younger than two years of age)
- Family history of IBD and/or immunodeficiency in multiple family members, usually with male predominance, or consanguinity

- Frequent attack of infections or unexplained fever
- Associated features suggestive for autoimmunity (eg, primary sclerosing cholangitis, arthritis, anemia, or endocrine dysfunction)
- Very severe IBD and/or resistance to conventional therapies for IBD
- Symptoms and/or signs suggestive of hemophagocytic lymphohistiocytosis (fever, hepatomegaly, cytopenias, high ferritin)
- Lesions of the skin, hair, or nails
- Current or previous history of cancer in the patient

Laboratory investigations include complete blood count with ESR, intestinal inflammatory markers, stool RME and C/S. For immunodeficiency, identification of immunological panel is important. For diagnosis of VEO-IBD, endoscopy of lower and upper GIT now remain the gold standard. Colonoscopy may show ulcer, pseudopolyps and histopathology confirms the diagnosis by showing features of chron's colitis or ulcerative colitis.[7] We hereby report a case of an 11 months old male infant who presented with blood and mucus mixed loose watery stool for 10 days and was diagnosed as very early onset IBD on the basis of laboratory, colonoscopy and histopathology findings.

CASE REPORT

A 11 months old male infant got admitted in the Department of Pediatric Gastroenterology and Nutrition, BSMMU with the complains of blood and mucus mixed loose watery stool for 10 days for 10-12 episodes per day. Occasionally he also complains mucoid stool without blood several episodes with moderate in amount. He had history similar type of illness for previous five months but not regularly. Duration of each attack persist for two weeks and managed with few antibiotics that results decrease the frequency of purging but not complete recovery. So that he visited several registered physician and condition not so improved. He had history of exclusive breast feeding (EBF) for first six months, then complementary feeding was started with formula milk for 1 month. But after starting complementary feeding, he developed watery diarrhea. Then after recovery only breast milk was continued with rice suji and occasionally chicken based diet was given. He had no history of cow's milk ingestion or related foods. On examination, baby was fretful, mildly pale and anicteric, all vitals were within normal limit, no signs of dehydration and bilateral pedal oedema absent, skin survey revealed normal findings, severe wasting was present (weight- 6.6 kg, length: 69 cm WLZ score -3.6), abdomen examination revealed no organomegaly and ascites was absent. Laboratory investigation showed haemoglobin (Hb)- 9.1 g/dl, WBC count- 16500/cmm, platelet count 8,50,000/cmm, ESR 90 mm in 1st hour, liver function test and fasting blood sugar were normal. Stool RME showed Mucus and RBC ++, pus cell plenty, stool C/S was normal, S. albumin was 27 gm/l, C-reactive protein 21 gm/l, fecal calprotectin was 850 µg/gm, S. tTG IgA was negative, stool for Clostridium difficile toxin negative, USG of whole abdomen showed loaded bowel loops having peristalsis. Primary immunodeficiency panel was normal and HIV testing was negative. Initially we managed this patient by giving lactose free diet with management of severe acute malnutrition due to its secondary cause and some antibiotics. But patient's condition did not improve rather there was persistent passage of mucoid stool, so we planned to do endoscopy of lower GIT. Upto transverse colon was seen through colonoscopy due to friable gut wall and there might be chance of bleeding. Macroscopically colonoscopy (Fig.1) showed erythematous mucosa, friable with shallow ulcer and few pseudopolyps in descending colon but there was no rectal involvement. For biopsy, tissue took from descending colon and sent for histopathologic examination. Histopathology report (Fig.2) showed infiltration of chronic inflammatory cell that suggestive of colitis with absence of crypt abscess, cryptitis, goblet cell depletion and absence of any granuloma. Usually for chron's disease getting definitive submucosal tissue by biopsy not always possible, so granuloma may be absent now a days. Then we treated the patient with oral prednisolone 1mg/kg/day and oral mesalazine 40mg/kg/day. Gradually, the frequency and amount of mucoid stool was reduced significantly, baby was gaining weight and he became playful. After 1 week CRP, was reduced to 18 mg/l, Hb 9.9 gm/dl, ESR 55 mm in 1st hour and platelet count 7,50,000/cmm. Our final diagnosis was very early onset IBD (Chron's disease) and we discharged the patient with advice for periodic follow up.

Fig.1 Colonoscopy showing erythematous mucosa, friable with shallow ulcer and few pseudopolyps in descending colon.

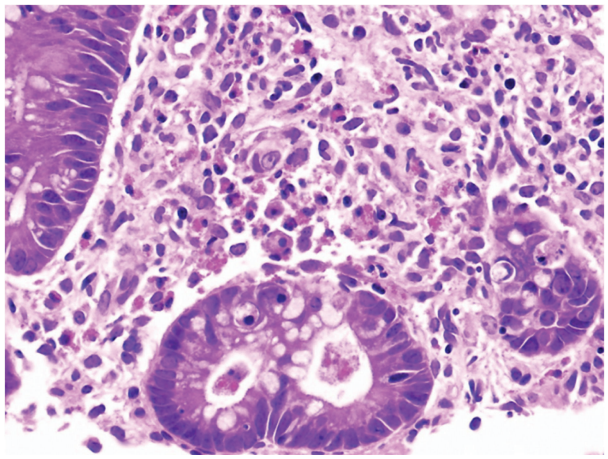

Fig.-2: Histopathology with features of Chron's colitis

DISCUSSION

Inflammatory bowel disease (IBD) in children below 6 years of age defined as very early-onset IBD (VEO-IBD). Infantile onset IBD also presents before 2 years of age and neonatal onset IBD present before <28 days of age. In pediatric IBD, around 6 to 15% of population presents at below 6 years of age.[4] The phenotype of VEO-IBD is considered to be heterogeneous and while some children have mild disease, others can present with aggressive and severe disease rather than adult IBD.[9-12] Due to more aggressive phenotype, strong family history and involving primary immunodeficiency gene, VEO-IBD is now considered to be a monogenic disease.[13-15] Our patient presented in his infancy period and we consider he had monogenic form, though he had no family history and his genetic study was not done due to financial constraints.

Variable presentation may show in pediatric IBD. Usually the onset is insidious, blood and mucus stained small volume loose watery stool may be present. Children with immune dysregulation polyendocrinopathy enteropathy X linked (IPEX) syndrome may presented with severe extensive volume of diarrhoea.[16] In children with IL-10 signalling defect, chronic granulomatous disease (CGD), and X-linked inhibitor of apoptosis protein (XIAP) may presented with intestinal fistula.[17] Children also may presented with repeated infections with lesions of the skin, nails, or hair.[6] On physical examination, pallor and tender abdomen may be present. Children must be evaluated for Perianal disease, folliculitis, arthritis, and gout. Some monogenic variants of VEO-IBD can present with palpable spleen or lymphnode.[18,19] Our patient presented with blood and mucus mixed loose watery stool and he was mildly pale, severely wasted.

The routine laboratory investigations for VEO-IBD include complete blood count (CBC) with ESR, important inflammatory markers. CBC picture may show low hemoglobin, high platelet count. Neutrophils defects can be associated with VEO-IBD, and low neutrophil as well as leukocytosis (seen in leukocyte adhesion deficiency) can be seen in some cases. There can be raised C-reactive protein. Looking for immunological panel is important for immunodeficiency disorders. Colonoscopy may show friable ulcer, pseudopolyps and histopathology confirms the diagnosis with features of chronic inflammation in

bowel wall and changes associated with IBD. Besides, monogenic form of VEO-IBD may show features of eosinophilic infiltrates, atrophied vilous, apoptosis, and increased intraepithelial lymphocytes.[7] Our patient had typical lab features of IBD (pallor, thrombocytosis and raised CRP). Other differentials- like allergic colitis, celiac disease, primary immunodeficiency disorder were excluded in this case. Colonoscopy showed ulcer and pseudopolyps in descending colon with no rectal involvement. Histopathology report showed features of Crohn's colitis.

Like other IBD, the treatment options for VEO-IBD include both medical (anti-inflammatory agents, immunomodulators, biologics, antibiotics) and surgical management (colectomy or ileal diversion). Hematopoietic stem cell transplantation (HSCT) is beneficial for specific genetic defect.[7] Our patient showed dramatic response both clinically and biochemically after treatment with steroid and mesalazine. So, now immunomodulatory therapy or biological agents were not required in our patient.

He was discharged with advice for periodic follow up.

CONCLUSIONS

Monogenic VEO-IBD has high rates of morbidity and mortality, and it might require different treatment strategies. So, starting the early pharmacologic treatment can be effective step. Early initiation vaccination therapy for children with VEO-IBD is necessary, due to the age of onset of disease. It is recommended to avoid immune suppressive drugs for at least 1 month for corticosteroid administration and 3 months for azathioprine/6-MP and biological medication.[20, 21]

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Obituary news May-2021

BMA would like to express deep condolence on deaths of the following notable physicians in recent past:

Sl. No.	Name	Date of Death
1	Dr. Jibesh Kumar Pramanik Assistant Professor, Respiratory Medicine Shahid Ziaur Rahman Medical College Bogura Ex. Student of Rajshahi Medical College (31th Batch)	06/01/2021
2	Dr. Md. Abdur Rashid Anesthesiology Specialist Ex. UH&FPO, Upazila Health Complex, Kahaloo, Bogra Ex Student of Rajshahi Medical College (K-15 Batch)	07/01/2021
3	Dr. Anwar Hossain Eye Specialist & Surgeon and Ex-consultant National Institute of Ophthalmology and Hospital, Dhaka Ex Student of Sher-E-Bangla Medical College, Barishal (4 Batch)	07/01/2021
4	Dr. Kazi Md Naser Ahmed Medical Officer, Square Hospital, Dhaka Ex Student of Sylhet MAG Osmani Medical College (6 Batch)	26/01/2021
5	Dr. Mahmudur Rahman Khandaker Professor of Anesthesiology, Northern International Medical College, Dhaka Ex, Assistant Professor of Anesthesiology, Dhaka Medical College Hospital Ex Student of Rahshahi Medical College (1972-73)	12/02/2021
6	Prof. Dr. Nazmul Haque Professor of Physiology, Northern International Medical College, Dhaka Ex, Head of Department, Physiology, Shahid Suhrawardy Medical College, Dhaka Ex Student of Chattogram Medical College (7 Batch)	09/03/2021
7	Professor (Dr.) M Sultan Ul Alam Freedom Fighter, Ex Head, Department of Community Medicine, Chattogram Medical College Ex Student of Chattogram Medical College (8th Batch)	15/03/2021
8	Dr. Abdul Hannan Associate Professor, Department of Surgery Rajshahi Medical College Ex Student of Rajshahi Medical College (31th Batch)	27/03/2021
9	Prof. Dr. Nur -E -Alam Patowary Professor of Anesthesiology and Ex Head, Department of Anesthesiology, Gonoshasthaya Somaj Vittik Medical College, Saver, Dhaka Ex Student of Dhaka Medical College (26th Batch)	02/04/2021
10	Professor Dr. Badrul Haque Titu Ex Professor of Neurology, Dhaka Medical College Ex Student, Mymensingh Medical College (12 Batch)	05/04/2021

Sl. No.	Name	Date of Death
11	Dr. Nurul Hasan Shoaib Ex Student of Sylhet MAG Osmani Medical College (27th Batch)	06/04/2021
12	Professor Dr. Mohammad Obaidullah Head, Department of Biochemistry, Rajshahi Medical College Islami Bank Medical College, Rajshahi Ex Student of Rajshahi Medical college (20th Batch)	08/04/2021
13	Dr. Abdul Latif Director, Chattogram Metropolitan Hospital Ex Student, of Chattogram Medical College (17th Batch)	09/04/2021
14	Dr. Gazi Saiful Alam Chowdhury Sapon Ex. Deputy Director, Rajshahi Medical college Hospital Life Member, BMA Ex. Student of Rajshahi Medical College (18th Batch)	09/04/2021
15	Dr. Mohammad Mozadded Mehdi Associate Professor and Sinior Consultant Department of Cardiac Surgery National Hard Foundation Hospital and Research Institute, Dhaka Ex. Student of Dhaka Medical College (K 44 Batch)	10/04/2021
16	Dr. Shariful Ahsan Medical Officer, Bangladesh Agricultural Research Council, Dhaka	11/04/2021
17	Dr. Upandra Nath Sheel Rtd. Upazila Health and Family Planning Officer Upazila Health Complex, Nagashree, Kurigram Life Member, BMA Ex. Student of Rangpur Medical College (4th Batch)	13/04/2021
18	Dr. Rezaul Karim Badal Ex. Upazila Health and Family Planning Officer Upazila Health Complex, Madhupur, Tangail Ex Student of Mymensingh Medical College (10th Batch)	16/04/2021
19	Dr. Mohammad Mujahid Hossain Ratan, Freedom Fighter Ex. Student of Dhaka Medical College (K-30 Batch	16/04/2021
20	Dr. Mominul Alam Ex. Student of Dhaka Medical College (K-21 Batch)	16/04/2021
21	Professor Dr. Abu Ahmed Asraf Ali Ex Principal, Shahid Ziaur Rahman Medical College Bogura Life Member, BMA Ex. Student of Rajshahi Medical College (10th Batch)	17/04/2021
22	Professor Dr. Abdul Majid, Freedom Fighter Ex. Professor, Department of Community Medicine Holy Family Red Crescent Medical College, Dhaka Life Member, BMA Ex. Student of Sir Salimullah Medical College (5th Batch)	20/04/2021

Sl. No.	Name	Date of Death
23	Professor Dr. Md. Fazlul Haque Director, Islamia Eye and Laser Center, Dhaka Ex. Head, Department of Ophthalmology, Dhaka Medical College, Dhaka Life Member, BMA Ex Student of Sir Salimullah Medical College (2nd Batch)	22/04/2021
24	Prof. Dr. Abul Khair Mohammad Shamsuzzaman Tushar Director, National Institute of Laboratory Medicine and Referral Centre, Dhaka Life Member, BMA Ex Student of Rajshahi Medical College (22nd Batch)	24/04/2021
25	Professor Dr. Md. Humayun Kabir Mukul Head of Department, Orthopaedic Surgery President Abdul Hamid Medical College, Kishoreganj Ex. Department of Head, Orthopaedic Surgery, Mymensingh Medical College Life Member, BMA Ex Student of Mymensingh Medical College (14th Batch)	25/04/2021
26	Dr. Ashis Kumar Bonik Emergency Medical Officer Shahid Ahsanullah Master General Hospital, Tongi Life Member, BMA Ex Student of Shahid Monsur Ali Medical College (Passing year 2005)	25/04/2021
27	Dr. Md. Mahbubul Islam Chief Cardiac Anesthesiologist and Director, Management Committee, Labaid Hospital Life Member, BMA Ex Student of Sir Salimullah Medical College (4th Batch)	26/04/2021
28	Professor Dr. ABM Shamsul Huda Ex. Principal and Head, Department of physiology and Biochemistry Sir Salimullah Medical College Ex Student of Dhaka Medical College (K-12 Batch)	26/04/2021
29	Dr. Faridul Alam Reza Shokrana Ex. Joint Managing Director Chattogram Managing Director Life Member, BMA Ex Student of Chattogram Medical College (8th Batch)	27/04/2021
30	Dr. Md. Abdul Ohab Tarafdar Chest Specialist and Chairman, Akota Hospital and Diagnostic Center pvt Ltd. Jashore Ex Student of Sylhet MAG Osmani Medical College (10th Batch)	27/04/2021

May Allah bless the departed souls.

Our heartiest commiseration to the deceased's family, our prayers are with them during this difficult moment of their life.

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