ISSN-0301-035X(Print)
2219-1607(Online)

Bangladesh Medical Journal

Official Organ of Bangladesh Medical Association

Vol. 49 No. 1 January 2020

BMA Executive Committee for The Year 2017-2018

Sl.	Name	Name of Post
1.	Dr. Mustafa Jalal Mohiuddin	President
2.	Dr. Kanak Kanti Barua	Vice President (Dhaka City)
3.	Dr. Jamal Uddin Khalifa	Vice President (Dhaka Division)
4.	Dr. Md. Kamrul Hassan (Salim)	Vice President (Barisal Division)
5.	Dr. Sheikh Mohammed Shafiul Azam	Vice President (Chittagong Division)
6.	Dr. Sk. Baharul Alam	Vice President (Khulna Division)
7.	Dr. Md. Mostafa Alam (Nannu)	Vice President (Rajshahi Division)
8.	Dr. Md. Delwar Hossain	Vice President (Rangpur Division)
9.	Dr. Murshed Ahmed Chowdhury	Vice President (Sylhet Division)
10.	Dr. A N M Fazlul Hoq Pathan	Vice President (Mymensingh Division)
11.	Dr. Md. Ehteshamul Huq Choudhury	Secretary General
12.	Dr. Mohd. Zahid Hussain	Treasurer
13.	Dr. Md. Kamrul Hasan (Milon)	Joint Secretary General
14.	Dr. Md. Tarique Mehedi Parvez	Organizing Secretary
15.	Dr. Shahryar Nabi (Shakil)	Scientific Secretary
16.	Dr. Md. SK. Shahid Ullah	Office Secretary
17.	Dr. Md. Mahbubur Rahman (Babu)	Publicity & Public Relation Secretary
18.	Dr. Sohel Mahmud	Social Welfare Secretary
19.	Dr. Purabi Rani Debnath	Cultural & Entertainment Secretary
20.	Dr. Kazi Shafiqul Halim (Zimmu)	Library & Publication Secretary
21.	Dr. Md. Abul Hashem Khan	International Affairs Secretary
22.	Dr. Mohammed Salim	Member, Central Executive Committee
23.	Dr. Md. Abdul Aziz	Member, Central Executive Committee
24.	Dr. Md. Moniruzzaman Bhuiyan	Member, Central Executive Committee
25.	Dr. Mohammad Mushtuq Husain	Member, Central Executive Committee
26.	Dr. Md. Jamal Uddin Chowdhury	Member, Central Executive Committee
27.	Dr. Md. Shafiqur Rahman	Member, Central Executive Committee
28.	Dr. Md. Sharfuddin Ahmed	Member, Central Executive Committee
29.	Dr. Qazi Shahidul Alam	Member, Central Executive Committee
30.	Dr. Md. Abu Raihan	Member, Central Executive Committee
31.	Dr. M Nazrul Islam	Member, Central Executive Committee
32.	Dr. Zahurul Huq Sachchu	Member, Central Executive Committee
33.	Dr. Md. Abu Yusuf Fakir	Member, Central Executive Committee
34.	Dr. Ehsanul Kabir Joglul	Member, Central Executive Committee
35.	Dr. Md. Zulfikar Ali (Lenin)	Member, Central Executive Committee
36.	Dr. Uttam Kumar Barua	Member, Central Executive Committee
37.	Dr. Chitta Ranjan Das	Member, Central Executive Committee
38.	Dr. Md. Jabed	Member, Central Executive Committee
39.	Dr. Hasanur Rahman	Member, Central Executive Committee
40.	Dr. Md. Babrul Alam	Member, Central Executive Committee
41.	Dr. Hossain Muhammad Mustafijur Rahman	Member, Central Executive Committee
42.	Dr. Muhammad Harun-Ar-Rashid	Member, Central Executive Committee
43.	Dr. Mahmud Hasan	Member, Central Executive Committee
44.	Dr. M Iqbal Arslan	Member, Central Executive Committee
45.	Dr. Syed Atiqul Haq	Chairman, Bangladesh Medical Journal & Member, Central Executive Committee
46.	Dr. Rokeya Sultana	Member, Central Executive Committee
47.	Dr. Badiuzzaman Bhuiyan (Dablu)	Member, Central Executive Committee
48.	Dr. Kamrul Hasan Khan	Member, Central Executive Committee
49.	Dr. Momenul Haq	Member, Central Executive Committee
50.	Dr. Md. Shahidullah Sikder	Member, Central Executive Committee
51.	Dr. Pabitra Kumar Debnath	Member, Central Executive Committee

Information for Authors

Submission of manuscripts:

Papers are accepted for publication with an understanding that they are submitted solely to the Bangladesh Medical Journal and are subject to peer review and editorial revision. Statement and opinions expressed in the papers, communications and letters herein are those of author(s) and not necessarily of the editors or publishers. Three hard copies along with a soft copy should be sent to the executive editor of Bangladesh Medical Journal, BMA Bhaban, 15/2, Topkhana Road, Dhaka-1000.

Bangladesh Medical Journal publishes the following:

Full papers, review articles, letters to the editors, debate and opinion papers, editorials, on being a doctor, medical news, medical jokes/poem.

Letters to the editor – letters are invited that discuss, criticize or develop themes on national or international issues related to doctors, medical science or medical profession. Clinical observations, original research presented in a research letter format or case reports or series may be included in letters to the editors. Comments on papers published in Bangladesh Medical Journal are also encouraged. Acceptance will be at the discretion of the editorial board, and editorial changes may be required. Wherever possible, letters from responding authors will be included in the same issue.

Form of full papers submitted for publication:

Full papers should be no more than 4000 words. The onus of preparing a paper in a form suitable for sending to press lies with the author. Authors are advised to consult a current issue in order to make themselves familiar with the journal regarding typographical and other conventions, layout of tables etc. Authors are encouraged to consult the latest guidelines produced by the International Committee of Medical Journal Editors (ICMJE), which contains a lot of useful generic information about preparing scientific papers (http://www.icmje.org/manuscript_a.html) Manuscripts should be typed on one side of white good quality A4 size paper, with wide margins of at least 2cm and using double space throughout, the preferred font being Garamond size 12. Words at the end of lines should not be hyphenated unless hyphens are to be printed. Page numbering is required. Spelling should generally be that of the Concise Oxford Dictionary, 11th ed. Oxford: Clarendon press. Each component of the manuscript should begin on a new page in the sequence of title page, abstract, text, reference, tables and legends for illustration. The title page should include the title of the paper, name of the author(s), and name of the departments(s) to which the work should be attributed. The first six authors of a work should be named, followed by "et al." if there are more than six.

The unstructured abstract of 150 words should follow the title page. It should provide the context or background for the study and should state the study's purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect size and their statistical significance, if possible), and principal conclusion.

The text should be presented in the form of Introduction, Methods, Results and Discussion.

References:

These should be given in the text using the Vancouver system. They should be numbered consecutively in the order in which they first appear in the text using superscript. If a reference is cited more than once the same number should be used each time. References cited only in tables and figures and not in the text should be numbered in sequence from the last number used in the text and in the order of mention of the individual tables and figures in the text. At the end of the paper, on a page(s) separate from the text, references should be listed in numerical order. The journal adheres closely to the Vancouver style of references (see http:// www.nlm. nih.gov/bsd/uniform_ requirements. html, updated 2013).

Sample references are given below –

1. Standard Journal Article

List the first six authors followed by et al:

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25; 347(4): 284-7

As an option, if a journal carries continuous pagination throughout a volume (as many medical journals do) the month and issue number may be omitted:

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002; 347:284-7

More than six authors:

Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6

Optional addition of a database's unique identifier for the citation:

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25;347(4):284-7. PubMed PMID: 12140307

Organization as author:

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.

4. Unpublished Material (In press or Forthcoming:)

Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. Proc Natl Acad Sci U S A. Forthcoming 2002.

5. Journal Article on the Internet

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [Internet]. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: http://www.annals.org/ cgi/reprint/ 145/1/62.pdf

Tables :

Table should have brief title for each, should be numbered consecutively using Roman numerals and be cited in the text in consecutive order. Internal horizontal and vertical rules should not be used.

Illustration :

All drawings should be made with black Indian ink on white paper. Photographs and photomicrographs should be supplied as glossy black and white prints unmoundted. All photographs, graphs and diagrams should be referred to as figures numbered consecutively in the text in Arabic numerals.

Abbreviation :

Except for units of measurement, abbreviations are discouraged. Consult scientific style and forma. The CBE manual for authors, editor and publishers (Sixth edition New York: Cambridge University Press, 1994) for lists of standard abbreviation. The first time an abbreviation appears, it should be preceded by the words for which it stands.

Drug names :

Generic name should generally be used. When proprietary brands are used in research, include the brand name in parentheses in the methods section.

Permission :

Materials taken from other source must be accompanied by a written statement from both author and publishers giving permission to the journal for reproduction. Obtain permission in writing from at least one author of papers that is still in press, unpublished data and personal communications.

The editor of Bangladesh Medical Journal reserves the customary right to style and if necessary shortens the material accepted for publication and to determine the priority and time of publication. Editor assumes that the manuscript submited by the author is based on honest observations. It is not a task of the editor to investigate scientific fraud paper.

Original Article

Serum C-reactive Protein Predicts Early Mortality in Patients with Decompensated Cirrhosis of Liver

*Islam MA[1], Alam SMN[2], Das DC[3], Khaleque N[4], Yousuf MAK[5], Mahtab MA[6]

Abstract

Serum C-reactive protein is a marker of systemic inflammation, which has been studied to predict mortality and cirrhosis related complication in decompensated cirrhosis of liver. To evaluate the role of serum C- reactive protein as a predictor of early mortality in patients with decompensated cirrhosis of liver. This was a prospective observational study, carried out in the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka between October 2017 to February 2019. A total of 89 patients with decompensated cirrhosis of liver were included in the study. Baseline serum CRP was measured and patients were longitudinally followed for a period of 30 days. Patients were divided into two groups, survival and non-survival. The groups were compared of CRP level, CTP score, MELD score and cirrhosis related complications. Chi-Square test was used to analyze the categorical variables and Student t-test was used to analyze continuous variables. Receiver-operator characteristic curve was used to detect serum CRP level for prediction of mortality within 30 days. The mean age was found 49.02±13.90 years in survival group and 47.52±11.30 years in non-survival group. Male patients were predominant in both groups. Total WBC count, serum CRP, serum sodium, serum bilirubin, CTP score & MELD score were statistically significant (p<0.05) between the groups. In multivariate analysis, only serum CRP level (OR 1.075, 95% CI, 1.027-1.122%, p=0.001) was found significantly associated with mortality within 30 days. Receiver-operator characteristic (ROC) was constructed, using serum CRP level, which gave a cut off value of 31mg/L, with 78% sensitivity and 90% specificity for prediction of mortality within 30 days. Elevated serum CRP level is an independent predictor of early mortality in patients with decompensated cirrhosis of liver. It was also observed that, high serum CRP level was associated with increased frequency of cirrhosis related complications.

Keywords: *Cirrhosis, decompensation, c-reactive protein (CRP), systemic inflammation.*

*1. Dr. Md. Atikul Islam, Medical Officer, Sheikh Russel National Gastroliver Institute and Hospital (SRGIH), Dhaka. E-mail: atikrazum@gmail.com
2. Dr. Sheikh Mohammad Noor-E-Alam, Assistant Professor, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka.
3. Dr. Dulal Chandra Das, Medical officer, Department of Hepatology, BSMMU, Dhaka.
4. Dr. Narwana Khaleque, Medical Officer, SRGIH, Dhaka.
5. Dr. M Abul Khair Yousuf, Resident, Hepatology, BSMMU, Dhaka.
6. Professor Mamun Al Mahtab, Chairman, Department of Hepatology, BSMMU, Dhaka.

*For Correspondence:

INTRODUCTION

Cirrhosis, a final pathway for a wide variety of chronic liver diseases is a pathologic entity defined as diffuse hepatic fibrosis with replacement of normal liver architecture by nodules. The rate of progression of chronic liver disease to cirrhosis may be quite variable, from weeks in patients with complete biliary obstruction to decades in patients with chronic hepatitis C.[1] Cirrhosis is classified into two main prognostic stages: compensated and decompensated cirrhosis. Median survival in the compensated stage exceeds 12 years whereas it is only 2 years in patients who develop decompensation.[2] Currently, liver transplantation is the only curative remedy for end stage cirrhosis.

The serum C-reactive protein (CRP) is an acute phase protein found in the blood stream. Its level rises in response to inflammation. It has been extensively studied in rheumatologic conditions, coronary artery diseases, tissue necrosis and bacterial translocation.[3,4] Several studies have been performed on the association of CRP with the severity of inflammation in liver disease, such as fatty liver and chronic hepatitis C.[5,6] Furthermore recent studies demonstrated that systemic inflammatory

response was a major prognostic factor in patients with cirrhosis and serum CRP can be used to reflect this exacerbated inflammation that coexist during the course of cirrhosis.[7]

In cirrhotic patients, once decompensation occurs, early mortality risk increases sharply. Predicting the mortality in such patients is of utmost important as depending on their prognosis, proper organ allocation for liver transplantation can be prioritized. Another important role of prognostic markers is to foresee probable complications e.g. spontaneous bacterial peritonitis and hepatorenal syndrome. Child-Pugh score and model for end-stage liver disease (MELD) have been used for many years for assessing the prognosis of cirrhosis. However, Child-Pugh score has important limitations and it only tells us about 1, 5 and 10 years mortality. The MELD score has been being used as a marker of prognosis of cirrhosis since long, even though 10 to 20% of patients are still misclassified and it only tells us about 3 month mortality.[8] On the context of our country a cheap, efficient and readily available marker to predict early mortality in cirrhotic patients can prove to be a boon, considering our socio economic status. Furthermore currently there are no established marker that can predict 30 days mortality in patients with decompensated cirrhosis of liver. Recent study suggested that serum CRP was able to predict early mortality in HBV related decompensated cirrhotic patients.[9] So, we have investigated whether serum CRP level could predict 30 days mortality in hospitalized patients with decompensated cirrhosis of liver.

MATERIALS AND METHODS

It was a hospital based prospective observational study. The study was carried out in the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh between October 2017 to February 2019. Patients with decompensated cirrhosis attending at Hepatology department were selected as study population. A total of 89 decompensated cirrhotic patients were observed during this study period. Initial investigations were done to meet up inclusion and exclusion criteria including liver chemistry (serum bilirubin, serum albumin, prothrombin time), ascitic fluid analysis, AFP, serum creatinine, urine R/E, CXR, ECG, abdominal ultrasonography, endoscopy of upper gastrointestinal tract. Decompensated cirrhosis was diagnosed with a combination of physical, biochemical and radiological findings and defined by history or presence of one or more of clinical ascites, variceal bleeding, jaundice, or hepatic encephalopathy.[10] The inclusion criteria were age > 18 years with decompensated cirrhosis of liver (cirrhotic patients with presence or history of one or more of clinical ascites, jaundice, variceal bleeding or encephalopathy). The exclusion criteria were acute on chronic liver failure, acute hepatitis, hematologic disorder, malignancy, pregnancy, ischaemic heart disease, renal failure, clinical infections, rheumatological condition associated with elevated CRP. The patients were chosen according to purposive sampling. Blood sample for serum CRP levels was collected and was measured in the department of Biochemistry, using Immunoturbidimetry. The patients were divided into two groups, survival and nonsurvival group. The selected patients were longitudinally followed to observe mortality or appearance of cirrhosis related complications (variceal bleeding, hepatic encephalopathy,hepatorenal syndrome and spontaneous bacterial peritonitis) for a period of 30 days. Follow up was done either in person or over telephone. End of study was considered after death or 30 days whichever one was shorter. The statistical analysis was carried out using SPSS version 22.0. Qualitative data were analyzed by Chi-square test & quantitative data were analyzed by student's t-test. Mann Whitney-U test was used to analyze non-parametric data. The discriminative ability of serum CRP to predict the outcome was evaluated by using the area under receiver operating characteristic curve (AUC). $P< 0.05$ was considered statistically significant.

Ethical consideration

Ethical clearance for the study was taken from the Institutional Review Board of BSMMU prior to commencement of this study. Approval paper was given by 146th Institutional Review Board, Bangabandhu Sheikh Mujib Medical University, meeting held on 07 October 2017 (No. BSMMU/2017/10935).

RESULTS

During the study period total 89 patients were enrolled. It was observed that 23 (25.84%) patients did not survive and 66 (74.16%) patients were found alive.

Table- I shows baseline characteristics of the patients, it was observed that mean age was found 48.63±13.23years. Male female ratio was 6.42:1. 56.2% patients had hepatitis B and 12.4% patients had Hepatitis C. Mean systolic BP was 103.65±8.18 mmHg, mean diastolic BP was 69.21±4.52 mmHg, mean Hb % was 9.87±1.81 g/dl, mean TC was 7.45±5.50x109/L, , mean platelet count was 111.94±83.65 x109/L, mean serum CRP was 23.67±25.11 g/L, mean serum creatinine 1.19±0.46 mg/dl, mean serum sodium was 132.01±6.36 mmol/L, mean serum potassium was 3.89±0.72 mmol/L, mean serum bilirubin 5.25±6.98 mg/dl, mean ALT was 59.53±41.79 U/L, mean prothrombin time was 19.52±7.10 sec, mean INR was 1.63±0.57, mean serum albumin was 2.51±0.56 g/dl, mean CP score 9.85±2.02 and mean MELD score 17.64±6.87.

Table I: Baseline characteristics of the study patients (n=89)

Baseline characteristics		Mean±SD	Min	Max
Age (Years)		48.63±13.23	22	80
Sex				
	Male	77		
	Female	12		
Cause of cirrhosis				
	Hepatitis B	50		
	Hepatitis C	11		
	Non-B non-C	28		
Systolic BP (mmHg)		103.65±8.18	90	130
Diastolic BP (mmHg)		69.21 ±4.52	60	80
Hb% (g/dl)		9.87±1.81	3.4	14.50
TC ($x10^9$/L)		7.45±5.50	1.50	34.00
Platelet count (x109/L)		111.94±83.65	15	450
CRP (mg/L)		23.67±25.11	0.32	98.05
S. Creatinine (mg/dl)		1.19±0.46	0.46	4.40
S. Sodium (mmol/L)		132.01±6.36	114	144
S. Potassium (mmol/L)		3.89±0.72	2.1	6.00
S. Bilirubin (mg/dl)		5.25±6.98	0.3	32.70
ALT (U/L)		59.53±41.79	13	233
Prothrombin time (Sec)		19.52±7.10	10.9	46.7
INR		1.63±0.57	0.91	4.00
Serum albumin (g/dl)		2.51±0.56	1.2	3.8
CP score		9.85±2.02	7	14
MELD score		17.64±6.87	7	38

Table-II shows distribution of the study patients by lab parameters, mean TC of WBC was found (6.76±5.42) x 109/L in survival group and (9.43±5.31) x 109/L in non-survival group, mean CRP was 13.65±14.40 in survival group and 52.40±27.32 in non-survival group, mean serum sodium was 133.13±5.45 mmol/L in survival group and 128.64±7.77 mmol/L in non-survival group, mean serum bilirubin was 5.23±7.79 mg/dL in survival group and 5.31±4.11 mg/dL in non-survival group, mean CTP score was 9.50±2.05 survival group and 10.81±1.66 in non-survival group, mean MELD score was 16.64±6.98 in survival group and 20.74±6.25 in non-survival group. 22.73% patients developed cirrhosis related complications in survival group and 82.61% in non-survival group.

Table II: Distribution of the study patients by lab parameters (n=89

Lab parameters	**Survival** Group (n=66) Mean ±SD	**Nonsurvival** Group (n=23) Mean±SD	**P value**
Hb% (g/dl)	9.76±1.98	10.15±1.18	0.271ns
TC (x109/L)	6.76±5.42	9.43±5.31	0.044s
Platelet count (x109/L)	98.49±64.29	151.68±117.67	0.054ns
S. CRP (mg/L)*	13.65±14.40	52.40±27.32	0.000s
S. Creatinine (mg/dl)	1.21±0.51	1.15±0.26	0.614ns
S. Sodium (mmol/L)	133.13±5.45	128.64±7.77	0.005s
S. Potassium (mmol/L)	3.84±0.67	4.05±0.84	0.250ns
S. Bilirubin (mg/dl)*	5.23±7.79	5.31±4.11	0.045s
ALT (U/L)	63.97±63.64	75.50±51.41	0.447ns
Prothrombin time(Sec)	18.66±6.28	21.91±8.72	0.059ns
INR	1.55±0.48	1.86±0.74	0.071ns
Serum albumin (g/dl)	2.57±0.55	2.31±0.57	0.057ns
CP score	9.50±2.05	10.81±1.66	0.011s
MELD score	16.64±6.98	20.74±6.25	0.016s

s= significant, ns=non-significant
P value reached from unpaired t-test
* P value reached from Mann Whitney-U test

Table-III shows the type of the cirrhosis related complications of the patients. It was observed that variceal bleeding developed in 6(9.1%) case in survival group and 3(13.04%) in non-survival group. Hepatic encephalopathy developed in 8(12.12%) cases in survival group and 14(60.87%) cases in non-survival group. HRS developed in 1(1.15%) case in survival group and (8.69%) in non-survival group. Total 15(22.73%) patients developed complications in survival group and 19(82.61%) in non-survival group which were statistically significant ($p<0.05$) between the groups.

Table III: Cirrhosis related complications in study patients within 30 days (n=89)

Name of the complication	Survival Group (n=66)		Non-Survival Group (n=23)		P value
	N	%	N	%	
Variceal bleeding	6	9.1	3	13.04	
HRS	1	1.51	2	8.69	0.000[s]
Hepatic encephalopathy	8	12.12	14	60.87	
Total complication	15	22.73	19	82.61	

s= significant, ns=non-significant

Table-IV shows high leukocyte count, low serum sodium, high serum bilirubin, high serum CRP level, high CTP and MELD score were independent risk factors for 30-day mortality in univariate logistic regression analysis.

Table IV : Univariate analysis for predictor of mortality within 30 days (n=89)

Lab parameters	Survive (n=66) Mean±SD	Not-survive (n=23) Mean±SD	P value
Age	49.02±13.90	47.52±11.30	0.644[ns]
Systolic BP (mmHg)	103.18±7.92	105.00±8.92	0.362[ns]
Diastolic BP (mmHg)	68.94±3.56	70.00±6.57	0.467[ns]
Hb% (g/dl)	9.76±1.98	10.15±1.18	0.271[ns]
TC (x10^9/L)	6.76±5.42	9.43±5.31	0.044[s]
Platelet count (x10^9/L)	98.49±64.29	151.68±117.67	0.164[ns]
S. CRP (mg/L)*	13.65±14.40	52.40±27.32	0.000[s]
S. Creatinine (mg/dl)	1.21±0.51	1.15±0.26	0.614 [ns]
S. Sodium (mmol/L)	133.13±5.45	128.64±7.77	0.005[s]
S. Potassium (mmol/L)	3.84±0.67	4.05±0.84	0.250[ns]
S. Bilirubin (mg/dl)*	5.23±7.79	5.31±4.11	0.045[s]
ALT (U/L)	63.97±63.64	75.50±51.41	0.447[ns]
Prothrombin time(Sec)	18.66±6.28	21.91±8.72	0.059[ns]
INR	1.55±0.48	1.86±0.74	0.071[ns]
Serum albumin (g/dl)	2.57±0.55	2.31±0.57	0.057 [ns]
CP score	9.50±2.05	10.81±1.66	0.011[s]
MELD score	16.64±6.98	20.74±6.25	0.016[s]

s= significant, ns=non-significant
P value reached from unpaired t-test
* P value reached from Mann Whitney-U test

Table-V shows in multivariate analysis only high serum CRP level (OR 1.075, 95% CI 1.027-1.122%, p=0.001) was significantly associated with mortality within 30 days.

Table V: Multivariable logistic regression analysis as predictor of mortality within 30 days (n=89).

Variables	Adjusted OR	95% CI		P Value
		Lower bound	Upper bound	
TC (x10^9/L)	0.999	0.880	1.191	0.557 [ns]
S. Sodium (mmol/L)	0.914	0.822	1.035	0.258[ns]
S. Bilirubin (mg/dl)	0.798	0.643	0.991	0.077 [ns]
CTP score	1.178	0.695	2.533	0.835 [ns]
MELD score	0.987	0.929	1.474	0.224[ns]
CRP	1.075	1.027	1.122	0.001s

OR=odds ratio, CI-Confidence interval, s=significant; ns=non-significant

Figure 1: Receiver-operator characteristic (ROC) curve of serum CRP level for prediction of mortality within 30 days:

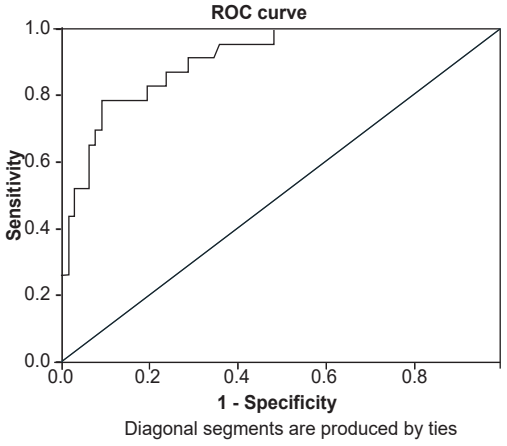


Fig.-1: Receiver-operator characteristic curves of Serum CRP level

Figure-1 shows based on the receiver-operator characteristic (ROC) curve, serum CRP level had an area under curve 0.907. Receiver operator characteristic (ROC) was constructed by using serum CRP level, which gave a cut off value 31, with 78% sensitivity and 90% specificity for prediction of mortality.

Table-VI shows mortality within 30 days is 4(6.06%) in serum CRP < 31 group but 17(73.91%) in serum CRP > 31 group and presence of complications is 14 (21.21%) in serum CRP <31 group but 16(69.56%) in serum CRP > 31 group.

Table- VI: Outcome of the study patients by CRP level within 30 days (n=89).

Parameters	Serum CRP <31 (n=66) N(%)	Serum CRP >31 (n=23) N(%)	P value
Mortality within 30 days	4(6.06%)	17(73.91%)	0.000s
Appearance of complications	14(21.21%)	16(69.56%)	0.000s

s= significant, ns=non-significant

P value reached from unpaired t-test and chi- square test

DISCUSSION

This prospective observational study was carried out with the aim to evaluate serum CRP level as a predictor of early mortality in patients with decompensated cirrhosis of liver. CRP is classically considered an important regulator of the innate immune system and a paramount mediator of the acute-phase response.[11] C-reactive protein is predominantly synthesized in the liver in response to proinflammatory cytokines and IL-6 appears to be the main regulator.[12] In cirrhotic patients, immune and inflammatory systems are activated and inflammatory markers, such as interleukin-6 and tumor necrosis factor-alfa, have been found to be elevated.[13] Inflammatory response activation may be caused by occult infections associated with bacterial translocation that complicates the increase of intestinal permeability in these patients.[14] Systemic inflammation has been shown to favor serious complications (variceal bleeding, encephalopathy and acute-on-chronic liver failure) and death in cirrhotic patients.[15,7]

In this study it was observed that majority of patients in surviving group 29(44%) and nonsurviving group, 13(56.50%) were within age 31-50 years. It was also observed that majority of patients both in survival and nonsurvival group were male which were 56(84%) and 21(91%) in survival and nonsurvival group respectively. Mean CRP was found 13.65±14.40 in survival group and 52.40±27.32 in non-survival group, mean CTP score was 9.50±2.05 survival group and 10.81±1.66 in non-survival group, mean MELD score was 16.64±6.98 in survival group and 20.74±6.25 in non-survival group. In this study it was observed that majority of study population both in survival and non-survival group had hepatitis B, which was 38(57.57%) and 12(52.17%) in survival and non-survival group respectively.

Univariate logistic regression analysis showed that high leukocyte count, low serum sodium, high serum bilirubin, high serum CRP level, high CTP and MELD score were independent risk factors for 30-day mortality.

In multivariate analysis, only high serum CRP level (OR 1.075, 95% CI 1.027-1.122%, p=0.001) was significantly associated with mortality within 30 days. Zhu et al. (2017) found that serum high CRP level at base line and MELD score were independent risk factor for 1-month mortality in HBV decompensated cirrhotic patients.[9] Martino et al. (2015) also found high serum CRP level at base line and at day 15 and MELD score predicted 3 month mortality independently in decompensated cirrhotic patients.[16] Cervoni et al. (2016) also found high serum CRP level at base line and at day 15 and MELD score predicted 6 month mortality in decompensated cirrhotic patients.[17]

In this study it was observed that based on the receiver-operator characteristic (ROC) curve, serum CRP level had an area under curve (AUC) at 0.907 and the best cut off value of CRP was 31 mg/L. Cervoni et al. (2016) found the best predictive value of CRP was 29 mg/L.[17] Martino et al. (2015) found the best cut off value of CRP was 32 mg/L.[16] Zhu et al. (2017) found that the median value of CRP was 29 mg/L[9] Cirrhosis related complications e.g. variceal bleeding, hepatic encephalopathy and HRS developed more frequently in higher CRP (>31) group. But previous studies, e.g. Zhu et al. (2017) and Martino et al. (2015) did not show any significant correlation between CRP and cirrhosis related complications.[9,16]

CONCLUSIONS

In this prospective study, we observed that CRP was able to predict short-term mortality in patients with decompensated cirrhosis of liver. It was also observed that, high CRP levels was associated with increased frequency of cirrhosis related complications. The prognostic value of CRP was independent of the usual prognostic criteria such as MELD and CTP scores. Hence, we assume that

measuring CRP is a simple and accurate way of diagnosing systemic inflammation and has a relevant impact on prognosis in cirrhotic patients.

Limitations

We did not investigate the relevance of serial measurements of CRP. Only one cross-sectional value of CRP was monitored. We were not able to determine whether CRP variation over time would perform better in predicting outcomes of decompensated cirrhotic patients. It was beyond of our scope to exclude all extra hepatic causes that could influence serum CRP level like subclinical infection.

REFERENCES

1. Feldman, M, Friedman, L & Brand, LJ (eds) 2015, 'Sleisenger and Fordtran's Gastrointestinal and Liver disease', Saunders, Philadelphia, pp. 1254.
2. D'Amico, G, Garcia-Tsao, G & Pagliaro, L 2006, 'Natural history and prognostic indicators of survival in cirrhosis. A systematic review of 118 studies', J Hepatol, vol. 44, PP. 217-231.
3. Shameem, M, Bhargava, R & Ahmad, Z 2011, 'Association between serum C - reactive protein levels and other important predictive markers of outcome in COPD', Acta Med Iran, vol. 49, pp. 18–20.
4. Garcia-Rio, F, Miravitlles, M & Soriano, JB 2008, 'systemic inflammation in chronic obstructive pulmonary disease, A population-based study', Respir Res, vol. 11, pp. 63.
5. Andreozzi, P, Viscogliosi, G & Colella, F 2012, 'Predictors of liver fibrosis in patients with non-alcoholic fatty liver disease', Recenti Prog Med, vol.103, pp. 570–574.
6. Atta, M, Cabral, M & Santos, G 2012, 'Inflammation biomarkers in chronic hepatitis C: association with liver histopathology, HCV genotype and cryoglobulinemia', Inflamm Res, vol.61, pp.1101 –1106.
7. Thabut, D, Massard, J, Gangloff, A, Carbonell, N, Francoz, C & Nguyen, KE 2007 'Model for end-stage liver disease score and systemic inflammatory response are major prognostic factors in patients with cirrhosis and acute functional renal failure', Hepatology, vol. 46, pp. 1872–1882.
8. Durand, F & Valla, D 2008, 'Assessment of prognosis of cirrhosis', Semin Liver Dis, vol. 28, pp. 110-122.
9. Zhu, SM, Waili, Y, Ting, X, Chen, YM, Lou, YF & Chen, B 2017, 'Serum C-reactive protein predicts early mortality in hospitalized patients with HBV-related decompensated cirrhosis', Medicine, vol. 96, pp. 1-4.
10. Liaw, YF, Tai, DI, Chu, CM & Chen, TJ 1988, 'The development of cirrhosis in patients with chronic type B hepatitis: a prospective study', Hepatology, vol. 8, pp. 493–496.
11. Ridker, PM 2009, 'C-reactive protein: eighty years from discovery to emergence asamajorriskmarker for cardiovascular disease', Clinical Chemistry, vol. 55, pp. 209–215.
12. Nanri, A, Moore, MA & Kono, S 2007 'Impact of C-reactive protein on disease risk and its relation to dietary factors', Asian Pacific Journal of Cancer Prevention, vol. 8, pp. 167–177.
13. Giron-Gonzalez, JA, Martinez-Sierra, C, Rodriguez-Ramos, C, Macias, MA, Rendon, P, Diaz, F, Fernández-Gutiérrez, C & Martín-Herrera, L 2004, 'Implication of inflammation-related cytokines in the natural history of liver cirrhosis', Liver International, vol. 24, pp. 437–445.
14. Cirera, TM, Navasa, M, Vila, J, Grande, L & Taura, P 2001, 'Bacterial translocation of enteric organisms in patients with cirrhosis', J Hepatol, vol. 34, pp. 32–37.
15. Shawcross, DL, Davies, NA, Williams & R, Jalan, R 2004, 'Systemic inflammatory response exacerbates the neuropsychological effects of induced hyper-ammonemia in cirrhosis', J Hepatol, vol. 4, pp. 247–254.
16. Martino, DI, V, Coutris, C & Cervoni, JP 2015, 'Prognostic value of C-reactive protein levels in patients with cirrhosis', Liver Transpl, vol. 21, pp. 753–60.
17. Cervoni, JP, Amoros, A, Banares, R, Luis Montero J, Sariano G, Weil D, Moreau R, Pavesi M, Thevenot T & Di Martino, V 2016, 'Prognostic value of C-reactive protein levels in patients cirrhosis', Eur J GastroenterolHepatol, vol. 28, pp. 1028-1034.

Original Article

Morbidities among Eclamptic Women of Lower Socioeconomic Community in a Selected Area of Bangladesh

Pervin R[1], Halim KS[2], Ara N[3], Islam SM[4], Nargis F[5]

Abstract

Eclampsia is a serious obstetric emergency with new onset of grand mal seizure during pregnancy or postpartum women having signs symptoms of pre-eclampsia. The sequel of severe pre-eclampsia and eclampsia includes organ failure, loss of consciousness and finally loss of lives of both mother and fetus. This study aimed to evaluate morbidity of eclamptic women at lower socioeconomic community in a selected area of Bangladesh. This descriptive cross sectional study was conducted at Sheikh Hasina Medical College Hospital (SHMC.T) of Tangail district during the period of January to December 2019. During this period 7918 admitted patients from different sub-districts (Upazilas) of this district in obstetrics ward of SHMC.T were observed and 205 diagnosed eclamptic patients were selected as respondents for this study to detect morbidities. The prevalence rate of eclampsia among the obstetrics patients was 2.6%, where 81% of them were found during antepartum/ intrapartum and rest of them during postpartum period. The mean age of the eclamptic cases was 23.78±4.94 years and more than half of them were in age group 21-30 years. Most of the cases (84%) were from primary level or able to sign or illiterate and rest was secondary level of education. Mean age of marriage and first pregnancy were 17.81±SD2.19 and 19.39±SD2.5 years respectively, where majority of patients were primigravida. Among the multi gravida about one fourth had 2-4 children, 16.09% had 5-6 children, where 1.46% had ≥7 children and more than three-fourth of cases had 34-37 weeks of gestational period. Among cases 95.1% had hypertension, 94.6% edema, 83.9% convulsion, 39.5% headache with blurring of vision, 22.4% severe abdominal pain, 79.0% proteinuria and 9.76% unconsciousness. Incidence of maternal morbidity during study period was 14.36%, among them 9.4% pulmonary edema, 1.5% renal failure, 0.98% HELLP (Hemolysis, Elevated liver enzyme level and Low Platelet level) syndrome, 0.98% coma and 1.5% placental abruption. Caesarean delivery was 79.2% and 11.70% was detected as postpartum haemorrhage. Among fetal morbidity 19.5% intrauterine growth restriction, 48.8% low birth weight, 39.6% birth asphyxia, and 58.5% preterm baby. During follow up only persistent hypertension was found as morbidity of eclampsia, 19.5%, 9.8% and 7.32% at 2nd week, at 6th week and at 6th months respectively. Regarding health care services 93.7% had available facility and 41.5%, 47.8% and 10.7% lived in >10 kilometers (kms), 5-10 kms and less than 5 km distance respectively. Regarding MCH services; only 5.9% patient received antenatal care (ANC) ≥4 times; more than half of them incompletely received ANC <4 times and 42.0% never visited for ANC. This study reveals various matters of maternal and fetal morbidities commencing from eclamptic condition in lower socioeconomic community. Here important factors for morbidities in eclamptic women like lack of ANC/ PNC, availabilities of MCHC services and others. Pulmonary edema, renal failure, HELLP syndrome, coma and placental abruption are important maternal morbidities. Prematurity, low birth weight, intrauterine growth restriction and birth asphyxia are foremost fetal morbidities. Availabilities of MCH services, complete visit for ANC/ PNC and early diagnosis and management of eclamptic women positively reduce morbidity and will prevent eclampsia.

Keywords: *Eclampsia, morbidities, lower socioeconomic community*

1. *Dr. Rehana Pervin, FCPS (Gynae), Assistant Professor, Department of Gynae & Obstretics Sheikh Hasina Medical College (SHMC.T), Tangail. E-mail: dr.rehanapervin73@gmail.com
2. Dr. Kazi Shafiqul Halim, Professor, Department of Epidemiology, National Institute of Preventive and Social Medicine (NIPSOM), Mohakhali, Dahaka.
3. Dr. Noor Riffat Ara, Deputy Program Manager, (DPM, MNC & AH), Director General of Health Services (DGHS), Mohakhali, Dhaka.
4. Dr. Syed Monirul Islam, Asstant Professor, Department of Cardiac Surgery, Sir Salimullah Medical College, Dhaka.
5. Dr. Fatema Nargis, Medical Officer, OSD, DGHS; Attached: BG Press Medical; Centre, Tejgaon, Dhaka

* For correspondence

INTRODUCTION

Eclampsia is a serious disease, especially in developing countries it is a major health issue and the second leading cause of maternal mortality in Bangladesh, according to report of BMMS 2010[1]; it contributes 20% of maternal mortality in Bangladesh.

In preeclampsia hypertension and proteinuria are present and when convulsions occur in addition to these sign the condition is referred to as eclampsia[2]. The clinical mani-

festations of maternal preeclampsia are hypertension and proteinuria with or without co-existing systemic abnormalities involving the kidney, liver or blood. There is also a fetal manifestation of preeclampsia involving fetal growth restriction, reduced amniotic fluid and abnormal fetal oxygenation. HELLP syndrome is severe form of preeclampsia which involve hemolytic anemia, elevated liver enzyme and low platelet count[2]. Most case of eclampsia occurs in third trimester of pregnancy, with about 80% of eclamptic seizures occurring intrapartum or within the first 48 hours following delivery[3]. Multiple risk factors are known for development of pre eclampsia, including primiparity, maternal age over 40 years, chronic hypertension or diabetes, multiple gestation and prior history of pre eclampsia[4]. Prognosis of eclampsia is uncertain which depends on many factors, these are long interval between onset of fit and start of treatment, number of fit, coma, temperature over102^{0}F with pulse rate>120minutes, Blood pressure >200mmHg systolic, oliguria (<400ml/24 hours) with proteinuria>5gm/24 hours, non-respond to treatment and jaundice. The perinatal mortality is very high to the extent is about 30-50%, causes are mainly prematurity-spontaneous or induce, intrauterine asphyxia, effects of drugs and trauma during operative delivery.[3]

This descriptive study determines pattern of morbidities of eclampsia occurred in lower socioeconomic community in a selected area of Bangladesh.

METHODOLOGY

This descriptive cross sectional study was conducted at Tangail district of Bangladesh and SHMC.T was selected as a focal point for data collection. Patients were referred from different sub-districts (Sub-D) of this district and uniform representation of sample collection was maintained for each Sub-D. This study was carried out during the period of January to December 2019. All the patients of pregnant and post-partum women admitted in obstetrics ward of SHMC.T were included in this study. During study period total 7918 patients were admitted to obstetrics ward, among them 205 were eclamptic patients and selected as respondents in this study to detect morbidities. Ethical approval was taken from Bangladesh Medical Research Council (BMRC) and both verbal and written consent of patient were taken prior to data collection. Data was collected by random sampling through semi-structured questionnaire and check list. Face to face interview of patient/ patient's attendance, patient's examination, record review and bed side urine albumin test were done. Morbidities were diagnosed by examining clinical signs/ symptoms and by investigations reports (bilirubin, SGPT, SGOT, LDH, platelets count). Patients were followed from admission to discharge then at 2nd weeks, 6th weeks and 6th months follow-up for long term morbidities. Data were analyzed by Statistical Package for the Social Science (SPSS).

RESULTS

The study result has been presented in tabular and graphical form as follows-.

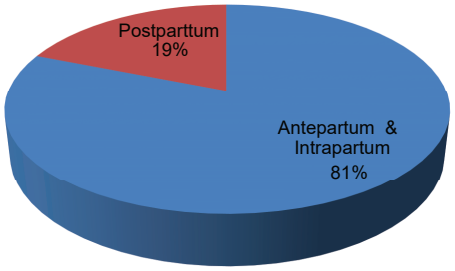


Fig.-1: *Distribution of respondents according to types of eclamptic women.*

Figure: 1 Shows that among 7918 admitted patients were in obstetrics ward of SHMC.T 205 patients were eclamptic. Appraised incidence of eclamptic women in this district was 26/ 1000 women of their natal period. Among them 166(81%) was antepartum intrapartum and 39(19%) postpartum period.

Table I shows participant's age, ranged from 11 years to 40 years with a mean of 23.78 (±4.94) years. The highest, lowest and median age was 45, 18 and 34 years respectively. About 110,(53.7%) of the respondents were in the age group of 21-30 years which is the highest among other groups. In contrast, 80 (39.0%) of the respondents in the 11-20 age group, and slightly more than that, 15 (7.3%) of the respondents represented the group of 31-40 years old.

Table I: Distribution of the respondents according to age of eclamptic women (n=205)

Age group (years)	Frequency (f)	Percentage (%)	Mean±SD
11-20	80	39.0	23.78 ± 4.94
21-30	110	53.7	
31-40	15	7.3	
Total	205	100.0	

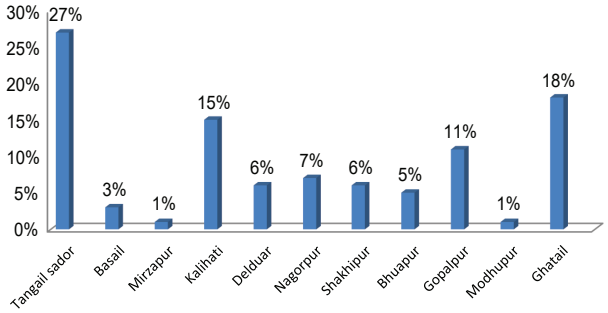


Fig.-2: *Distribution of respondents according to area (n=205).*

Figure: 2 shows the distribution of respondents in different Sub-D, 55(27%) were from Tangailsadar, 7(3%) fromBasail, 01(1%) Mirzapur, 30(15%) Kalihat, 12(6%) Delduar, 15(7%) Nagarpur, 13(6%) Shakhipur, 12(5%) Bhuapur, 21(11%) Gopalpur, 2(1%) Modhupur, and 37(18%) Ghatail sub-districts.

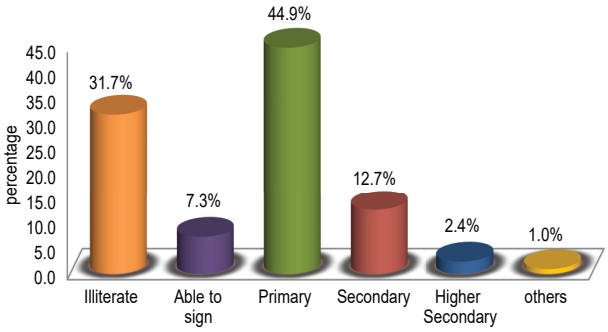


Fig.-3: *Distribution of respondents according to educational status (n=205).*

Figure: 3 shows the distribution of educational status; 92 (44.9%) had completed primary level, 65 (31.7%) were illiterate, 26 (12.7%) had completed secondary level, 15 (7.3%) was able to sign their name, 5 (2.4%) had completed higher secondary and rest of the respondents 2 (1.0%) were in others level of education.

Table II shows the distribution of occupation and family income, 201 (98.0%) were housewives, 2 (1%) others occupation, where 1 (0.5%) service and business. Monthly family income ranged from 00.00 Tk-30000TK with a mean of 9129.27 (±4493.91) Tk, median incomes was 8000Tk. The monthly income 00.0-10000Tk was 161 (78.5%), then 10001-20000Tk was 42 (20.3%), and the rest 2 (4%) of them 20001Tk and above.

Table II: istribution of respondents according to occupation and family income. (n=205)

Characteristics Occupation of respondents	Frequency (f)	Percentages (%)
Housewife	201	98.0
Service	1	0.5
Business	1	0.5
Others	2	1.0
Total	205	100.0
Monthly Family Income		
Upto 10000	161	78.5
10001-20000	42	20.5
20001 to above	2	1.0
Total	205	100.0

Table III shows the distribution of first marriage and age at first pregnancy; the mean age at first marriage was 17.81 years± SD 2.19 and age range at first marriage 11-29 years. The mean age at first pregnancy was 19.39 years± SD 2.58 and age range first pregnancy was 14-30 years.

Table- III : Distribution of respondents according to age at marriage and age at First Pregnancy. (n=205)

	Age at marriage	Age at first pregnancy
Mean	17.81	19.39
Std. Error of Mean	.153	.180
Std. Deviation	2.191	2.577
Range	18	16
Minimum	11	14
Maximum	29	30

Table IV shows the distribution of parity, 117 (57.07%) were primipara, 88 (42.93%) multipara; according to number of children, 52 (25.37%) had 2-4 children, 33 (16.09%) had 5-6 children and 3 (1.46%) had more than 7 children. Time duration between present and previous pregnancy, 59 (28.78%) had 1-5 years' time space between past and present pregnancies, 12(5.85%) had more than 5 years, 17 (8.3%) had less than 1 year. Primigravida was 117 (57.07%).

Table IV : Distribution of respondents according to parity: (n=205)

Characteristics	Frequency (f)	Percentages (%)
Parity		
Primipara	117	57.07
Multipara	88	42.93
Total	205	100.0
Number of Children		
Primigravida	117	57.07
2-4 children	52	25.37
5-6 children	33	16.09
=>7 children	03	1.46
Total	205	100.0
Duration of present and previous pregnancy		
<1 year	17	8.3
1-5 year	59	28.78
> 5 year	12	5.85
Not applicable	117	57.07
Total	205	100.0

Table V shows the distribution of history of (H/O) eclampsia, 193 (94.14%) had no H/O of and 12 (5.86%) had H/O of eclampsia.

Table V: Distribution of respondents according to H/O eclampsia (n=205)

Characteristics	Frequency (f)	Percentages (%)
History of eclampsia		
No	193	94.14
Yes	12	5.86
Total	205	100.0

Table VI shows the distribution of gestational period, 159 (77.6%) were in moderate to late preterm (34-37 weeks), 19 (9.3%) were in very preterm period (28-33 weeks) and 27 (13.2%) were in full term (≥38 weeks).

Table VI : Distribution of respondents gestational period during delivery (n=205)

Characteristics	Frequency (f)	Percentages (%)
Gestational Period		
Very preterm (28-33) weeks	19	9.3
Moderate to late Preterm (34-37) weeks	159	77.6
Full term(≥38 weeks)	27	13.2
Total	205	100.0

Table VII shows the distribution of denger signs, 195 (95.1) had hypertension, 194 (94.6%) had edema, 172 (33%) had convulsion, 14 (6.8%) had P/V bleeding, 81(39.5%) had headache with blurring of vision, 46 (22.4%) had severe abdominal pain, 162 (79.0%) had proteinuria, 33 (16.1%) difficulty of breathing and 20 (9.76) unconsciousness.

Table VII: Distribution of Respondents according to Danger Sign (n=205)

Danger sign during pregnancy	Present f (%)	Absent f (%)
Hypertension	195(95.1)	10(4.9)
Edema	194 (94.6)	11 (5.4)
Convulsion	172(83.9)	33(16.1)
Headache with blurring vision	81(39.5)	124 (60.5)
Severe abdominal pain	46 (22.4)	159 (77.6)
Per vaginal bleeding	14(6.8%)	191(93.2%)
Proteinuria	162(79.0)	43(21.0)
Difficulty in breathing	33(16.1)	172(83.9)
Unconsciousness	20(9.76)	185(90.23)

*multiple responses

Table VIII shows the distribution of maternal of eclamptic women, 19 (9.4%) had pulmonary edema, 3 (1.5%) had Renal failure, 02 (0.98%) had HELLP syndrome, 02 (0.98%) had Coma, 3 (1.5%) had placental abruption, 160 (79.2%) Cesarean delivery and 24 (11.70%) PPH.

Table VIII: Information related to maternal morbidities due to eclampsia (n=205)

Maternal morbidities	Frequency (%)	Percentage (%)
Pulmonary edema	19	9.4
Renal Failure	3	1.5
HELLP Syndrome	2	0.98
Coma	2	0.98
Placental abruption	3	1.5
Cesarean delivery	160	79.2
Postpartum hemorrhage (PPH)	24	11.70

*multiple responses

Table IX shows the distribution of fetal morbidity, 40 (19.5%) had intrauterine growth restriction, 100 (48.8%) had LBW baby, 80 (39.6%) had problem with birth asphyxia and 120 (58.5%) had preterm baby.

Table IX: Information related to fetal morbidities due to eclampsia(n=205)

Fetal Morbidities	Frequency (f)	Percentage (%)
Intrauterine growth restriction	40	19.5
Low birth weight (LBW)	100	48.8
Birth asphyxia	80	39.02
Preterm baby	120	58.5

*multiple respones

Table X shows the morbidities during follow up, 40 (19.51%), 20 ((9.75%) and 15(7.32%) had persistent hypertension at 2nd week, 6th week and at 6th month of follow up respectively. Others morbidities, anemia, secondary PPH, wound infection, 6 (2.92%) had at 2nd weeks, and 8(4.9%) had at 6th weeks.

Table X: Distribution of respondents according to morbidities during follow up (n=205)

Morbidities	2nd weeks	6th weeks	6th months
Persistent hypertension	40(19.51%)	20(9.76%)	15(7.32%)
Others Morbidities (anemia, PPH wound infection)	6(2.92%)	8(3.90%)	00
Nomorbidities found	159(77.57%)	177(86.34%)	190(92.68%)

Table XI shows the information related to health care service from respondents, 192 (93.7%) had availability of health care facility, 13 (6.3%) had no availability. Distance of health care facility from the residence of respondents 98 (47.8%) came from 5-10 Kilometers (kms) distance, 85 (41.5%) from more than 10 kms and 22 (10.7%) from less than 5 kms distance to health care facility. Regarding ANC visits, 107 (52.2%) partially (less than 4 times) visited for ANC during gestational period, 86 (42.0%) never visited for any type of ANC, 12 (5.9%) completed the full ANC visit (≥ 4 times).

Table II: Information related to health care service (n=205)

Characteristics	Frequency (f)	Percentages (%)
Availability of health care facility		
Yes	192	93.7
No	13	6.3
Total	205	100.0
Distance of health care facility		
<5km	22	10.7
5-10 km	98	47.8
≥10 km	85	41.5
Total	205	100.0
H/O ante-natal checkup		
Complete(≥ 4 times)	12	5.9
Partial (< 4 times)	107	52.2
Never	86	42.0
Total	205	100.0

LIMITATIONS OF THE STUDY

The study population was included from one selected district of Bangladesh and data were collected from one health facility. Some patients of the selected district attended to other health facilities and some patients from border areas receive MCHC services form adjoining districts. Findings of this study may infrequently match with the actual data of the whole district and even whole country. Most of patient didn't attend any postnatal follow up; hence in some cases we collected information electronically. The study was conducted for short period with moderate sample size.

DISCUSSION

Eclampsia is still one of the important and common obstetrics Emergency in developing country like Bangladesh which has significant role of maternal and Fetal morbidities and mortalities. In this study incidence of eclampsia was 2.6% which is comparable to other developing countries with the incidence of 1 in 100 to 1 in 1700 pregnencies.[5,6,7]. Simillar study done by Raji et al[8] found incidence of eclampsia 0.83%. In our study 81% respondents were antepartum and intrapartum, 19% were postpartum eclampsia; similar to study Tamina et al[9], reported that antepartum and intrapartum eclampsia 92%, postpartum 10%. This study observed that majority (53.7%) respondents belonged to age 21-30 years. The mean age of respondents was 23.78(±4.94) years. NADEEM SHAZAD et al[10] observed mean age 25.17±4.9

years and maximum age group 26-30 years. Ahmed Mahran et al[11] showed that maternal age was major risk factor with 42.2% patients aged <20 years. In this study all respondents came from rural area of Tangail district and 27% from Tangail sadar, 3% Basail, 1% Mirzapur, 15% Kalihati, 6% Delduar, 7% Nagarpur, 6% shakhipur, 5% Bhuapur, 11% Gopalpur, 1% Modhupur and 18% Ghatail. Nearly half of respondents (44.9%) had completed primary level of education and 31.7% were illiterate 12.7% had completed secondary level and 7.3% able to sign. Most of respondents were housewives and belong to lower economic condition (had monthly income up to 0-10,000 taka). Ahmed mahar et al[11] showed that low socioeconomic standard obviously affected the incidence of the eclampsia. Two-third patient had no education at all and 24.8% received primary education. Meleseet al[12] showed that higher the women's educational status, lower the perinatal unfavorable outcomes of severe eclampsia. The mean age at marriage was 17.81 years ±SD 2.19 and the mean age at first pregnancy was 19.39±SD2.57. Maximum age during first pregnancy was 30 years where minimum age was 14 years. Ahmed Meharan et al.[11] showed short duration of marriage was found increase risk of eclampsia. In this study 57.07% were primipara, 42.93% multipara. Among multiparous 25.3% had 2-4 children, 16.09% had 5-6 children and 1.46% had ≥7 children. Space between present and previous pregnancy 28.78%) had 1-5 years, 5.85% had ≥5years and 17(8.3%) had <01 year gap. Pipkin FB et al[13], Duckit k et al[14] observed nulliparity is a well-known risk factor for eclampsia. Raji et al[8]found 69.2% had primigravida, 27.4% had parity 2-4 while 3.4% had parity between p_5 and p_6. NADEEM SHAHZAD et al[10] found 63% was primigravida and 28% had parity 2-4, whereas 6% was p_5 –p_6 and 3% had ≥7. In this study 5.86% had previous H/O pre eclampsia. Ahmed Mahranet al[11] identified previous H/O pre eclampsia in 59.6% cases. This study observed more than three-fourth had 34-37 weeks of gestation, 13.2% had ≥38 weeks and 9.3%) had 28-33 weeks of gestation. Study by NADEEM SHAHZAD et al[10] showed, 39% of patient presented at gestational age of 31-36 weeks while 39% had gestational age of 37 weeks or above. It is observed that risk of eclampsia in third trimester is more. In this study 95.1% hypertention, 94.6% edema, 83.9% convulsion, 6.8 per vaginal bleeding, 39.5% headache with blurring of vision, 22.4% abdominal pain, 79.0% proteinuria, difficulty in breathing in 16.1% and 9.76% had unconsciousness; similar to study Mattar F et al[15]. Raji et al[8] and Ahmed mahran et al[11]. Among the maternal morbidity (14.63%) this study finds of pulmonary edema 9.4%, Renal failure 1.5%, HELLP syndrome 0.98%, coma 0.98% and abruption placentae 1.5%, chMadhuri et al.[16] and Mosammot Rashida Begum et al[17] found incidence of eclampsia with different complication was 21% which included renal failure 0.7%, hepatic failure 0.5%, heart failure 0.5%, coma 2.9%, pulmonary edema 10.3% and DIC 1.0% which was similar to this study. CS and PPH are not complication of eclampsia but risk for this complication is high. In this study 79.2% had CS and 11.70% developed PPH. Tulfinel et al[18] reported 72% CS which is similar to this study. chMadhuri et al[16] reported 6.53% PPH. In this study fetal morbidities was high and among them, 58.5% had preterm baby, 48.8% LBW, 19.5% intrauterine growth restriction and 39.02% had problem with birth asphyxia. chMadhuri et al[16] reported 30.49% prematurity, 41.47% LBW, 10% IUGR , 14.17% intrauterine death. Eclampsia is reported with high perinatal mortality and morbidity. It is established that early delivery reduce maternal morbidity but induced fetal prematurity. During follow up period as sequel of eclampsia only persistent hypertension was found but other morbidities like wound infection, anemia secondary PPH found in some cases; 19.5% at 2nd weeks, 9.75% at 6th weeks and 7.32% had persistent hypertension at 6th months. Others morbidities were observed in 2.92% at 2nd weeks, and 4.9% at 6th weeks. Others morbidities are not complication of eclampsia but these worsen patient condition. We observed information related to health service, 93.7% had availability of health care facilities and 6.3% had no availability, where 41.5% had ≥10Km distance, 47.8% had 5-10 Km and 10.7%) had <5Km. Study finds that 5.9% completed ≥4 ANC, 52.2%) taken partial (<4) ANC and 42% never received ANC. Ahmed Mahran et al[11] showed, 30% did not attend ANC throughout pregnancy, 64.4% had <4 ANC. Antenatal care is important point to identify preeclamptic state.

CONCLUSION

This study reveals that eclampsia is still important cause of maternal and fetal morbidity in lower socioeconomic community. Nulliparity, primigravida, less interval in between pregnancy, pregnancy at early age, lack of education, lack of ANC and lack of health care service availabilities are important factors for morbidities in Eclamptic women. Pulmonary edema, renal failure, HELLP syndrome, coma and placental abruption are important maternal morbidities slowing to achieve MDG goal. Prematurity, low birth weight, intrauterine growth restriction and birth asphyxia are important fetal morbidities adding bulge in child health care. Proper

antenatal care, available health care facility, early diagnosis of pre eclamptic condition, proper treatment of pre eclampsia and appropriate referreal can prevent eclmpsia and its morbidity.

RECMMONDATION

The huge prevalence rate of eclampsia during antepartum/ intrapartum period might be the major concern of health care providers. Assurance of MCH services for every pregnant women throughout their natal period by continuous upgrading their database and by settling ANC & PNC (postnatal care) at Community Clinic. Prompt referral of eclamptic women to higher level health care facilities would reduce the morbidities and mortality during natal period. Thus complete visit to MCH services during natal period, early diagnosis and management of pre-eclamptic condition positively will reduce morbidity and will prevent eclampsia.

REFERENCES:

1. NIPORT (2012) Bangladesh maternal mortality and health care survey 2010.
2. Kejersti M . Aagaardtilery, md, phd and Micheal A. Belfort, md, phd, eclampsia :Morbidity Mortality , and management, Clinical obstetrics And Gynaecology, volume 48,Number 1,12-13.
3. DC Dutta Hiralal Konar, The Text book of obstetrics, 7th edition. Hypertensive Disorder in Pregnancy: 219-240.
4. Sijaus A, Mckeen DM, George RB. Hypertensive disorders of pregnancy. Can J Anaesth.2016; 63: 1075-97(pubmed)[Google scholar
5. World Health Organisation International Collaborative Study of Hypertensive Disorders of pregnancy. Geographic variation in the incidience of hypertension in Pregnency. Am J Obstet Gynaecol 1958: 158:80-3.
6. Crowther CA Eclampsia at Harare Maternity Hospital- An epidemiological study. S AfrMed. J. 1985; 68:927-9.
7. Bergstom S, Povey G, Songane F, chingC. Seasonal incidence of eclampsia and its relationship to meterological data in Mozambique; J Perinat Med. 1992;20:153-8.
8. Raji C. , poovathi M., Nithya D. Prospective study of fetomaternal outcome in eclampsia in a tertiary care hospital .Int. J Reprod Contracept Obstet Gynaecol. 2016 Dec ;5(12):4329-4334.www.ijrcog org.
9. Tahinma HZ, Shahid AR , Hosna AU, Alam A. Study on outcome of eclampsia patients in District Hospital in Bangladesh. J Dhaka Med coll. 2014; 23(2): 223-226.
10. Nadeem Shazad, Uzma Yaqoo, Asif Hanif. Feto-Maternal Outcome in Patients with Eclampsia at A Tertiary Care Hospital. PJMHS Vol.7 No.1 Jan-Mar 2013:76-79.
11. Ahmad Mahran, Hashem Fares, Reham Elkhateeb, Mahmoud Ibrahim, Haitham Bahaa, Ahmad Sanad, et al. Risk factors and outcome of patients with eclamsia at a tertiary hospital in Egypt BMC pregnancy Childbirth. 2017;17:435. DOI 10.1186/s 12884-017-1619-7.
12. Misganaw Fikirie Melese, Marta Berta Bari and Getie lake Aynale. Perinatal outcomes of severe pre-eclampsia/ eclampsia and associated factors among mothers admitted in Amhara Region referral hospitals, North West Ethiopia,2018.BMC Res Notes (2019)12:147 https/doi.org/10.1186/s 13104-019 -4161-z.
13. Pipkin FB. Risk factors for pre-eclampsia. NEngl J Med. 2001,344.
14. Duchit K, Hamington D. Risk factor for pre eclampsia at antenatal booking system review of controlled studies.Bmj.2005;339(749)565.pubMed PMID:15743856.pubmed central PMCID.554027.
15. Mattar F, Sibai BM. Eclampsia .V111.Risk factors for maternal morbidity. Am. J Obstet Gynaecol.2000 Feb.182 (2):307-12.
16. Ch. Madhuri , Y. Varalakshmi. Retrospective study on fetomaternal outcome in gestational hypertension, pre eclampsia and eclampsia in a tertiary care centre. Indian Journal of Basic and Applied Medical Research, September 2019;vol.8 Issue-4,p. 246-255.
17. Mosammat Rashida Begum, MBBS,FCPS, MS (MED-EDU), Anowara Begum MBBS,FCPS, Ehsan Quadir, MBBS,DCH, Sayeba Akther, MBBS, FCPS and Latifa Shamsuddin, MBBS, FCPS, Eclampsia : Still a problem in Bangladesh, National Institute of Health Journal,6(4);2004 PMC1480554.
18. Tufnell DJ. Jankowiez D, Lindow SW, Lyons G, Mason GC, Russell IF, et al. outcome of severe pre eclampsia/eclampsia. Yorkshire 1999/2003. Br J Obstet Gynecol.2005;112:875-80.

Original Article

A Comparative Study of Rotaviral Antigen Detection by ELISA and ICT in Children below Five Years with Acute Diarrhoea in A Tertiary Care Hospital

*Habib FB[1], Rahman MM[2], Haque MM[3], Sinha SP[4], Dey S[5], Tanni NN[6], Nabi MA[7], Jhuma AA[8], Hasan MN[9]

Abstract

Rotavirus is responsible for acute severe watery diarrhoea in young children. Early and rapid detection of rotavirus infection can help to reduce inappropriate administration of antibiotics and has future positive impact on prevention of drug resistance. This cross-sectional study was designed to determine the role of rotaviral antigen detection by ICT from stool sample of acute diarrhoeal children below five years admitted in Sylhet MAG Osmani Medical College Hospital, Sylhet and was carried out in the department of microbiology in collaboration with the department of paediatrics during the period from 1st January to 31st December, 2018. Total 184 children of under five years of age with acute watery diarrhoea were enrolled in this study. Rotaviral antigen was detected by ELISA (Enzyme Linked Immunosorbent Assay) and ICT (Immunochromatographic test) from stool samples. Out of 184 stool samples, rotaviral antigen was found positive in 84 and 86 cases by ICT and ELISA methods, respectively. ICT showed sensitivity of 90.70% and specificity of 93.88% when compared with ELISA. The rotavirus infection was found highest in male children (61.90%) and in age group of 7 to 12 months (51.89%). Considering the importance of rotaviral diarrhoea, rapid detection of rotavirus infection by ICT is essentially needed and should be practiced routinely as it is relatively reliable, easy to perform and cost-effective. It is particularly important in Bangladesh, where diarrhoea is still contributing a significant proportion of mortality and morbidity in under five children.

Keywords: *Rota virus, diarrhoea, ICT, ELISA, sensitivity, specificity*

1. *Dr. Farjana-Binte-Habib, Lecturer, Department of Microbiology, Dhaka Medical College (DMC), Dhaka, E-mail: farjanahabib33@gmail.com, Mobile- 01767846944
2. Dr. Mohammed Mirazur Rahman, (MD Phase-B), Pulmonology, Bangabandhu Sheikh Mujib Medical University Hospital (BSMMU), Dhaka.
3. Professor Dr. Md. Moynul Haque, Professor & Head of the Department of Microbiology, Sylhet MAG Osmani Medical College (SOMC), Sylhet.
4. Dr. Shib Prasad Sinha, Lecturer, Department of Virology, SOMC, Sylhet
5. Dr. Suborna Dey, Lecturer, Department of Microbiology, Sylhet Women's Medical College (SWMC), Sylhet
6. Dr. Nusrat Noor Tanni, Lecturer, Department of Microbiology, DMC, Dhaka
7. Dr. Muhammad Arif-un Nabi , Assistant Professor, Department of Microbiology, Sheikh Hasina Medical College, Habiganj.
8. Dr. Azima Akter Jhuma, Assistant Professor, Department of Microbiology, SOMC, Sylhet
9. Dr. Md. Nazmul Hasan, Assistant Professor, Department of Internal Medicine, BSMMU, Dhaka.

*For Correcpondence

INTRODUCTION

Acute diarrhoeal disease is a major public health problem leading to high morbidity and significant mortality in both developed and developing countries[1]. In Bangladesh, diarrhoea is the second commonest cause of death in children below five years after pneumonia. UNICEF estimated that diarrhoea is responsible for 6% of total under five deaths in the year 2013 in Bangladesh[2]. Among hospitalized children, most of the deaths are due to diarrhoeal complications[3]. There are several bacterial, parasitic and viral agents are responsible for acute gastroenteritis. Among viral agents, Rotavirus is the major cause of acute severe dehydrating diarrhoea in young children.[1,4]

Rotavirus is transmitted from one person to another through the faeco-oral route having a very low infective dose.

Rotaviruses infect and multiply in the cytoplasm of enterocytes in the villi of small intestine. NSP4, one of virus encoded protein, is an enterotoxin which induces secretion by triggering a signaling transduction pathway. Damaged villus cells are replaced by non-absorbing immature crypt cells which leads to impaired glucose and sodium absorption. Consequently, there is loss of water and electrolyte which leads to dehydration, acidosis, shock and even death. Restoration of normal gut function requires 3 to 8 weeks.[5,6]

Rotaviral infection is responsible for significant morbidity and mortality. Globally, this pathogen alone causes approximately 215,000 under five deaths. In Bangladesh, rotavirus causes 1000-2700 deaths each year in children below 5 years of age.[7]

There are different methods used in rotavirus diagnosis like tissue culture, electron microscopy, enzyme linked immunosorbent assay (ELISA), latex agglutination techniques, immunochromatographic test (ICT) and reverse transcriptase polymerase chain reaction (RT-PCR).[8]

Direct detection of viral particles by electron microscopy is conclusive evidence of rotaviral infections but it is not available everywhere. Rotavirus can be isolated from stool sample by culture but it is a cumbersome process and needs equipped laboratories and skilled personnel[9]. RT-PCR although a very sensitive diagnostic tool, is available in only few reference and research centers and is particularly used for identification of outbreaks.[8]

Detection of antigen in stool sample is easy, rapid, relatively inexpensive and very sensitive method. It is a non-invasive procedure and there is no need of specialized laboratory facilities. So, the recent advancement of antigen detection methods based on immunological techniques like ELISA and ICT have gained the attention of researchers and clinicians.[9]

A study conducted by Agarwal and coresearchers in Delhi, India used both ELISA and ICT to detect stool antigen of rotavirus and showed that ICT had a sensitivity of 96.97% and specificity of 100% when compared to ELISA as a standard method.[10]

Rapid and accurate methods for the detection of rotavirus is important both for diagnosis and management of acute gastroenteritis. Rapid diagnosis also has a role in preventing spread of the disease. Due to high morbidity and significant mortality rate of rotavirus infection, there is a need for rapid and reliable methods like ELISA and ICT for Rotavirus detection in routine diagnostic laboratories.

ELISA is a sensitive method for detection of Rotaviral antigen and is ideal for screening of large number of fecal specimens in single sitting. Though it is a reliable method, it requires proper laboratory facilities and is time consuming. On the other hand, ICT is rapid, easy, single step procedure and can be done for a single specimen even at bed side. it can save time, labour and cost. It will help the clinician to take prompt decision regarding management.

So, this study was designed to compare between ICT and ELISA and also to evaluate the efficacy of ICT as a sensitive, rapid and easy diagnostic tool in diagnosis of Rotaviral diarrhoea among children less than 5 years.

MATERIALS AND METHOD

This cross-sectional study was carried out in the department of Microbiology in collaboration with the department of Paediatrics, Sylhet MAG Osmani Medical College Hospital from 1st January 2018 to 31st December 2018. All admitted children under 5 years of age with acute watery diarrhoea were included in this study. Children suffering from chronic diarrhea (diarrhoea for ≥ 14 days) and bloody diarrhea were excluded. After explaining the purpose of the study, informed written consent was taken from legal guardians of the patients. Prior to the beginning of this study, approval of the research protocol was obtained from the Ethical Review Committee of Sylhet MAG Osmani Medical College, Sylhet.

Specimen collection

Fresh stool samples were collected from the patients after admission in properly labeled clean, dry, wide mouthed, leak-proof plastic containers were used. Stool samples were carried within 1 to 2 hours to the virology laboratory of the department of microbiology.

Laboratory procedure

Macroscopic examination was done for colour, consistency, presence of mucus, blood or worms in stool samples. Then ICT was done in fresh samples. After performing ICT, samples were stored at -20°C until ELISA was done.

Antigen detection:

- **Detection of rotavirus by ELISA**:
  Monoclonal antibodies against the product of the sixth viral protein (VP6) used in a sandwich type method. The assay was carried out according to the manufacturer's instructions.
- **Detection of rotavirus by ICT:**
  ICT is a single-step, immuno-chromatographic lateral-flow test. Two bands (red and blue band) appear to indicate rotavirus positive. If only the blue band is visible, it is Rotavirus negative. It was carried out according to the manufacturer's instructions.

For data analysis, χ^2 test was done and $p<0.05$ was considered significant.

RESULTS

Table-I Shows It was revealed from our study that, prevalence of Rotaviral diarrhoea (ICT positive) was highest (51.89%) among 7-12 months of age group children followed by 13-24 months of age group children (36.36%) .

Table I : Prevalence of Rotavirus diarrhoea (ICT +ve) among under 5 years old children according to age group (n=184)

Variable	ICT (+ve)		ICT (-ve)		P value
	N	(%)	N	(%)	
Age (months)					
0-6	8	30.77	18	69.23	0.004*
7-12	55	51.89	51	48.11	
13-24	16	36.36	28	63.64	
25-59	2	20.00	6	80.00	

Table-II Shows It was found from our study that, prevalence of ELISA positive Rotaviral diarrhoea was highest among 7-12 months age group (50.56%) followed by 13-24 months age group (48.28%) .

Table II: Prevalence of Rotavirus diarrhoea (ELISA +ve) among under 5 years children according to their age (n=184)

Variable	ELISA (+ve)		ELISA (-ve)		P value
	n	(%)	N	(%)	
Age (months)					
0-6	2	11.11	16	88.89	
7-12	50	50.56	40	49.44	0.004*
13-24	28	48.28	30	51.72	
25-59	6	33.33	12	66.67	

From our study, we found that prevalence of Rotaviral diarrhoea (both ELISA and ICT positive) was found higher among male children (61.90%) compared to female children (38.10%) (p= 0.247).

Table-III showed that stool antigen was found positive in 84 (45.65%) and negative in 100 (54.35%) patients by ICT and was positive in 86 (46.74%) and negative in 98 (53.26%) patients by ELISA.

Table III: Distribution of study population according to stool antigen test by ICT and ELISA

Diagnostic test	Positive	Negative	Total
ICT	84(45.65%)	100(54.35%)	184 (100.0)
ELISA	86(46.74%)	98(53.26%)	184 (100.0)

Table-IV showed that stool antigen was found positive in 78 cases by both ICT and ELISA and negative in 92 cases by both ICT and ELISA. However, 6 cases were false-positive as these 6 cases were positive by ICT but found negative in ELISA. Again, 8 cases were false-negative as these 8 cases were negative by ICT but found positive in ELISA.

Table IV: Cross tabulation between total number of positive and negative cases observed by ICT and ELISA

Diagnostic Test ICT	ELISA		Total
	Positive	Negative	
Positive	78	6	84
Negative	8	92	100
Total	86	98	184

Considering ELISA as the gold standard diagnostic test, ICT revealed 90.70% sensitivity and 93.88% specificity. Positive predictive value (PPV), negative predictive value (NPV) and accuracy of ICT were found as 92.86%, 92.00% and 92.39% respectively.

DISCUSSION

In the present study, highest prevalence of Rotaviral diarrhoea was found in children of 7-12 months of age group (51.89%). This is in agreement with the results of a study done in Nigeria by Junaid et al. (2011) where most of the infected children (42%) were found between 7 to 12 months of age group[11]. Ahmed (2009), Salwa (2014) and Dhiman (2015) also reported the same.[12,13,14] It appeared that infants below 6 months of age are initially protected to some extent against rotavirus diarrhoea due to presence of maternal antibodies. After 6 months when maternal antibody decreases, rate of infection increases (Majumder et al., 2018).[15] In this age group (7 – 12 months), children start crawling and develop tendency to put almost everything into mouth which can increases the chance of infection (Ahmed et al., 2009).[12] Another reason can be that the weaning is started at this age. So, there is chance of contamination of food during preparation if hand washing and food hygiene is not maintained properly. Frequency of rotaviral infection was less in higher age group due to acquisition of antibody by natural infection (Junaid et al., 2011).[11]

In this study, highest prevalence of rotaviral diarrhoea was found among male (61.90%). This result is in agreement with previous Bangladeshi studies, where it was reported that around 58% (Roy et al., 2012)[9] and 54% (Verkerke et al., 2016)[16] children were male. Similar result was found from an Indian study done by Agarwal and co-workers where 62.7% male children were affected (Agarwal et al.,

2016)[10]. This male predominance is not clearly understood. It can be explained by social reason that the tendency of parents to prioritize their male children than female in seeking any kind of health care. This finding can also be explained by more resistance to infection in females due to XX chromosome (Dhiman et al., 2015).[14]

Present study found that ICT is 90.70% sensitive and 93.88% specific for diagnosis of Rotaviral diarrhoea compared to ELISA. This finding is in agreement with Momenzadeh[17] and Salwa.[13] Considering ELISA as gold standard, Momenzadeh et al. compared ICT with ELISA and found the sensitivity and specificity of ICT to be 87.7% and 98.6%, respectively and Salwa et al. found sensitivity and specificity of ICT 90.0% and 100%, respectively. Rougemont et al. tested ICT in comparison to ELISA and found sensitivity and specificity of ICT 83.0% and 99.9%, respectively. They suggested that ICT and ELISA were fairly comparable. They also suggested ICT as an effective and alternative diagnostic test for Rotaviral infection and it is also good for ambulatory practice.[18] Kim and his co-workers compared ICT with ELISA, ELFA (enzyme linked fluorescent assay), real-time PCR, and mRT-PCR (multiplex reverse transcription PCR) and found that the ICT had no interference and an acceptable agreement rate with the ELISA, ELFA, real-time PCR and mRT-PCR. Therefore, ICT method can be useful in clinical practice for the rapid detection of Rotavirus infection.[19] Considering ELISA as standard test, Agarwal et al. (2016) compared ICT with ELISA and found ICT was equivalent to ELISA regarding sensitivity and specificity. It is rapid, easy to perform, requires less handling of the sample and easy to interpret in the routine clinical laboratory and made the diagnosis simple, rapid, cost-effective and convenient. ICT has another important advantage that it can be kept in room temperature. On the other hand, ELISA is relatively expensive and equipments are not readily available in the health facilities of low resource countries.[10]

CONCLUSION

This study demonstrated that ICT is a useful method for the rapid screening of rotaviral antigen as it has the advantage of being quicker, convenient application, cost-effective, easy to perform, long shelf life, useful for testing single specimen, not requiring additional equipment and easy interpretation. As rotaviral infection causes severe dehydrating diarrhoea, rapid diagnosis by applying ICT may help in prompt treatment decision. It is particularly important in Bangladesh, where diarrhoea is still contributing a significant proportion of mortality and morbidity in under five children.

REFERENCES

1. Pang X and Hodinka RL. In Gastroenteritis Viruses. Manual of clinical microbiology. Jorgensen JH and Pfaller MA (eds). 11th Ed, Washington, DC: ASM press. 2015: 1617-1632.
2. UNICEF. Committing to Child Survival: A Promise Renewed. Progress Report 2015. New York, 2015: 8-25.
3. Chisti MJ, Pietroni MA, Smith JH, Bardhan PK and Salam MA. Predictors of death in under-five children with diarrhoea admitted to a critical care ward in an urban hospital in Bangladesh. Acta Paediatr. 2011; 100 (12): 275-279.
4. Zuccotti G, Meneghin F, Dilillo D, et al. Epidemiological and clinical features of rotavirus among children younger than 5 years of age hospitalized with acute gastroenteritis in Northern Italy. BMC Infect Dis. 2010; 10 (218): 1-8.
5. Estes MK and Greenberg HB. In Rotaviruses. Fields Virology. Knipe DM and Howley PM (eds). 6th ed, Philadelphia: Lippincott Williams & Wilkins. 2013; 1347-1401.
6. Miller S. In Virology. Jawetz, Melnick & Adelberg's Medical Microbiology. Carroll KC, Morse SA, Meitzner TA and Miller S (eds). 27th Ed, New York: McGraw-Hill. 2016; 532-536.
7. World Health Organozation (2013): Rotavirus deaths by country 2000-2013. web page at www.who.int/immunization/monitoring_surveillance/rotavirus [accessed on 12/08/2018].
8. Obi RK, Oke BO, Anjorin AA, et al. Evaluation of techniques for the diagnosis of Rotavirus gastroenteritis in paediatric patients. Asian Med J. 2015; 1 (1): 6-27.
9. Roy S, Shamsuzzaman SM and Mamun KZ. Rapid detection of Rotavirus antigen in stool sample of acute diarrheic children. Ban J Med Microbiol. 2012; 6 (1): 11-13.
10. Agarwal JK, Garg SP, Dayachand and Agarwal D. Comparative Analysis of Enzyme-Linked Immunosorbent Assay and Rapid Card Test for Diagnosis of Rotavirus Antigen in Acute Diarrhea Below Five Years Children. Int J Curr Microbiol Applied Sci. 2016; 5 (7): 289-294.

11. Junaid SA, Umeh C, Olabode AO and Banda JM. Incidence of rotavirus infection in children with gastroenteritis attending Jos university teaching hospital, Nigeria. Virol J. 2011; 8: 1-8.

12. Ahmed S, Kabir ARM, Rahman A, et al. Severity of Rotavirus diarrhea in children: One Year Experience in a Children Hospital in Bangladesh. Iran J Pediatr. 2009; 19: 107-116.

13. Salwa IB, El-Bialy AA, Mohamed MS, et al. Comparative study of Rotavirus detection. Zag Uni Microbiol J. 2014; 20 (6): 807-815.

14. Dhiman S, Devi B, Singh K, et al. Comparison of Enzyme-Linked Immunosorbent Assay and Immunochromatography for Rotavirus Detection in Children Below Five Years with Acute Gastroenteritis. J Clin Diagn Res. 2015; 9: 6-9.

15. Majumder N, Barbhuiya NI, Majumder T and Datta SS. Prevelence of Rotaviral infection among children admitted with acute diarrhea in a tertiary care hospital of Tripura. Int J Sci Res. 2018; 7: 105-107.

16. Verkerke H, Sobuz S, Ma JZ, et al. Malnutrition Is Associated with Protection from Rotavirus Diarrhea: Evidence from a Longitudinal Birth Cohort Study in Bangladesh. J Clin Microbiol. 2016; 54: 2568-2574.

17. Momenzadeh A, Modarres S, Faraji A, et al. Comparison of Enzyme Immunoassay, Immuno-chromatography, and RNA-Polyacrylamide-Gel Electrophoresis for Diagnosis of Rotavirus Infection in Children with Acute Gastroenteritis. Iran J Med Sci. 2008; 33 (3): 173-176.

18. Rougemont A, Kaplon J, Billaud G, et al. Sensitivity and specificity of the VIKIA Rota-Adeno immune-chromatographic test (bioMérieux) and the ELISA IDEIA Rotavirus kit (Dako) compared to genotyping. Patho Biol. 2009; 57 (1): 86-89.

19. Kim J, Kim HS, Kim H, et al. Evaluation of an Immunochromatographic Assay for the Rapid and Simultaneous Detection of Rotavirus and Adenovirus in Stool Samples. Ann Lab Med. 2014; 34 (3): 216-222.

Original Article

Comorbidity and it's Impact on COVID-19 Affected Patients in COVID-19 Dedicated Hospital of Bangladesh

*Hossain I[1], *Mullick AR[2], Khan MH[3], Halim KS[4], Aktaruzzaman MM[5], Nabi SG[6], Rahman S[7], Shahin M[8]

Abstract

The Wuhan City of China evidenced unknown aetiology pneumonia cases at the end of December 2019. On 7 January 2020, the causative agent was identified as a novel coronavirus (2019-nCoV), currently referred to as SARS-CoV-2, and coronavirus disease as COVID-19. Older adults and people of any age who have underlying medical conditions, such as hypertension and diabetes, have shown worse prognosis. The aim of this study to evaluate the risk of serious adverse outcomes in patients with COVID-19 by stratifying the comorbidity status. We conducted a retro-prospective study of 405 patients admitted into the Mugda Medical College and Hospital, Dhaka,Bangladesh. Among 405 cases, mean age was 46.33 years. About 216 (53.3%) patients were male. Almost 322 (79.5%) patients were managed inside Dhaka city. The most common symptom was fever on or after hospitalisation (71.9%). Of the 405 cases the prevalence of specific comorbidities was: hypertension (n=141, 34.8%), other cardiovascular diseases (n=42, 10.4%) cerebrovascular diseases (n=7, 1.7%), diabetes (n=140, 34.6%), COPD (n=4, 1.0%), chronic kidney diseases (n=65, 16.0%), malignancy (n=4, 1.0%) and asthma (n=51,12.6%). Overall, 307 (75.8%) patients discharged alive during the time frame of this study. 98(24.2%) patients died, 63 (15.6%) were admitted to the ICU and 16 (4.0%) received invasive ventilation. Patients with comorbidities should take all necessary precautions to avoid getting infected with SARS CoV-2, as they usually have the worst prognosis. There is a need for a global public health campaign to raise awareness, on reducing the burden of these comorbidity illnesses causing deaths in COVID-19- infected patients.

Keywords: *Co-morbidity, impact of COVID-19, COVID-19 pandemic*

1. *Dr Irin Hossain, Assistant Professor, Department of Occupational and Environmental Health (OEH), National Institute of Preventive and Social Medicine (NIPSOM), Dhaka. E-mail: irin.hossain @gmail.com
2. *Dr Ashekur Rahman Mullick, Field Supervisor, NIPSOM, Dhaka
3. Prof. Dr. Manzurul Haque Khan, Consultant, CDC, DGHS, Dhaka
4. Prof. Dr. Kazi Shafiqul Halim, Professor & Head, Department of Epidemiology, NIPSOM, Dhaka
5. Dr M M Aktaruzzaman, Assistant Director, Dhaka Medical College and Hospital, Dhaka
6. Dr Shah Golam Nabi, Principal, Mugda Medical College, Dhaka
7. Dr. Md. Shafiur Rahman, Assistant Professor and Head, Department of OEH, NIPSOM, Dhaka
8. Dr Md. Shahin, Medical Officer (OSD), DGHS, Dhaka

*For Correcpondence

INTRODUCTION

The Wuhan City of China evidenced unknown aetiology pneumonia cases at the end of December 2019[1-10]. On 7 January 2020, the causative agent was identified as a novel coronavirus (2019-nCoV)[3-5], currently referredto as SARS-CoV-2[4-6], and coronavirus disease as COVID-19[4-10]. The disease over runentire China[2-5] and surpassed international borders inno time[2.3], extending the world tally to >27 million confirmed cases and >0.9 million deaths[11-13].

Older adults and people of any age who have underlying medical conditions, such as hypertension and diabetes, have shown worse prognosis[14]. Diabetic patients have increased morbidity and mortality rates and have been linked to more hospitalization and intensive care unit (ICU) admissions[14-17]. People with chronic obstructive pulmonary disease (COPD) or any respiratory illnesses are also at higher risk for severe illness from COVID-19[18]. The risk of contracting COVID-19 in patients with COPD is found to be four fold higher than patientswithout COPD[18-20]. There are significant differences between Bangladesh, China and the US in population demographics,[21] smoking rates,[22] and prevalence of comorbidities.[23-25] In this study we tried to evaluate the risk of serious adverse outcomes in patients with COVID-19 by stratifying the comorbiditystatus.

METHODS AND MATERIALS

Study Population, Setting, and Design

We conducted a retro-prospective study of 405 patients admitted into the Mugda Medical College and Hospital, Dhaka, Bangladesh. All patients who were diagnosed with COVID-19 according to WHO interim guidance[26] were screened, and those who died or were discharged between May 1, 2020 and June 31, 2020, were included in this study.

Data collection

Epidemiological, demographic, clinical and outcome data were obtained from patient charts and the hospitals' admission records using a structured questionnaire which was adopted from Novel Coronavirus (COVID-19 Rapid Version) by Global COVID-19 Clinical Platform which was previously used for same purpose in United Kingdom[27] and China[9]. All data were collected by expert physicians and public health specialist.

Statistical analysis

We used the $\chi 2$ test, or Fisher's exact test to compare differences between survivors and non- survivors where appropriate and also for severe and non-severe patients. The level of significance was set at 0.05. SPSS 26.0 was used to analyse the data.

RESULT

Table I : Demographic findings, comorbidities and related sigh-symptoms of patients on admission

Variables		Severe (n=197)	Non-severe (n=208)	p value
Gender	Female	89 (47.1%)	100 (52.9%)	0.559
	Male	108 (50.0%)	108 (50.0%)	
Current Smoker		30 (40.5%)	44 (59.5%)	0.280
	Chronic Cardiac Disease	21 (50%)	21 (50%)	0.980
	HTN	83 (58.9%)	58(41.1%)	0.011
Comorbidity	Asthma	22 (43.1%)	29 (56.9%)	0.552
	CKD	41 (63.1%)	24 (36.9%)	0.035
	DM	89 (63.6%)	51 (36.4%)	0.000
	Others	13 (13.3%)	11 (4.3%)	0.184
Fever		137 (47.1%)	154 (52.9%)	0.315
Cough		118 (48.2%)	127 (51.8%)	0.595
Cough with sputum		23 (42.6%)	31 (57.4%)	0.531
Sore throat		83 (56.8%)	63 (43.2%)	0.021
Runny nose		8 (22.9%)	27 (77.1%)	0.006
Wheezing		17 (63.0%)	10 (37.0%)	0.270
Chest pain		33 (62.3%)	20 (37.7%)	0.033
Muscle ache		35 (43.2%)	46 (56.8%)	0.333
Joint pain		22 (45.8%)	26 (54.2%)	0.545
Fatigue		93 (52.5%)	84 (47.5%)	0.166
Shortness of breath		125 (59.0%)	87 (41.0%)	0.000
Inability to walk		67 (74.4%)	23 (25.6%)	0.000
Chest in-drawing		55 (85.9%)	9 (14.1%)	0.000
Headache		23 (37.1%)	39 (62.9%)	0.142
Altered consciousness		39 (75.0%)	13 (25.0%)	0.000
Abdominal pain		16 (40.0%)	24 (60.0%)	0.191
Nausea/Vomiting		36 (40.4%)	53 (59.6%)	0.128
Diarrhoea		32 (50.8%)	31 (49.2%)	0.585

Table I shws taht among 405 cases, mean age was 46.33 years. About 216 (53.3%) patients were male. Almost 322(79.5%) patients were managed inside Dhaka city. Themost common symptom was fever on or after hospitalisation (71.9%), followed by dry cough (60.5%). Shortness of breath (52.3%), fatigue (43.7%) and sore throat (36.0%) were also found. Of the 405 cases the prevalence of specific comorbidities was: hypertension (n=141, 34.8%), other cardiovascular diseases (n=42, 10.4%) cerebrovascular diseases (n=7, 1.7%), diabetes (n=140, 34.6%), COPD (n=4, 1.0%), chronic kidney diseases (n=65,16.0%), malignancy (n=4, 1.0%) and asthma (n=51, 12.6%). Hypertension was seen more commonly in severe cases than in non-severe cases (58.9% versus 41.1%) followed by chronic kidney disease (63.1% versus 36.9%), diabetes (63.6% versus 36.4%). In case of on treatment complications the pattern of distribution was sore throat (56.8% versus 43.2%), fatigue (52.5% versus 47.5%), shortness of breath (59.0%% versus 41.0%), diarrhoea (50.8% versus 49.2%), and alteration of consciousness (75.0% versus 25.0%).

Table II shows that overall, 307 (75.8%) patients discharged alive during the time frame of this study. 98 (24.2%) patients died, 63 (15.6%) were admitted to the ICU and 16 (4.0%) received invasive ventilation. Hypertension was seen more commonly in patients who has been discharged alive than in decease case (61.0% versus 39.0%) followed by asthma (78.4% versus 21.6%), chronic kidney disease 55.4% versus 44.6%), diabetes (60.7% versus 39.3%).

DISCUSSION

In our study circulatory and endocrine comorbidities were common among patients with COVID-19. Patients with at least one comorbidity, or even more so, were associated with severe health status. These findings have provided further objective evidence, with a large sample size and extensive coverage of the geographic regions across Bangladesh, to take into account baseline comorbid diseases in the comprehensive risk assessment of prognosis among patients with COVID-19 on hospital admission. Overall, our findings have rebounded the recently published studies in terms of the commonness of comorbidities in patients with COVID-19[27-32]. Despite considerable variations in the proportion in individual studies due to the limited sample size and the region where patients were managed, circulatory diseases (including hypertension and coronary heart diseases) remained the most common category of comorbidity[27-30]. Apart from circulatory diseases, endocrine diseases such as diabetes were also common in patients with COVID-19[29,30]. Not with standing the commonness of circulatory and endocrine comorbidities, patients with COVID-19 rarely reported having comorbid respiratory diseases (particularly COPD)[30]. Consistent with recent reports[27-30], the percentage of patients with comorbid renal disease and malignancy was relatively low. Our findings have therefore added to the existing literature on the spectrum of comorbidities in patients with COVID-19 based on the larger sample sizes and representativeness of the whole patient population in Bangladesh.

A number of existing literature reports have documented the escalated risks of poorer clinical outcomes in patients with avian influenza[31-35], SARS-CoV[36] and MERS-Co

Table II : Relationship between comorbidity and health outcome

Variables		Survivor (n=307)	Non-survivor (n=98)	p value
	Chronic Cardiac Disease	26 (61.9%)	16 (38.1%)	0.070
	HTN	86 (61.0%)	55(39.0%)	0.000
Comorbidity	Asthma	40 (78.4%)	11 (21.6%)	0.823
	CKD	36 (55.4%)	29 (44.6%)	0.000
	DM	85 (60.7%)	55 (39.3%)	0.000

Vinfections[37-45]. The most common comorbidities associated with poorer prognosis included diabetes[44,46], hypertension[47], respiratory diseases[32,46], cardiac diseases[32,40], pregnancy[35], renal diseases[31,36]and malignancy[33]. Our findings suggested that, similar with other severe acute respiratory outbreaks, comorbidities such as COPD, diabetes, hypertension and malignancy predisposed to adverse clinical outcomes in patients with COVID-19. The strength of association between different comorbidities and the prognosis, however, was less consistent when compared with the literature reports[28,35,40,47]. For instance, the risk between cardiac diseases and poor clinical outcomes of influenza, SARS-CoV or MERS-CoV infections was inconclusive[28,40,46]. Except for diabetes, no other comorbidities were identified to be the predictors of poor clinical outcomes in patients with MERS-CoV infections[42].

Our findings suggested that patients with comorbidities had greater disease severity compared with those without. Furthermore, a greater number of comorbidities correlated with greater disease severity of COVID-19. The proper triage of patients should be implemented by carefully inquiring about the medical history because this will help identify patients who would be more likely to develop serious adverse outcomes of COVID-19. Moreover, better protection should be given to the patients with COIVD-19 who had comorbidities upon confirmation of thediagnosis.

CONCLUSIONS

Patients with comorbidities should take all necessary precautions to avoid getting infected with SARSCoV-2, as they usually have the worst prognosis. There is a need for a global public health campaign to raise awareness, on reducing the burden of these comorbidity illnesses causing deaths in COVID-19-infected patients.

ACKNOWLEDGEMENTS

We would like to thank all of our colleagues and other personnel of National Institute of Preventive and Social Medicine (NIPSOM), Mugda Medical College (MuMC) for their constructive cooperation. In addition, we would like to thank all of our co-authors for their valuable contribution for this work. We also acknowledge all of those helping hands, as without their valuable contribution this work couldn't see the light of success.

LIMITATIONS

A main limitation was the self-reporting of comorbidities on admission. We did not approach patients to obtain additional history or biologic samples for laboratory measurement. Because of the rapid evolving outbreak globally, ongoing studies with the inclusion of more patients would be needed to increase the statistical power and lend support to subgroup analyses stratified by the specific comorbidities and their association with the risk of death.

Declarations

Funding: No funding.

Conflict of interest: No competing interests relevant to this study to disclose for all authors. Full forms submitted and on file for allauthors.

Ethical approval: All the procedures were conducted following the ethical guidelines of institution's ethical committee (IRB) at Mugda Medical College Hospital, Bangladesh (Memo No/MUMC/2020/617). The ethical standards as laid down in the 1964 Declaration of Helsinkiand its later amendments or comparable ethical standards will be followed whereverapplicable.

REFERENCES

1. Yang X, Yu Y, Xu J, et al.Clinicalcourseand outcomes of critically ill patients with SARS- CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020;8: 475-81.
2. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA 2020 Apr.6. doi: 10.1001/jama. 2020.5394.
3. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. COVID-19 in critically ill patients in the Seattle region - case series. N Engl J Med 2020 Mar. 30, doi: 10.1056/NEJMoa2004500.
4. Richardson S, Hirsch JS, Narasinhan M, etal. Presenting characteristics, comorbidities,and outcomes among 5700 patients hospitalized with COVID-19 in the New York CityArea. JAMA 2020 Apr. 22, doi: 10.1001/ jama.2020.6775.
5. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease- 2019 (COVID-19): The epidemic and the challenges. In J Antimicrob

Agents. 2020;55(3):105924. DOI:10.1016/j. ijantimicag. 2020.105924

6. Qiu H Tong Z Ma P et al., Intensive care during the coronavirus epidemic. Intensive Care Med. 2020; 46:576-578

7. ICU Care Management Challenges and Recommendations for COVID-19,Infectious Disease Advisor, access on: 19.07.2020 Available at:https:// www. infectious diseaseadvisor.com/home/ topics/covid19 /icu-care-management-challenges- and- recommendations-for-covid- 19/

8. Docherty, A. B., Harrison, E. M., Green, C. A., Hardwick, H. E., Pius, R., Norman, L., Holden, K. A., Read, J. M., Dondelinger, F., Carson, G., Merson, L., Lee, J., Plotkin, D., Sigfrid, L., Halpin, S., Jackson, C., Gamble, C.,Horby,P.W., Nguyen-Van-Tam,J.S.,M. G. (2020). Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. The BMJ, 369. https://doi.org/10.1136/bmj.m1985

9. Fei Zhou (2020) Clinical Course and Risk Factors for Mortality of Adult in Patients with COVID-19 in Wuhan, China: A Retrospective Cohort Study. J Med Stud Res 3:015.

10. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y,ZhangL,FanG,XuJ,GuX,ChengZ,Yu T,XiaJ, WeiY, WuW, XieX,YinW,LiH, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J and CaoB. Clinical features of patients infectedwith 2019 novel coronavirus in Wuhan, China. Lancet, 2020; 395: 497-506.

11. Novel Corona Virus 2019 Update, World-O- Meter, access on,02.09.2020. Available at: https://www. worldometers.info/

12. Daily Live Updates of Corona Virus: Aljazeera Television, access on, 02.09.2020. Available at:https://www.aljazeera.com/news/2020/06/eu-bar-travellers-brazil-coronavirus-live-updates-20062 7002953075.html.

13. Coronavirus India Live Updates, The India Express, access on,02.09.2020. Available at: https://indianexpress.com/article/india/coronavirus-india-news-live-updates-covid-19-tracker-corona-cases -in-india-today-update-lockdown-extension-state-wise-latest-news-tamil-nadu-delhi-6479588/

14. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: prevalence, pathophysiology, prognosis, and practical considerations. Diabetes Metab Syndr Clin Res Rev. 2020;14(4):303 –10https: //reader. elsevier.com/reader/sd/pii/S18 71402120300631? token=9053C7A9DEA8F 9AD35620DE8A76E569 E800C744D2785B F1F3E13C425A07B78B480145 B9E04D94 BE41439983005F17A52

15. Hossain I, Mullick AR, Khan MH, Aktaruzzaman M, Rahman S, Tuhin SGN, et al. Impacts of Conventional OxygenTherapy on COVID-19 Patient in Intensive Care Unit (ICU). JMedSci ClinRes. 2020;08(08):183– 9.

16. Hossain I, Khan MH, Ahmad SA, Aktaruzzaman M, Tuhin SGN, Rahman S, et al. Characteristics of Inpatients' Fatality Due to Covid -19 Pandemic : Experience From Mugda Medical College and Hospital , Dhaka ,. World J Adv Heal care Res. 2020; 4(5):11–5.

17. Hossain I, Mullick AR, Khan MH, Ahmad SA, Rahman S, Aktaruzzaman M. Epidemiologyof Coronavirus Disease :Past, Present , Future Prospects and Its Journey Towards Bangladesh. Int Med J. 2020; 25(06):2517–29.

18. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, et al. The impact of COPD and smoking history on the severity of COVID-19: a systemic review and meta-analysis. J Med Virol. 2020. 10.1002/jmv. 25889 [Accessed April 18, 2020,https://www. ncbi.nlm.nih.gov/pubmed/3229 3753].

19. YangJ, ZhengY, GouX, Pu K, Chen Z, Guo Q, Ji R, Wang H, Wang Y, Zhou Y. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int J Infect Dis. 2020; S1201–9712 (20): 30136– 30133. doi:10.1016/j.ijid.2020.03.017.

20. Franki R. Comorbidities the rule in New York's COVID-19 deaths. Hospitalist. 2020; [Accessed June 1, 2020,https://www.the- hospitalist.org/hospitalist/ article/ 220457/coronavirus-updates/ comorbidities -rule-new- yorks-covid-19-deaths].

21. United Nations Department of Economicand Social Affairs Population Dynamics. World population prospects2019. AccessedApril6, 2020.https://

population. un.org/wpp/Graphs/ Demographic Profiles/ Pyramid/840

22. Chen Z, Peto R, Zhou M, et al; China Kadoorie Biobank (CKB) collaborative group. Contrasting male and female trendsin tobacco-attributed mortality in China: evidence from successive nationwide prospective cohort studies. Lancet. 2015; 386(10002):1447-1456. doi:10.1016/S0140- 6736 (15)00340-2

23. Institute for Health Metrics and Evaluation. GBD Compare/Viz Hub. Accessed April 6, 2020. https://vizhub.healthdata.org/gbd-compare/

24. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics,Comorbidities, and Outcomes Among 5700 Patients Hospitalized with COVID-19 in the New York City Area.JAMA. 2020; 323(20):2052– 2059. doi:10.1001/ jama.2020.6775

25. Li Q Guan X Wu P et al., Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020; (published online Jan 29.) DOI:10.1056/NEJMoa20013168.

26. World Health Organization. Coronavirus disease (COVID-19) technical guidance: laboratory testing for 2019-nCoV inhumans. [cited 2020 Jan24]. Available at: https://www.who.int/ emergencies/ diseases/ novel-coronavirus- 2019/technical-guidance /laboratory-guidance

27. Docherty, A. B., Harrison, E. M., Green, C. A., Hardwick, H. E., Pius, R., Norman, L., Holden, K. A., Read, J. M., Dondelinger, F., Carson, G., Merson, L., Lee, J., Plotkin, D., Sigfrid, L., Halpin, S., Jackson, C., Gamble, C.,Horby,P.W., Nguyen-Van-Tam,J.S.,M. G. (2020). Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. The BMJ, 369.https://doi.org/10.1136/bmj.m1985

28. Huang C, Wang Y, Li X, et al. Clinical features of patients with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395:497–506. doi:10.1016/ S0140 -6736(20)30183-5

29. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395: 507–513. doi:10.1016/S0140-6736(20)30211-7 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

30. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novelcoronavirus-infected pneumonia in Wuhan, China. JAMA 2020; in press [https://doi.org/ 10.1001/jama.2020.1585]. doi:10.1001 /jama.2020. 1585

31. Kui L, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J 2020; in press [https://doi.org/10.1097/CM9.0000000000000744]. doi:10.1097/CM9.0000000000000744

32. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case studies. BMJ 2020; 368: m606. doi:10.1136/bmj.m606

33. PlaczekHED,MadoffLC.Associationofage and comorbidity on 2009 influenza A pandemic H1N1-related intensive care unit stay in Massachusetts. Am J Public Health 2014; 104: e118–e125. doi:10.2105/AJPH.2014.302197

34. Mauskopf J, Klesse M, Lee S, et al. The burden of influenza complications in different high-risk groups. J Med Economics 2013; 16: 264–277. doi:10. 3111/13696998.2012.752376

35. Shiley KT, Nadolski G, Mickus T, et al. Differences in the epidemiological characteristics and clinical outcomes of pandemic (H1N1) 2009 influenza, compared with seasonal influenza. Infect Control HospEpidemiol 2010; 31: 676–682. doi:10. 1086/653204

36. Martinez A, Soldevila N, Romeo-Tamarit A, et al. Risk factors associated with severe outcomes in adult hospitalized patients according to influenza type and subtype. PLoS One 2019; 14:e0210353.

37. Gutiérrez-González E, Cantero-Escribano JM, Redondo-Bravo L, et al. Effect of vaccination, comorbidities and age on mortality and severe disease associatedwith influenza during the season 2016–2017 in a Spanish tertiary hospital. J Infect Public Health 2019; 12: 486–491. doi: 10.1016/j.jiph.2018.11.011

38. Booth CM, Matukas LM, Tomlinson GA, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. JAMA 2003; 289: 2801–2809. doi:10.1001/jama. 289.21. JOC30885

39. Alqahtani FY, Aleanizy FS, Ali Hadi Mohammed R, et al. Prevalence of comorbidities in cases of Middle East respiratory syndrome coronavirus: a retrospective study. Epidemiol Infect 2018; 5:1–5.

40. Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV). Int J Infect Dis 2016; 49:129–133. doi: 10.1016/j.ijid.2016.06.015

41. Rahman A, Sarkar A. Risk factors for fatal Middle East Respiratory Syndrome coronavirus infections in Saudi Arabia: analysis of the WHO line list, 2013–2018. Am J Public Health 2019; 109: 1288–1293. doi:10. 2105/AJPH.2019.305186

42. Alanazi KH, Abedi GR, Midgley CM, et al. Diabetes mellitus, hypertension, and death among 32 patients with MERS-CoVinfection, Saudi Arabia. Emerg Infect Dis 2020; 26: 166–168. doi:10. 3201/eid2601.190952

43. Yang YM, Hsu CY, Lai CC, et al. Impact of comorbidity on fatality rate of patients with Middle East Respiratory Syndrome. Sci Rep 2017; 7:11307. doi:10.1038/s41598-017-10402-1

44. Garbati MA, Fagbo SF, Fang VJ, et al. A comparative study of clinical presentation and risk factors for adverse outcome in patients hospitalised with acute respiratory disease due to MERS coronavirus or other causes. PLoS One 2016; 11:e0165978. doi: 10.1371/journal.pone.0165978

45. Rivers CM, Majumder MS, Lofgren ET. Risks of death and severe disease in patients with Middle East Respiratory Syndrome coronavirus, 2012–2015. Am J Epidemiol 2016; 184: 460–464. doi:10.1093/aje/ kww013

46. Kulscar KA, Coleman CM, Beck S, et al. Comorbid diabetes results in immune dysregulation and enhanced disease severity following MERS-CoV infection. JCI Insight 2019; 20:e131774.

47. Matsuyama R, Nishiura H, Kutsuna S, et al. Clinical determinants of the severity of Middle East respiratory syndrome (MERS): a systematic review and meta-analysis. BMC Public Health 2016; 16: 1203. doi:10.1186/s12889-016-3881-4

Original Article

Study on Early Childhood Adversities of Orphans Rearing in Orphanages

*Mahmood F[1], Khan NR[2], Islam MZ[3], Shahreen T[4], Zaman NA[5]

Abstract

Orphans spread a significant mass of our absolute child folks and this study was planned to determine the early childhood adversities of orphans that may attract them in various violence and perilous fortune lead further that in the end have a long-standing psycho-social impact on their adulthood. This was a cross-sectional study that was completed among 301orphans of both genders. The subjects were chosen by convenient sampling technique based on specific inclusion criteria and maintaining ethical issues. The study was directed from January to December 2017 in different orphanages of Chittagong and Dhaka city. The examination uncovered, maximum (84%) of participants were male and the rest (16%) were female. Among them, around 44.9% of them were matured from 10-12 years followed by 37.9% matured between 13-15 years. The majority (62%) of the participants had education up to primary/equivalent level. A maximum (69.77%) of them lost their father and 17.94% of them lost both of their parentages. The study revealed, physical assault (30.2%), serious domestic accident (27%), and life-threatening illness/injury (33.6%) had higher frequencies than other events that happened with the participants personally. Additionally, events like traffic transportation accidents (47.3%), serious domestic accidents (36.8%), and physical assault (28.3%) had higher frequencies than other events experienced through observing to transpiring. Then again, transportation accidents, domestic accidents ($\chi 2$ =32.673, p<0.05), physical assault, life-threatening illness/injury were experienced among 16-18 years of aged orphans personally where assault with a weapon and sexual assault ($\chi 2$ =14.637, p< 0.05) were more frequent among 13-15 years old gathering.

Keyword: *Orphan, childhood adversity*

1. *Dr. Fahad Mahmood, Lecturer, Department of Community Medicine, National Institute of Preventive and Social Medicine (NIPSOM), Dhaka. Email: fahadmahmud999@gmail.com
2. Dr. Nirmeen Rifat Khan (Rtd.), Professor, Department of Community Medicine, NIPSOM, Dhaka.
3. Dr. Md. Ziaul Islam PhD, Professor and Head of the Department of Community Medicine, NIPSOM, Dhaka.
4. Dr. Tasmia Shahreen, Medical Officer, Lab Call Centre, DGHS, Dhaka
5. Dr. Md. Noor Ashad-Uz-Zaman, Lecturer, Department of Public Health & Hospital Administration, NIPSOM, Dhaka.

*For Correspondence

INTRODUCTION

UNICEF and global partners outlined an orphan as a child under 18 years of age who has lost one or both parents to any cause of death. According to this outlining, there were nearly 140 million orphans worldwide in 2015, including 61 million in Asia, 52 million in Africa, 10 million in Latin America and the Caribbean and 7.3 million in Eastern Europe and Central Asia.

This outsized number speaks to youngsters who have lost the two guardians as well as the individuals who have lost their dad however have an enduring mother or have lost their mother yet have an enduring father. Of this around 140 million kids delegated orphans, among them about 15.1 million have lost the two guardians. Proof obviously shows that by far most of orphans are living with an enduring guardian grandparent or with other relative for endurance.[1]

According to UNICEF, about 95 per cent of all orphans globally are over five years of age.[1] Some of them are lucky enough of getting possibility of being raised up in orphanages having convenience and instructive offices and the rest spend their adolescence in streets, railroad stations, and ghettos in a random way. These vulnerable children including orphans are especially defenseless as they often experience physical abuse from their employers. Moreover, the number of orphans and children living on streets is increasing. Orphans in our country are struggling to survive in harsh conditions surrounded by everyday violence.[2]

At the point when guardians bite the dust, kids miss their physical presence, yet additionally miss the numerous positive things they gave them when they were alive, for example, love, care and insurance. By and large, orphans and weak kids have nobody to share their hopelessness. This can numerous their feeling of powerlessness. Absence of help during the lamenting cycle and deficient assistance in acclimating to a domain without their folks may lead

kids to become discouraged which leaves a solid, negative impacts on the wellbeing and improvement of the person.[3]

Orphans receiving orphanage/foster care report more depressive symptoms and have a higher prevalence of clinically significant depressive symptoms than children reared at home.[4] Halfway houses like orphanages are liable for the training and care of the youngsters that live in them, and regularly become related with a low norm of care. A significant part of the time, they are obliged with an absence of emotional wellness and backing administrations, helpless food, and inadequate financing. Approximately 250,000 children are adopted annually, but 14,505,000 children develop up as orphans and age out of the system by age of 16 and of this number 60% of the girls become prostitutes and 70% of the boys become involved in criminal acts. The consequences of child abuse are vast, particularly when such abuse is prolonged and repeated including acute and severe outcomes such as death, injury, traumatic brain injury, as well as long-term developmental outcomes such as substance abuse, risky sexual behaviors, depression, and youth violence. These brutality and encounters are regularly neglected as they are parentless and none to gripe.[5] Child abuse is a serious issue with long-lasting effects. The National Data Archive on Child Abuse and Neglect estimated that, 772,000 children were victims of abuse and neglect, worldwide; furthermost of them are living in developing countries.[6] Entities who have adverse childhood experiences can be more vulnerable to disease development through both differences in physiological development and adoption and persistence of health-damaging behaviors. The orphans in orphanage institutions take more risks, have more threats, and have poorer peer influences. Male-controlled values and power structures that result in different socialization headways of the children lead them to adopting different coping mechanisms and manifesting the impression of abuse and trauma in different ways on them. They are likely to experience low self-esteem and poor psychosocial care and support. So, the children are rising up, experiencing unsafe and in secure living condition and stereotyping their sociocultural practices.[7] In any case, intercessions zeroing in on both improving consideration quality and forestalling abuse are scant in our nation. Each child is honorable of having a free from any danger youth that is regardless of their economic wellbeing. Regardless of being such a colossal number that is scaling up each day, not many studies were endeavored on orphans to see the continuous unfriendly encounters that may jeopardize their physical, mental, and social development and regularly drives them towards a hazardous future life. The investigation was endeavored to decide different antagonistic encounters of orphans who reside in various orphanages in Bangladesh as it has long-standing psycho-social effect on their adulthood which frequently stays unnoticed.

MATERIALS AND METHODS

This cross-sectional study was conducted in Kodom Mubarak orphanage, Baytush Sharaf Muslim orphanage at Chittagong, and Sir Salimullah orphanage, Dhaka from 1st January to 31st December 2017. Interviewed orphans were between 10-18 years old from the above-mentioned orphanages who were resident over there for at least three years. The sample size was calculated 384 and convenient sampling technique was applied but due to unavailability 301 participants were included in this study. A pre-tested semi-structured questionnaire was used to collect data for this research. The questionnaire was prepared based on the Life Events Checklist for DSM-5 (LEC-5) and Survey questions of 'Child violence experiences in institutionalized/orphanage care' study. Data were collected through face-to-face interviews with the orphans. Permission was taken from the orphanage authority informing them of the purpose, objective and utilization of results, and ensuring of the privacy of the respondents. Informed written consent was obtained from the respondent orphans ensuring them of their privacy before data collection. The interview was conducted by visiting their classrooms and hostels. Privacy was maintained as much as possible during the collection of data. Data were collected according to the working schedule. Descriptive statistics included distribution, percentage, mean, range, standard deviation, etc. For inferential statistics, non-parametric Chi-Square test was performed to determine the association between different variables. A p-value of <0.05 was considered statistically significant. The analysis plan was developed following the objectives of the study. In this study, an ethical clearance certificate was taken from the Ethical Review Board (ERB) of the National Institute of Preventive and Social Medicine (NIPSOM).

RESULTS

Table I Shows the out of 301 participants, male (84%) outnumbered the female (16%) participants. Among them, majority were (44.9%) aged between 10-12 years followed by 37.9% aged between 13-15 years of age. About 62 % of participants were educated up to primary/ equivalent level and 25% had up to secondary/ equivalent level of education. Maximum (82.06%) participants had lost any of their parents and the rest lost both of their parents

Table I: Socio-demographic characteristics of the orphans (N=301)

Attributes	Category	Frequency (n)	Percentage (%)
Sex	Male	254	84
	Female	47	16
Age (in groups)	10-12	135	44.9
	13-15	114	37.9
	16-18	52	17.3
Level of education	Primary /Equivalent	188	62
	S.S.C./Equivalent	38	13
	Secondary/Equivalent	75	25
Nature of orphan	Single orphan	247	82.06
	Double orphan	37	12.29

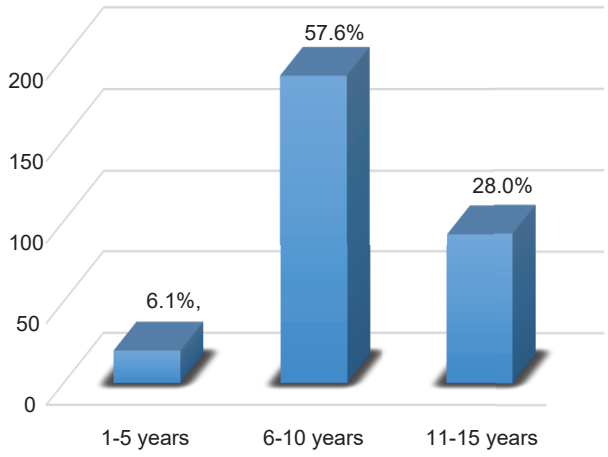


Figure 1: Duration of staying in orphanages (N= 301)

Figure 1 Shows the about 189 (57.6%) orphans were staying in orphanage for 6-10 years, 92 (28%) orphans were staying for 11-15 years and rest 20 (6.1%) were there for 1-5 years. Maximum duration of staying in orphanage was 15 years and minimum duration 5 years .Mean (± SD) duration was 7.98± 2.31 years

Table II Shows the according to the table, about 8.2% of participants said terrific transportation accidents happened with themselves but a maximum (47.3%) of them saw this event happening to someone. About 36.8% participants saw serious domestic accident happening to someone followed by 27% of them said the event happened with their own. Experience of physical assault was the highest (30.2%) among them who responded this event happened with their own and 28.3% said they saw this event happening to someone. About 26.9% participants experienced exposure to toxic substances by hearing from someone and 6.2% of them were exposed personally. Of the participants, about 23% of them encountered attack with a weapon by observing it happening followed by 30.3% heard of this event happening to someone. Result shows, 4.6% participants experienced sexual assault personally and maximum (26.1%) heard of this event happened to someone. Life-threatening illness/injury happened personally with 33.6% of participants. Almost 22.2% of participants said they experienced the event of sudden violent deaths by observing it happening to somebody and 34.4% of them heard of this event. Experience of domestic accidents by oneself was highest among the 16-18 age group and 39.2% of participants of 10-12 years of age saw that event happening to someone which was found statistically significant ($\chi 2 = 32.673$, $p < 0.05$)

Table II: Distribution of participants according to the nature of experiencing events (multiple responses)

Attributes	Category	Frequency (n)	Percentage (%)
Experience of terrific transportation accident (n=317)	Happened with oneself	26	8.2
	Saw happening to someone	150	47.3
	Heard from someone	88	27.8
	Didn't experience	53	16.7
Experience of serious domestic accident (n=318)	Happened with oneself	86	27.0
	Saw happening to someone	117	36.8
	Heard from someone	73	23.0
	Didn't experience	42	13.2
Experience of physical Assault (n=318)	Happened with oneself	96	30.2
	Saw happening to someone	90	28.3
	Heard from someone	72	22.6
	Didn't experience	60	18.9
Experience of exposure to toxic substances (n=305)	Happened with oneself	19	6.2
	Saw happening to someone	72	23.6
	Heard from someone	82	26.9
	Didn't experience	132	43.3
Experience of assault with a weapon (n=304)	Happened with oneself	9	3.0
	Saw happening to someone	70	23.0
	Heard from someone	92	30.3
	Didn't experience	133	43.8
Experience of sexual assault (n=303)	Happened with oneself	14	4.6
	Saw happening to someone	54	17.8
	Heard from someone	79	26.1
	Didn't experience	26	51.5
Experience of life threatening illness/injury (n=307)	Happened with oneself	150	33.6
	Saw happening to someone	88	26.7
	Heard from someone	53	22.8
	Didn't experience	86	16.9
Experience of sudden violent death (n=302)	Saw happening to someone	117	22.2
	Heard from someone	73	34.4
	Didn't experience	42	43.4

Table III. Shows the study also revealed, the experience of exposure to toxic chemicals by both personally and seeing it transpiring was the highest among 10-12 years of age members ($\chi 2 = 18.650$, $p < 0.05$). It was evident from the study that, the experience of sexual assault personally was the highest among 13-15 years age group followed by 10-12 years aged participants. The variety of this event by age was found significant statistically ($\chi 2 = 14.637$, $p < 0.05$). Experience of domestic accidents personally was highest among 16-18 years old orphans compared to other groups ($\chi 2 = 32.673$, $p < 0.05$). Experience of physical assault personally was highest within the same age group though this relation wasn't statistically significant. Furthermore, orphans aged from 10-12 years experienced sexual assault ($\chi 2 = 14.637$, $p < 0.05$) and physical assault through seeing it transpiring than other age groups that were evident from the study

Table III: Age of the participants and nature of experiencing events (N= 301)

Age group	Happened with oneself f(%)	Saw happening f(%)	Heard from someone f(%)	Didn`t experience f(%)	Total f(%)	Significance
Transportation accident						
10-12	12 (9.2)	71 54.6)	30 (23.1)	17 (13.1)	130 (100.0)	χ^2=5.729
13-15	10 (8.0)	54 (43.2)	35 (28.0)	26 (20.8)	125 (100.0)	df= 6
16-18	4 (8.7)	19 (41.3)	13 (28.3)	10 (21.7)	46 (100.0)	p= .454
Domestic accident						
10-12	29 (22.3)	51 (39.2)	41 (31.5)	9 (6.9)	130 (100.0)	χ^2=32.673
13-15	34 (27.2)	41 (32.8)	23 (18.4)	27 (21.6)	125 (100.0)	df= 6
16-18	23 (50.0)	15 (32.6)	2 (4.3)	6 (13.0)	46 (100.0)	p= .000
Physical assault						
10-12	36 (27.7)	40 (30.8)	31 (23.8)	23 (17.7)	130 (100.0)	χ^2 =5.628
13-15	42 (33.6)	30 (24.0)	23 (18.4)	30 (24.0)	125 (100.0)	df= 6
16-18	18 (39.1)	11 (23.9)	10 (21.7)	7 (15.2)	46 (100.0)	p= .466
Exposure to toxic chemicals						
10-12	13 (10.0)	40 (30.8)	33 (25.4)	44 (33.8)	130 (100.0)	χ^2 =18.650
13-15	6 (4.8)	25 (20.0)	35 (28.0)	59 (47.2)	125 (100.0)	df= 6
16-18	0 (0.0)	7 (15.2)	10 (21.7)	29 (63.0)	46 (100.0)	p= .005
Assault with a weapon						
10-12	3 (2.3)	29 (22.3)	45 (34.6)	53 (40.8)	130 (100.0)	χ^2 =6.109
13-15	5 (4.0)	29 (23.2)	37 (29.6)	54 (43.2)	125 (100.0)	df= 6
16-18	1 (2.2)	11 (23.9)	8 (17.4)	26 (56.5)	46 (100.0)	p= .411
Sexual assault						
10-12	7 (5.4)	32 (24.6)	30 (23.1)	61 (46.9)	130 (100.0)	χ^2 =14.637
13-15	7 (5.6)	19 (15.2)	35 (28.0)	64 (51.2)	125 (100.0)	df= 6
16-18	0 (0.0)	2 (4.3)	13 (28.3)	31 (67.4)	46 (100.0)	p= .023
Life threatening injury/illness						
10-12	42 (32.3)	34 (26.2)	35 (26.9)	19 (14.6)	130 (100.0)	χ^2 =5.433
13-15	41 (32.8)	32 (25.6)	27 (21.6)	25 (20.0)	125 (100.0)	df= 6
16-18	20 (43.5)	12 (26.1)	6 (13.0)	8 (17.4)	46 (100.0)	p= .490

DISCUSSION

This study which was conducted to assess the adverse childhood experiences among orphans who reside in different orphanages. It was a cross sectional study where 301 orphans participated from different orphanages in Chittagong and Dhaka city. According to this study, majority of them (44.9%) were between 10-12 years, 37.9 % were between 13-15 years and on the other hand 17.3 % orphans were aged between 16-18 years which was the minority group. In this study, male were 84% and female 16%. This study was done among the orphans who`s age were in the range of 10-18 years. Mean (± SD) age of this orphans were 13.31 ± 1.696 years. Study by Hermenau *et al.*, (2015) conducted a study on maltreatment in institution rearing children among 14 female orphans with mean± SD was 9.79± 1.45 years.[8] Gray et al., (2015) conducted a study on traumatic experiences among orphans in institutional and family-Based settings orphans

where 1063 was his sample size among whom 51.83 % were female and almost 48.16% male which was aimed to assess violence experiences among institutional cared orphans aged between 10-12 years.[9] Gray *et al.*,(2015) conducted their study between 6-12 years age range of orphans.[9] According to a study of Tadesse *et al.*,(2014) in Ethiopia on psychosocial wellbeing of orphan in orphanages where age range of the participant orphans was 10-17 years which almost coincides with this study.[10] However, variation in study findings may be due to variation of places, duration of study period. Only female orphanages are not easy to access and less available. Moreover, we can hardly get male and female orphans together in a very few orphanage in our country`s perspective. Maybe it is a reason of this disproportionate ratio of male and female orphans in this study. Maximum age limit was 18 as up to this year orphans are considered as so and after this age they are not allowed to stay in orphanages in our country.

In this study, among this 301 orphans, majority of this orphans lost one their parents (82%) than both of them (18%) where 210 (64%) orphans lost only their father/ paternal orphan, 37 (11.3%) lost their mother/maternal orphan and about 54 (16.5%) lost both of them. Orphans who loses both of their parents are forced by their fate to earn their livelihood rather than getting shelter in orphanages as they have none to take them in orphanages. Moreover, after losing their father, it becomes difficult for their mother to bear his/her expenses as father earns mostly in a family in our country`s perspective. Maybe it is a reason for what there are more single and paternal orphans in this study. This study included the data of the orphans of duration of their staying in orphanage. Here 20(6.1%) of them were staying for 1-5 years, 189(57.6%) for 6-10 years and 92(28.0%) orphans were staying for 11-15 years. Maximum duration was 15 years and minimum 5 years where mean (± SD) was 7.98 (± 2.231) years. Tadesse *et al.*, (2014) on orphans where study population should had at least 1 year experience of staying in orphanage.[10]

The study showed, experience of physical assault was the highest (30.2%) among them who responded this event happened with their own and 28.3% said they saw this event happening to someone and this experience wasn't associated with age. Again, 4.6% participants experienced sexual assault personally and maximum (26.1%) heard of this event happened to someone. The experience of sexual assault personally was the highest among 13-15 years age group followed by 10-12 years aged participants which was significant statistically. A similar study conducted by Gray et al., (2015) found 50.3% of 1053 children in institutional care across 5 countries experienced physical or sexual abuse with no differences by gender, but more abuse among the younger age groups.[9] Cristine *et al.*, (2015) conducted a longitudinal study where by using Life Event Checklist assessed different adverse experiences. They found more than half of children in institutions (50.3% [95% CI=42.5, 58.0]) and in family-based care (54.0% [95% CI=50.2, 57.7]) had experienced physical or sexual abuse by age 13 out of 1,357 institution-dwelling and 1,480 family-dwelling orphaned and separated children.[11]

In this study, orphans said they experienced threatening or injury by weapon, among whom 3 % of them experienced through happening with themselves, 23 % by seeing while occurred with others and 30.3% learned from someone about this event and in case of 43.8 % orphans this event didn't happen. Maximum orphans (43.8 %) didn't experienced this event and minimum (6%) orphans experienced it personally. Experience of assault with a weapon one way or another didn't have statistical significance. Possible explanation can be as they reside at orphanage and little chance of involvement in political, criminal activities as well as victimization of terrorism where firearms, knife, gun are usually used. Almost 22.2% of orphans saw someone to suicide or homicide but 34.4% of orphans had learnt about that from someone close to him/her and 43.4% of them didn't experience this event. It is very likely that they share stories of experiencing of suicide or homicide that they witnessed or learnt from someone like neighbors or people around them. Maybe this a cause for what 34.4% orphans said they learnt of this event from someone else rather than seeing it by own self.

CONCLUSIONS

Experience of life-threatening illness/injury that required hospitalization was the most frequent event revealed by this study. The experience of physical abuse had the second-highest frequency and was pretty much incessant in all age groups.

LIMITATIONS

1. This study was confined to metropolitan orphanages of two urban areas because of time limitations. So the result probably won't be generalized.
2. Male and female participants were disproportionate due to the difficulty of access to the female orphanages.

RECOMMENDADTION

Further studies are required in bigger degree to survey their actual need with the goal that specific strategies can be embraced explicitly to defeat the deterrent for guaranteeing their privileges and benefit.

REFERENCES

1. UNICEF for every child: Orphans. accessed at: https://www.unicef.org/media/orphans [Cited on 2019 June 26]
2. Radenkovic M. 11-countries-with-highest-orphan-population. [Internet]. New Jersey, USA: January 11, 2016. Available from: https://www.insidermonkey.com/blog/ -
3. Allen E, Orme T, McCarter R, Grossman L. Self-reported depressive symptoms in school-age children at the time of entry into foster care. Ambulatory Child Health. 2000; 6(1):45-57
4. Shiferaw G, Bacha L, Tsegaye D. Prevalence of Depression and Its Associated Factors among Orphan Children in Orphanages in Ilu Abba Bor Zone, South West Ethiopia. Psychiatry Journal. 2018 October 15. Available from: https://doi.org/10.1155/2018/6865085
5. Kumsta R, Kreppner J, Rutter M, Beckett C, Castle J, Stevens S, Sonuga-Barke EJS. Deprivation-specific psychological patterns. Monographs of the Society for Research in Child Development. 2010; 75: 48–78. Available from: http://dx.doi.org/10.1111/j.1540-5834.2010.00550.x
6. National Data Archive on Child Abuse and Neglect (NDACAN), (Ed.), National child abuse and neglect data system (NCANDS) child file, FFY 2011, NDACAN dataset number 169, user's guide and codebook (Brofenbrenner Center for Translation Research ed.). Ithaca, NY: Cornell University.2011 Available from: https://pdfs.semanticscholar. org/c606/099735c52b048d95a3c9e0f029d9d22496a5.pdf
7. Glenn D.WolfnerRichard J.Gelles. A profile of violence toward children: A national study. Child Abuse & Neglect. 1993 Mar-Apr;17(2):197-212
8. Hermenau K, Kaltenbach E, Mkinga G, Hecker, T. Improving care quality and preventing maltreatment in institutional care – A feasibility study with caregivers. Frontiers in Psychology. 2015; 6:1–7. doi:10.3389/fpsyg.2015.00937.
9. Gray CL, Pence BW, Ostermann J, Whetten RA, O'Donnell K, Thielman NM, et al. Prevalence and incidence of traumatic experiences among orphans in institutional and family-based settings in 5 low- and middle-income countries: a longitudinal study. Glob Health Sci Pract. 2015; 3(3):395-404.
10. Tadesse S, Dereje F, Belay M. Psychological wellbeing of orphan and vulnerable children at orphanages in Gondar Town, North West Ethiopia. Journal of Public Health and Epidemiology. 2014; 6:293-301.
11. Christine L Gray, Brian W Pence, Jan Ostermann, Rachel A Whetten, Karen O'Donnell, Nathan M Thielman, Kathryn Whetten. Prevalence and Incidence of Traumatic Experiences among Orphans in Institutional and Family-Based Settings in 5 Low- and Middle-Income Countries: A Longitudinal Study. Global Health: Science and Practice. Sep 2015; 3 (3) 395-404; DOI: 10.9745/GHSP-D-15-00093

Original Article

Effects of Iron and Amloki (Emblica Officinalis) on Serum Zinc Level in Anaemia with Pregnancy

*Akter T[1], Akter QS[2], Lisa SH[3], Sultana MA[4], Sultana F[5], Nahar S[6], Suma SA[7], Kamal ST[8], Habib TB[9], Rahman F[10]

Abstract

Pregnancy is associated with several trace elements deficiency in developing countries. Supplementation of iron in iron deficiency anaemia (IDA) has several side effects including alterations of serum zinc level. Traditionally, amloki is used as a well known supplement in pregnancy, which is rich in trace elements. To determine the effects of iron and amloki on serum zinc level in IDA with pregnancy. The study was a non blind, non random sampling interventional type of clinical trial. This study was performed in the Department of Physiology, Dhaka Medical College, Dhaka on 43 pregnant women between 13th to 20th weeks of gestation with IDA from July 2016 to June 2017. They were recruited from Outpatient Department of Obstetrics and Gynaecology of Dhaka Medical College Hospital. Anaemic pregnant women supplemented with oral iron and amloki were considered as study group (A) and control group (B) were with only iron supplementation for 45 days. Serum zinc level was estimated in the laboratory of the Department of Soil, Water and Environment, University of Dhaka, Bangladesh. For statistical analysis, Paired Student's 't' test and Unpaired Student's 't' test were considered using SPSS 22.0 version. Significant decrease ($p<0.001$) of serum zinc level was observed after intervention of iron in both groups. In this study, there was no significant difference in serum zinc level in between study and control group. It can be concluded that oral iron supplementation causes decrease in serum zinc level in IDA with pregnancy. Amloki shows no significant role in preventing decrease of serum zinc level in this study. Emblica officinalis (amloki) is traditionally used to treat iron deficiency anaemia. It can increase haemoglobin concentration and decrease side effects of iron supplementation.

Keywords: *Iron deficiency anaemia, pregnancy, amloki, zinc.*

1. *Dr. Tahmina Akter, M.Phil (Physiology)Lecturer (Physiology) Dhaka Medical College and Hospital (DMCH), Dhaka. Email: tahmina.runa.akter1@gmail.com
2. Dr. Qazi Shamima Akther. M.Phil, Professor and Head, Department of Physiology, DMCH, Dhaka.
3. Dr. Saima Haque Lisa, M.Phil, Assistant Professor, Department of Physiology, Parkview Medical College and Hospital, Sylhet.
4. Dr. Mst. Ariza Sultana, M.Phil, Assistant Professor, Department of Physiology, National Institute of Neurosciences and Hospital, Dhaka.
5. Dr. Farhana Sultana, M.Phil. Assistant Professor (CC), Department of Physiology, Dhaka Community Medical College, Moghbazar, Dhaka.
6. Dr. Sharmin Nahar, M.Phil. Assistant Professor, Department of Physiology, DMCH, Dhaka.
7. Dr. Sunjida Akter Suma, M.Phil. Lecturer, Department of Physiology, DMCH, Dhaka.
8. Dr. Sayeda Tasnim Kamal, M.Phil. Lecturer, Department of Anatomy, DMCH, Dhaka.
9. Dr. Tamanna Binte Habib, M.Phil. Lecturer (Physiology), DMCH, Dhaka.
10. Dr. Farhana Rahman, M.Phil. Lecturer (Physiology), DMCH, Dhaka. Email:

**For correspondence*

INTRODUCTION

Qualitative or quantitative deficiency of haemoglobin or red blood cells in circulation is called anaemia which leads to decreased oxygen carrying ability of blood to organ and tissues.[1] Iron deficiency anaemia (IDA) is the most common type and considered for one-half of anaemia cases. Low iron stores in the body causes decreased red blood cell production. [2,3]

In organisms after iron, zinc is the second most important transitional metal. Zinc is the only metal presents in all enzyme classes and required for catalytic activity of many enzymes. For normal growth and development of pregnancy, childhood and adolescence zinc is essential. Even at low concentration it is an effective antimicrobial agent. For proper sense of taste and smell zinc is required. Dietary zinc is absorbed from the duodenum to blood through DMT1. In blood, zinc is transported by albumin (60%) and transferrin (10 %). Zinc is excreted through

Pregnancy with IDA is usually associated with decreased serum zinc level. Serum zinc reduces due to increased demand and haemodilution in pregnancy, and also for formation of zinc-protoporphyrin due to deficiency of iron.[6,7] There are some interactions between iron and zinc during absorption and transport in the blood. The divalent metal transporter1 (DMT1) is the common transporter for both ferrous iron and zinc in the proximal small intestine from lumen to the enterocyte.[8] So, dietary intake of iron can influence the absorption of zinc. Different iron preparations are used to treat IDA in pregnancy which can lead to zinc deficiency.[9]

Indian mythology believes amloki as the first tree to be created in the universe. It is a medium sized tree. Leaves are small, oblong, narrow and pinnately arranged. Fruits are globose ½ - 1 inch in diameter with central depression, fleshy and 6-lobed, with 6 small seeds. The tree is 30-40 ft in height and circumference of stem usually extends up to 3-6 ft and rarely up to 9 ft. Stem is usually curved, branches are strong and extended. Bark is thin and brownish in colour. Leaves resemble to tamarind leaves. Raw fruits are green in colour and become greenish yellow on ripening. Tree is known as *Phyllanthus emblica*, Emblica officinalis (latin name) from the Family: Euphorbiaceae.[10,11,12]

In India, so many researches have done on Emblica officinalis as an important ingredient of different ayurvedic preparation to cure IDA in pregnancy. Most of these researches have proved that Amloki has the efficacy to increase haemoglobin level and improves iron status during pregnancy.[13,14,]

Amloki is renowned for its nutritional elements, which is rich in polyphenols, minerals (0.7%) , considered as one of the richest source of vitamin C.[11,12] Many researchers have found presence of significant amount of zinc and other trace elements in amloki.[15,16] So, The study was undertaken to observe the effect of iron and amloki supplementation on serum zinc level in iron deficient pregnant women.

MATERIAL AND METHODS

On 43 pregnant women with IDA, this prospective interventional type of clinical trial was done. This study conformed to the Helsinki Declaration and was approved by the concerned departments, Research Review committee and Ethical Review Committee of Dhaka Medical College, Dhaka. After, fulfilling all the ethical aspects this study was performed in the department of Physiology of Dhaka Medical College. Subjects were in between 18 to 36 years having gestational age of 13th to 20th weeks. They were recruited from the outpatient department of Obstetrics and Gynaecology of DMCH, Dhaka on the basis of inclusion and exclusion criteria. Subjects were explained about the nature, purpose and benefit of the study in details. They were counselled for voluntary participation and allowed to withdraw from the study whenever they feel like. Informed written consent was taken from the participants. All the informations were recorded in a prefixed questionnaire. A detailed of pregnant females including socio economic condition, food habit, parity, menstrual history were taken along with haematological examination. They were free from any known cardiac, renal, liver and endocrine disorders. Compliance to the supplementation was monitored by regular telephonic communications. Amloki capsules and iron tablets were given in boxes for 45 days and participants were encouraged to continue the supplied medicine daily. Serum zinc level was estimated in the laboratory of the Department of Soil, Water and Environment, University of Dhaka, Dhaka. This parameter was studied 2 times in all subjects of control and study groups, i.e. at the beginning of the study (baseline) and after 45 days of study period. Diet and physical activity of the patients remained unchanged during the course of study. Clinically diagnosed and confirmed (Hb 8 to <11 gm/dl) patients of iron deficiency anaemia were selected and divided into two groups, 25 pregnant women with IDA, were supplemented with oral amloki capsules (1.072 gm) thrice daily and iron tablet [ferrous fumarate (200mg) + folic acid (0.02 mg)] once daily for 45 days, were considered as study group (Group A). Again, 21 pregnant women with IDA, supplemented with only iron tablet once daily for 45 days were considered as control group (Group B). One subject discontinued the study due to reluctance in group A after two weeks, while 2 subjects from control group left Dhaka after 4 weeks of study. So, finally 24 subjects of study and 19 subjects of control groups completed the study.

The amloki capsule (Amlahills) was authentified by the Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Dhaka, which was manufactured by Isha Agro Developers PVT.LTD, India.

Paired Student's't' test and Unpaired Student's't' test were performed using SPSS Version 22.0 for statistical analysis. Mean ± SD were used for data expression. The *p* value < 0.05 was taken as level of significance.

RESULTS

The results are shown in table I and Figure 1. In this study, the mean serum zinc level was almost similar in A_1 and B_1 groups, and no statistically significant differences were observed. In group A_2, the serum zinc (p<0.001) level was found significantly decreased in comparison to that of A_1. Again, in group B_2, the serum zinc (p<0.001) level was found significantly decreased in comparison to that of B_1. While, in group A_2, decreases in serum zinc (p=0.286) was not statistically significant in comparison to that of B_2.

Table-I shows the serum zinc level in respective groups. Results are shown as mean ± SD. Paired t- test was considered for comparison within groups and unpaired t- test to compare between groups. The significance of the tests were calculated & *p* value < 0.05 was considered as level of significance.

Table I Serum zinc level in respective groups (n=43)

Parameter	Groups			
	A_1 (24)	A_2 (24)	B_1 (19)	B_2 (19)
Zinc(µg/dl)	57.18 ± 12.03	54.28 ± 11.08	53.30 ± 16.17	50.09 ± 14.30
Statistical analysis				
Parameter		*p* value		
	A_1 vs A_2	A_1 vs B_1	B_1vs B_2	A_2 vs B_2
Zinc	<0.001	0.372	<0.001	0.286

N= Total number of subjects, n = number of subjects in each group;

A_1: Study group (At baseline)

A_2: Study group (After intervention with Amloki and iron tablet)

B_1: Control group (At baseline)

B_2: Control group (After intervention with iron tablet)

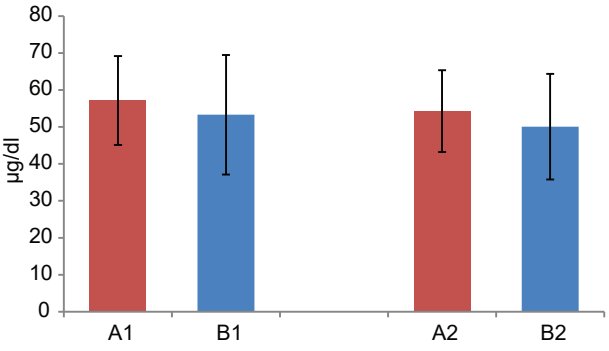


Fig.- 1: Mean serum zinc level in different groups (n=43)

N= Total number of subjects

A_1: Study group (At baseline)

A_2: Study group (After intervention with amloki and iron tablet)

B_1: Control group (At baseline)

B_2: Control group (After intervention with iron tablet)

DISCUSSION

In this study, the decrease in serum zinc (p=0.286) level was not statistically significant in amloki and iron supplemented group in comparison to that of only iron supplemented group. But decrease in serum zinc level (p<0.001) was found statistically significant in both groups in comparison to their baseline value.

O´Brien et al. (1999) also found no significant difference in serum zinc level in between (iron + zinc) supplemented group and only iron supplemented group.[9] They found significant decrease in serum zinc level in iron supplemented group in comparison to without iron supplemented group. Different researchers also found that, supplementation of iron during pregnancy causes decreased zinc absorption.[17,18]

In pregnancy, serum zinc level decreases due to increased demand and hemodilution. Normally, iron bind with protoporphyrin IX to form haem. But, in case of iron deficiency, zinc replaces iron and combines with protoporphyrin IX. This combination further decreases serum zinc level in pregnant women with iron deficiency anaemia.[19,6,20]

Some researchers suggested that, supplementation of iron can inhibit the absorption of zinc. Divalent metal

transporter 1 (DMT1) in the duodenal enterocyte, is the common transporter for iron and zinc. These three elements compete to bind with the same transporter. When iron is supplemented, there is increased iron concentration at the site of absorption. Increased concentration of iron causes competitive displacement of zinc and copper from DMT1. Again, exposure to supplemental iron leads to down regulation of DMT1. That will subsequently decrease zinc absorption.[21,7] In this study, no significant differences were observed in serum zinc level in between amloki with iron supplemented group and only iron supplemented group, after 45 days of supplementation. Though amloki contain significant amount of zinc, it could not prevent the decrease of serum zinc level in iron deficient pregnant women. The cause may be due to improper iron and zinc ratio, as iron-zinc ratio > 2:1 can impair zinc absorption. Again, supplementation of iron during pregnancy may decrease zinc absorption.[9]

Though, the actual mechanisms responsible for decreased serum zinc by oral amloki supplementation cannot be explained from the present experiment as the phytochemical study of amloki powder was not done.

CONCLUSIONS

The results concluded that oral iron intervention for the treatment of IDA in pregnancy causes decreased serum zinc level. In this study, Amloki shows no significant effect on serum zinc level.

ACKNOWLEDGEMENT

The authors acknowledge Department of Pharmaceutical Chemistry, Faculty of Pharmacy and Department of Soil, Water and Environment, University of Dhaka for their kind cooperation.

REFERENCES

1. Roy A, Dwivedi M. Dhatrilauha: right choice for iron deficiency anemia in pregnancy. Ayu 2014; 35(3): 283-288.
2. Short MW, Domagalski JE. Iron deficiency anemia: evaluation and management. Am Fam Physician 2013; 87(2):98-104.
3. Layeeq S, Thakar AB. Clinical efficacy of amloki rasayana in the management of pandu (iron deficiency anemia). Ayu 2015; 36(3): 290-297.
4. Ugwuja EI, Ejikeme BN, Ugwu NC, Obido O. A comparative study of plasma trace elements (copper, iron and zinc) status in anaemic and non-anaemic pregnant women in Abakaliki, Nigeria. Online J of Health Allied Sci 2011; 10(2):1-3.
5. Osredkar J, Suster N. Copper and zinc, biological role and significance of copper/ zinc imbalance. J Clinic Toxicol 2011; S3(001): 1-18.
6. Upadhyaya C, Mishra S, Ajmera P, Sharma P. Serum iron, copper and zinc status in maternal and cord blood. Indian J of clinical Bio Chem 2004; 19(2): 48-52.
7. Arredondo M, Martinez R, Nunez MT, Ruz M, Olivers M. Inhibition of iron and copper uptake by iron, copper and zinc. Biol Res 2006; 39:95-102.
8. Nelson JC, Westwood M, Allen KR, Newton KE, Barth JH. The ratio of erythrocyte zinc-protophyrin to protophyrin IX in disease and its significance in the mechanism of lead toxicity on haem synthesis. Ann Clin Biochem 1994; 35: 422-426.
9. O´Brien KO, Zavaleta N, Caulfield LE, Yang DX, Abrams SA. Influence of prenatal iron and zinc supplements on supplemental iron absorption, red blood cell iron incorporation, and iron status in pregnant Peruvian women. Am J Clin Nutr 1998; 69: 509-15.
10. Govind P, Pandey SP. Phytochemical and toxicity study of Emblica officinalis (Amla). Int Res J Pharmacy 2011; 2(3): 270-272.
11. Yadav V, Duvey B, Sharma S, Devi B. Amla (Emblica officinalis)- medicinal food and pharmacological activity. Int J Pharm Chem Sci 2014; 3(3): 616-619.
12. Jain R, Pandey R, Mahant RN, Rathore DS. A review on medicinal importance of Emblica officinalis. Int J Pharm Sci Res 2015; 6(1): 73-84.
13. Khot BM, Patil AJ, Kakad AC. Comparative clinical study of dhatri lauha and navayasa lauha in garbhini panduroga with reference to anemia in pregnancy. Int Org Sci Res J Dental Med Sci 2013; 11(1): 28-33.
14. Ramadevi G, Jonah S, Prasad UN. A clinical study on the effect of dhatri lauha in garbhinipandu (iron deficiency anaemia). Int. J. Res. Ayurveda Pharm 2014; 5(6): 708-712.
15. Singh NKS, Devi CB, Singh TS, Singh NR. Trace elements of some selected medicinal plant of Manipur. Indian J Nat Prod Resour 2009; 1(2): 227-231.
16. Kumar VN, Vibha, Ashwani K. A comparative study of heavy metals in Emblica officinalis, Phyllanthus

emblica and Azadirachta indica. Int Res J Biological Sci 2013; 2(8):16-19.

17. Hambidge KM, Krebs NF, Jacobs MA, Favier A, Guyette L, Ikle DN. Zinc nutritional status during pregnancy: a longitudinal study. Am J Clin Nutr 1983; 37: 429-442.
18. Fung EB, Ritchie LD, Woodhouse R, Roehl R, King JC. Zinc absorption in women during pregnancy and lactation: a longitudinal study. Am J Clin Nutr 1997; 66:80-88.
19. Hastka J, Lasserre JJ, Schwarzbeeck A, Hehlmann. Central role of zinc protopophyrin in staging iron deficiency. Clin Chem 1994; 40(5):768-773.
20. Ozhan O, Erdem N, Aydogdu I, Arkurt A, Kuku I. Serum zinc levels in iron deficient women: a case-control study. Turk J Hematol 2016; 33: 156-158.
21. Arredondo M, Munoz P, Mura CV, Nunez MT. DMT1, a physiologically relevant apical Cu1+ transporter of intestinal cells. Am J Physiol 2003; 284(C):1525-1530.

Original Article

Stress and Coping Status among Caregivers of Major Psychiatric Patients

Tasmin S,[1] Sultana H,[2] Haque A,[3] Islam MM,[4] Alam MR[5], Halim KS[6], *Abbas MG[7]

Abstract

Caregivers play an important role for the treatment and wellbeing of the psychiatric patients. Constant caregiving role exert stress on the caregiver which is usually handled by them. This cross-sectional study aimed to assess the level of stress and coping status among conveniently selected 171 care givers of major psychiatric patients at National Institute of Mental Health (NIMH), Dhaka. Data was collected by the pre-tested semi-structure questionnaire blended with perceived stress and coping scale through face to face interview. Average coping status was found in most of the (70%) care givers; good coping status was found in more than one fifth (21%) of the caregivers and few (02%) caregivers had poor coping status. Stress and coping status was found ($p<0.05$) significantly related. This study finds the perceived stress among all the caregivers under study population; where high level of stress were perceived by more than three fourth of the caregivers and moderate to low level of stress were perceived by most of the caregivers. Caregiver-centric interventions, services and programs are recommended to plan and implement so that they should not compromise their caregiving work.

Keywords: *Stress, coping status, caregiver, psychiatric patient.*

1. Dr. Sinthia Tasmin, Lecturer, Institute of Public Health, Mohakhali, Dhaka.
2. Dr. Hafiza Sultana, Professor and Head, Department of Health Education, National Institute of Preventive and Social Medicine (NIPSOM), Mohakhali, Dhaka.
3. Dr. Aysha Haque, Lecturer, Department of Health Education, NIPSOM, Mohakhali, Dhaka
4. Dr. Md. Moinul Islam, Resident Surgeon, Department of Neurosurgery, Dhaka Medical College (DMC)
5. Dr. Mohammad Rashidul Alam, Assistant Professor (Community Medicine), Department of Health Education, NIPSOM, Mohakhali, Dhaka
6. Prof. Dr. Kazi Shafiqul Halim, Professor and Head, Department of Epidemiology, NIPSOM, Mohakhali, Dhaka
7. *Dr. Md. Golam Abbas PhD, Assistant Professor, Department of Occupational and Environmental Health (OEH), NIPSOM, Mohakhali, Dhaka. Email: abbasgolam@yahoo.com

*Corresponding author

INTRODUCTION

Mental disorder accounts for 13% global burden of disease.[1] About 1 in 17 people worldwide suffers from a serious mental illness.[2] Depression, psychosis, schizophrenia and bipolar disorder are the four out of six leading causes for the years lived with disability.[3] According to the World Health Organization (WHO), mental illness is found in at least one member of any one of the four families which results in family members providing care towards their sick member as a primary caregiver.[3] Although there is no valid data about the number of people suffering from the major psychiatric condition, the prevalence of mental disorder is varied from 6.5% to 31% and 13.4% to 22.9% respectively among adults and children in Bangladesh .[1]Bangladesh has been trying to provide institutionalized based health-care services to the mentally ill population since its independence. Of these, establishment of National Institute of Mental Health (NIMH) in 2000, and adoption of a mental health policy, strategy and plan in 2006 is significant. Although it was well known that appropriate medication is the principal element for optimizing a patient's function, it is also the case that the quality of care provided by family caregivers is important.[4]

A family caregiver may be a family member, a parent, a spouse, a son, a daughter, or other relatives or friends.[5] The caregiver not only stays with the patients but also allocates time to take proper care of them.[6] Uninterrupted caregiving can cause caregivers to create stress or strain, and lower levels of physical and mental well-being, and limit the caregivers' ability to perform their caregiving tasks. It is evident that moderate to severe stress is developed among caregivers of psychiatric patients.[2] Consequently, stress can lead to deterioration of physical and mental health. Mant et al (2005) state that caregivers are at high risk in developing physical and mental illness because of having excessive depression and stress resulting from performing psychiatric patients' daily activities.[7] Prior studies have shown that the development of depression among caregivers is a very common mental illness. [8, 9] In addition to this, anxiety and stress symptoms are also experienced by the caregivers.[10] Lack of motivation, less or nil financial support and social isolation have been described as the most problematic area for caregivers.[11] Because of the deficiency of social, psychological and financial support, the quality of life of caregivers can be negatively affected; as a result, their effectiveness as caregivers is disrupted which can result in deterioration of the health of the sick family member.

Coping is understood as the process of managing demands (external or internal) that are appraised as taxing or exceeding the resources of the person which is seen as a process involving at least two stages: Primary appraisal (is this something to bother about?), and secondary appraisal (what can I do about it?).[12] It is proposed to serve two distinct purposes: To do away with the problem (i.e., problem-focused coping), and to regulate emotional reactions (emotion-focused coping).[13] Previous studies have not used the same assessment scale to identify coping strategies; as a result, it is difficult to compare their results with each other. A study using family coping questions found that more than half of caregivers adopted information, positive communication, patient social involvement, and resignation as their coping strategies.[14] Social involvement of the patient and positive communication as coping strategies were most frequently reported by both key relatives and other relatives in another study based on the family coping questionnaire.[15] On the other hand, a study used a combination of three coping frameworks namely cognitive or behavioral, social or non-social, problem-centered or emotion-centered suggesting that relatives often use behavioral coping responses more than cognitive, more socially than non-social and more emotionally than problem-focused coping strategy.[16] Other studies have reported most frequent use of problem focused coping.[17] self-controlling, positive reappraisal and escape-avoidance coping .[18] In Bangladesh, no studies have been conducted so far in regards to the coping status and strategies among the caregivers of psychiatric patients.

Caregivers play a significant role in the treatment and wellbeing of the patient. When caregivers suffer from stress, it may be difficult for the patient to recover from illness. If the caregivers are not being able to cope with the stress, the situation becomes complicated. In our country almost, all psychiatric illness patients depend on the care provided by their family members. Every patient needs a compulsory all-time caregiver from their family during his or her hospital stay especially in public hospitals. This study has aimed to provide policy makers and healthcare providers with some essential information that will help planning programs and services to alleviate the suffering of caregivers and build support for them that will ultimately contribute to the recovery of mental patients.

MATERIALS AND METHODS

This cross-sectional study was conducted among the caregivers of major psychiatric patients of National Institute of Mental Health (NIMH), Dhaka lasting from 1st of January to 31st of December, 2019. The inclusion criteria for psychiatric patients was the duration of disorder >= 6 months. Caregivers whose age was> = 18 years, and who spent at least 30 minutes a day and ≥2 months with a psychiatric patient were included in the study. On the other hand, smokers, diabetic, psychiatric and physically ill, and unwilling caregivers were excluded from the study. In order to select the sample size of the study, a standard equation was used .[19] Al though a total of 179 caregivers were scheduled to be interviewed, 171 were set as the final number due to the reluctance of caregivers to participate in the study. Data were collected through a semi-structured questionnaire blended with perceived stress and coping scale. This questionnaire contained four parts such as socio-demographic status of caregivers, caregiving and care recipient related questions, caregiver's stress and coping information. Caregiver stress related question by using perceived stress scale PSS 10 version scale used. PSS Scale 10 version comprises 10 Question. Here cut off point is 0 = never,

1=almost never,2=sometimes,3=Fairly often,4=very often Here 0-13= Low stress, 14-26= moderate stress, 27-40= High perceived stress. Caregiving coping related question by using coping scale. Coping scale 13 question. Each answer category was assigned a value from 4 to 1. The total score can be a sum or mean of all items .we used Z-score of the in our analyses. Higher score indicates higher levels of coping. Here 4= Mostly true about me, 3= somewhat true about me, 2= A little true about me, 1= Not true about me. Score 13-25 poor coping, 26-38 average, 39-52 good coping. Prior to the implementation of questionnaire, a pretest was carried out at the Dhaka Medical College to check the validity and credibility of the questionnaire. A face to face interview was taken from the caregivers of mentally sick patients at the ward or cabin of NIMH after the final modification of the questionnaires. After receiving written consent from the caregivers, the interview proceeded. The data were checked for consistency and completeness and inserted, cleaned and recorded in the SPSS version 20 before moving to analysis. Descriptive statistics of frequency, percentage, means, medians, mode, standard deviation, tables and graphs were used to summarize the data. Chi-square ($\chi 2$) test was used to explore the association and correlation between variables. A P-value of<0.05 was considered as significant. Before commencing the study, the necessary approval was taken from the ethical committee of the National Institute of Preventive and Social Medicine (NIPSOM). Further, permission was also sought from the authority of the NIMH before implementing the interview towards the caregivers of major psychiatric patients.

RESULTS

Table I Shows illustrates the socio-demographic status of the caregiver. Among them, 90.6 % caregivers mentioned their religion as Islam. 28.7 % of caregivers were over 47 years, representing the higher age group of caregivers among other age groups. The Mean ± SD of caregivers' age was 40.09(±13.31) years. Among the caregivers, the percentage of female and male was 74% and 26 % respectively. About

33% of caregivers identified them as illiterate, while only 4% caregivers had a master's degree. 57.9% of participants cited housewives as their occupation which was the highest among other occupations of caregivers. At the time of the interview, 77.2 percent of the participants were married and 65% were living as a nuclear family. Further, 43.9% of caregivers monthly family income was <=10,000.

Table I: Socio-demographic status of caregiver (n=171)

	Variables	Percentage (%)
Age group (in years)	18-27	19.3
	28-37	24.6
	38-47	27.5
	>47	28.7
	Mean ± SD 40.09(±13.31) years	
Gender	Male	26
	Female	74
Educational status	Illiterate	33
	Primary	22
	Secondary	24
	Higher Secondary	8
	Honor's	9
	Master's	4
Occupation	Housewife	57.9
	Service holder	18.7
	Business	6.4
	Farmer	5.3
	Student	5.3
	others	6.4
Marital Status	Unmarried	14.6
	Married	77.2
	Separated	1.2
	Widow/Widower	7.0
Family type	Nuclear	65
	Joint	35
Family Income	<=10,000	43.9
	10,001-20,000	32.2
	20,001-30,000	14
	>30,001	9.9
Relationship with the patients	Husband/wife	18.7
	Son/daughter	49.7
	Son/daughter in law	2.9
	Siblings	19.9
	Brother/sister in law	3.5
	Other	5.3
Religious status	Muslim	90.6
	Hindu	9.4

Table II: Shows it is noticed that complete independence with no longer was identified by the participants of 53.8% in eating, 48.5% in daily activities and 64.3% in bowel/bladder, while at eating 4.7%, at daily activities 4.7% and at bowel/bladder management 5.3% of respondents had required minimal assistance with helper.

Table II : Activities related to caregiver and care recipients

Activities related to caregiver and care recipients	Percentage
Eating	
Total assistance with helper	7.0
Moderate assistance with helper	9.4
Minimal assistance with helper	4.7
Supervision with helper	25.1
Complete independence with no longer	53.8
Daily activities	
Total assistance with helper	6.4
Moderate assistance with helper	9.4
Minimal assistance with helper	4.7
Supervision with helper	31.0
Complete independence with no longer	48.5
Bowel/bladder management	
Total assistance with helper	3.5
Moderate assistance with helper	6.4
Minimal assistance with helper	5.3
Supervision with helper	20.5
Complete independence with no longer	64.3

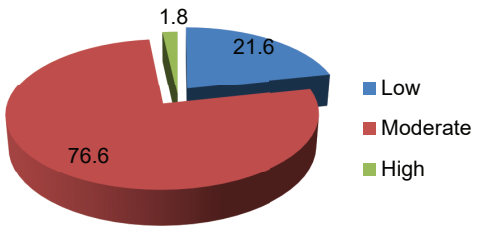


Figure 1 : Stress percentage of different levels considered by the caregiver (n=171)

Figure 1 illustrates the stress percentage of different levels considered by the caregiver. It is seen that low, moderate, and high levels of stress were perceived by 21.6%, 76.6%, and 1.8% of caregivers respectively.

Table III: Shows the caregivers previously employed were 20 (11.7%), had to leave the job 13 (7.6%) & took financial support 5 (2.9%). Mean duration of caregiving (months) 45.76 months (±SD 59.38) & Mean caregiving time was (hours/day) 18.56 (± SD 8.07).

Table III: Distribution of caregiver their caregiving related information (n=171)

Attributes	Frequency	Percentage
Caregiver employed previously	20	11.7
Caregiver had to leave the job	13	7.6
Financial support	5	2.9
Caregiving duration (months)	45.76±59.38	
Caregiving time (hours/day)	18.56±8.07	

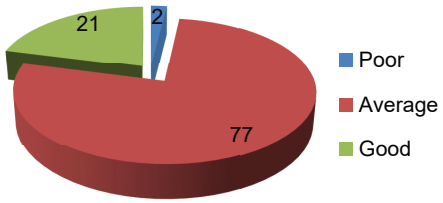


Figure 2 : Percentage of caregivers coping status

The pie chart above presents the status of the caregiver in terms of coping as a percentage (Figure 2). Most of the participants' (77%) coping status was average followed by good (21%) and poor (2%).

Table IV: Shows the p-value for age was (0.241) followed by the marital status (0.241), educational status (0.122) and income level (0.044). Since income level's p-value was less than 0.05, representing it is as statistically significant. Therefore, income level has an association with the stress.

Table IV: Association between socio-demographic status and perceived stress of caregiver (n=171)

Variables	Low stress	Moderate Stress	High stress	χ2 Value	P-value
Age groups (years)	N (%)	N (%)	N (%)		
18-27	6 (16.2)	25(19.1)	2(66.7)		
28-37	8(21.6)	33(25.2)	1(33.3)	6.907	0.241
38-47	8(21.6)	39(29.8)	0(0.0)		
>47	15(40.6)	34(26.0)	0(0.0)		
Educational status					
Illiterate	9 (24.3)	49 (37.4)	0 (0.0)		
Primary	8 (21.6)	27 (20.6)	0 (0.0)		
SSC	7 (18.9)	28 (21.4)	1 (33.3)	13.2	0.122
HSC	4 (10.8)	11 (8.4)	1 (33.3)		
Graduation	5 (13.5)	12 (9.2)	0 (0.0)		
Post graduation	4 (10.8)	4 (3.1)	1 (33.3)		
Monthly Income (BDT)					
<10,000	14(37.8)	61(46.6)	0(0.0)		
10,001-20,000	10(27.0)	44(33.6)	1(33.3)	10.685	0.044
20,001-30,000	8(21.6)	16(12.2)	0(0.0)		
>30,000	5(13.5)	10(7.6)	2(66.6)		

Table V shows the association between socio-demographic and coping status. The p-value for educational status, profession, income level, and type of family was 0.235, 0.070, and 0.085 respectively. As none of the variables' p-value was lower than 0.05, therefore, there is no association between these with the coping status.

Table V: Association between socio-demographic and coping status (n=171)

Variables	Poor Coping	Average Coping	Good Coping	χ2 Value	P-value
	N (%)	N (%)	N (%)		
Educational status					
Illiterate	1 (50.0)	45 (33.3)	12 (35.3)		
Primary	0 (0.0)	28 (20.7)	7 (20.6)		
SSC	0 (0.0)	25 (18.5)	11 (32.4)	11.57 *	0.235
HSC	0 (0.0)	15 (11.1)	1 (2.9)		
Graduation	0 (0.0)	14 (10.4)	3 (8.8)		
Post graduation	1 (50.0)	8 (5.9)	0 (0.0)		
Monthly Income (BDT)					
<10,000	0 (0.0)	60 (44.4)	15 (44.1)	9.996	0.070
10,001-20,000	0 (0.0)	43 (31.9)	12 (35.3)		
20,001-30,000	0 (0.0)	18 (13.3)	6 (17.6)		
>30,000	2 (100.0)	14 (10.4)	1 (2.9)		
Family Type					
Nuclear	2 (100.0)	91 (67.4)	18 (52.9)	3.174	0.085
Joint	0 (0.0)	44 (32.6)	16 (47.1)		

Table VI shows 50% (n=1) had poor coping, 23.7 % (32) had average coping and 11.8% (4) had good coping status among the respondents having low stress. In contrast, 0.0% (0), 74.8% (101) and 88.2% (30) moderately stressed respondents had represented poor; average and good coping status respectively. Respondents having high perceived stress had 50% (1) poor coping, 1.5% (2) had average coping and 0.0% (0) had good coping status. This difference was statistically significant (p value: 0.009). So there was an association between level of stress and coping status

Table VI: Relationship between stress and coping status (n=171)

Stress Level	Coping			χ^2 Value	p-value
	Poor	Average	Good		
Low stress	1 (50.0)	32 (23.7)	4 (11.8)	12.669	0.009*
Moderate stress	0 (0.0)	101 (74.8)	30 (88.2)		
High perceived stress	1 (50.0)	2 (1.5)	0 (0.0)		

DISCUSSION

Current study found that 49 (28.7%) of caregivers aged over 47 years followed by 47(27.5%), 42 (24.6%), and 33 (19.3%) within the age group 38-47years, 28-37 years, and 18-27 years respectively. Unlike this finding, 45.9% of participants were between 18-30 years of age group, and 30.6% and13.8% were between 31-40 years and 41-50 years age group respectively in a study conducted by Karim et al (2011).[20] Differences in the results of the two studies have been observed due to the different criteria of inclusion for the study and the lack of a universal scale for age-based group selection. Therefore, it is important to introduce a standard scale for selecting the participants based on the age-based group.

To classify gender-based caregivers, one piece of research proves that there were more women than men as caregivers.[21] which support the current study. As a result, women are more at risk of developing mental illness than men. In addition, the study reveals the normal state of culture in Bangladesh, especially marital and religious status, as most caregivers expressed themselves as Muslims (90.6%) and married (77.2 %). Further, this study also presents that parental bonding is stronger in Bangladesh like other studies[22] since 49.7 % of caregivers were found as the parents of the patients. Despite this study being carried out in a tertiary hospital situated in the capital of Bangladesh, most of the participants' occupational and educational status were identified as housewife (57.9%) and illiterate (33.9 %). These findings are different from the prior studies conducted in the same country.[23] Differences in study methods and locations may be responsible for this difference.

Psychiatric patients cared for by participants were found to be suffering from schizophrenia, bipolar disorder, anxiety, psychosis, and depression. This finding upholds another study conducted in Bangladesh which implies that a mentally ill person in this country usually suffers from the above mentioned major mental illnesses. [22] Thus, the training and awareness raising program focusing only on the mentioned disorders would be cost effective and time non-consuming and will be able to retain the caregiver on certain issues. On the other hand, the present study reveals some important information about hospitalization and medications of mentally ill persons, and activities of caregivers and care-recipients that will give other researchers some insight into conducting studies on this topic.

This study presents that most of the caregivers were experiencing moderate level of stress. No participants were found to be unstressed. This implies that the role of caregivers exerts pressure on caregivers. In regards to coping status, it is found that maximum participants had average levels of this condition. Although how caregivers approache for coping were not under investigation in this study; thus, research on coping strategies and its significance is recommended to carry out. In addition, stress reduction intervention may help to reduce stress and cope up with their conditions. The present study looked for a link separately between the socio-demographic status and stress or coping status. Except for income levels, none of the aspects of the socio-demography had found to be associated with the stress or coping status of caregivers. Since money plays a direct role in getting people access to various public and private services, there can be a direct relationship between income and stress or coping with it. Further study is recommended to understand in depth how income regulates the stress and coping position of caregivers.

In order to examine the psychological status and its relationship with coping styles among the caregivers of individuals with intellectual disability and psychiatric illness, Panicker and Ramesh (2019) conducted a study and found that use of positive reinterpretation and growth was associated with lower levels of depression and stress symptoms.[24] The current study supports this finding as an association was found between the stresses and coping status among the caregivers. In addition, it is evident that caregivers with low stress do not seek enough coping style. Similarly, Kaur (2015) concluded that caregivers with low stress level had poor coping style.[25] This study suggests the health professional to focus on the care giving situation to provide better support to them and also suggests that it shall be advisable to provide equivalent services for caregivers. Failure to find timely coping styles can lead to increased levels of stress later among caregivers which can ultimately have a detrimental effect on the proper care of mental patients.

CONCLUSIONS

In Bangladesh, major psychiatric conditions usually refer to schizophrenia, bipolar disorder, anxiety, psychosis, and depression. Person suffering from these conditions is labeled as a major psychiatric patient and the person who is cared for by these patients is regarded as a caregiver. In this country, parents play as the caregiver for most ill people. Caregivers of major psychiatric patients can experience low, moderate and high levels of stress because of their constant care giving role. On the other hand, poor, average and high coping conditions are found among the caregivers of mentally sick people. Except for income levels, none of the aspects of the socio-demography had found to be associated with the stress or coping status of caregivers. But caregivers stress and coping status are found

to be interrelated. The Caregivers who experienced low stress showed poor coping status. Failure to plan and implement the proper intervention, services and program for the caregiver may negatively affect their care giving performance which can deteriorate the wellbeing of major psychiatric patients.

REFERENCES

1. Hossain MD, Ahmed HU, Chowdhury WA, Niessen LW, Alam DS. Mental disorders in Bangladesh: a systematic review. BMC Psychiatry 2014; 14(1):1-8.
2. Darlami K., Ponnose R ,Jose P. .Caregiver's stress of psychiatric patients. Journal of Universal College of Medical Sciences (2016); 3(2):39–43.
3. WHO (World Health Organization).Investing in mental health.Investing in mental health (2003): 3–49.
4. Nuri NN, Sarker M, Ahmed HU, Hossain MD, Beiersmann C, Jahn A. Pathways to care of patients with mental health problems in Bangladesh. Int J Ment Health Syst. (2018);12 (39):1-12.
5. Bugge C, Alexander H, Hagen S. Stroke patients informal caregivers. Patient,caregiver and service factor that affect caregiver. (2000); 30 (8): 15-23.
6. Pinquart M, Sörensen S. Differences between caregivers and non-caregivers in psychological health and physical health: A meta-analysis. Psychology and Aging. (2003);18 (2):250–67.
7. Mant J, Winner S, Roche J, Wade DT. Family support for stroke: one year follow up of a randomised controlled trial. J Neurol Neurosurg Psych. (2005);76 (7):1006–1008.
8. Derajew H ,Toless d ,Feyissa G ,Addsu F , Sobaka M. Prevalence of depression and its associated factors among primary caregivers of patients with severe mental illness in southwest, Ethiopia. BMC Psychiatry. (2017); 17(1): 1–8.
9. Harrison KL, Ritchie CS, Patel K, et al. Care Settings and Clinical Characteristics of Older Adults with Moderately Severe Dementia. J Am Geriatr Soc. (2019); 67(9):1907-1912.
10. Panicker AS, Ramesh S. Psychological status and coping styles of caregivers of individuals with intellectual disability and psychiatric illness. J Appl Res Intellect Disabil. (2019);32(1):1-14.
11. Vasileiou K, Barnett J, Barreto M, et al. Experiences of Loneliness Associated with Being an Informal Caregiver: A Qualitative Investigation. Front Psychol. (2017);8 (585):1-12.
12. Lazarus RS, Folkman S. Stress, Appraisal, and Coping.New York: Springer; 1984.
13. Scherer KR. Appraisal considered as a process of multi-level sequential checking. In: Scherer KR, Schorr A, Johnstone T, editors. Appraisal Processes in Emotion: Theory, Methods, Research. New York: Oxford University Press; 2001. p. 92-120.
14. Magliano L, Veltro F, Guarneri M, Marasco C. Clinical and socio-demographic correlates of coping strategies in relatives of schizophrenic patients. Eur Psychiatry (1995); 10 (2):155-8.
15. Magliano L, Fadden G, Fiorillo A, Malangone C, Sorrentino D, Robinson A, et al. Family burden and coping strategies in schizophrenia: Are key relatives really different to other relatives? Acta Psychiatr Scand (1999);99 (1):10-5.
16. Mueser KT, Valentiner DP, Agresta J. Coping with negative symptoms of schizophrenia: Patient and family perspectives. Schizophr Bull (1997);23(2):329-39.
17. Scazufca M, Kuipers E. Coping strategies in relatives of people with schizophrenia before and after psychiatric admission. Br J Psychiatry (1999); 174 (3):154-8.
18. Hassan WA, Mohamed II, Elnaser AE, Sayed NE. Burden and coping strategies in caregivers of schizophrenic patients. J Am Sci (2011);7(5):802-11.
19. Hoque MM . ABC of research methodology and bio-statistics, 3rd ed. Dhaka: Bangladesh medical book seller association; 2019.
20. Karim E ,Alam M ,Rhman AHM ,Hussain AAM ,Uddin Mj ,Firoz AHM. Prevalence of Mental Illness in the Community', TAJ. Journal of Teachers Association. (2011) ;19(1):18–23.
21. Ahmed A, Green BA, Clark CB, Stahl KC, Mcfarland M. Latent structure of unipolar and bipolar mood symptoms. Bipolar Disorders 2011; 13(5-6):522-36.
22. Sunita Mahtani Stewart, Michael Harris Bond, Abu Saleh M. Abdullah and Stefan S. L. Gender, Parenting, and Adolescent functioning in Bangladesh. Ma Merrill-Palmer Quarterly (2000);46 (3): 540-64.
23. Firoz AHM, Karim MDE, Alam MF, Rahman AHMM, Zaman MM, Rabbani MG. Awareness, Care and Acceptance of Mental Patients: A Nationwide Multicentric Community Survey in Bangladesh. Journal of NIMH. (2009);1(1):9–30.
24. Panicker AS, Ramesh S. Psychological status and coping styles of caregivers of individuals with intellectual disability and psychiatric illness. Journal of Applied Research in Intellectual Disabilities 2018; 32(1): 1-14 .
25. Kaur S, Kiran UV. Stress among parents and caregivers of differently abled children.Journal for Studies in Management and Planning. (2015);1(7):172–184.

Case Report

Autoimmiune Hepatitis in Children: Two Case Report

*Benzamin M[1], Sonia ZF[2], Rukunuzzaman M[3], Nahid KL[4], Dey BP[5], Hossen K[6], Fathema K[7], Khadga M[8], Islam MM[9]

Abstract

Autoimmune hepatitis (AIH) is the disease of immune mediated inflammation of liver. Presentation of AIH in children is variable, ranging from acute hepatitis to cirrhosis of liver and also as only asymptomatic raised ALT. AIH can present at any age and female are more affected. Here we are presenting two cases. Case 1 presented with jaundice and H/O epistaxis, having cutaneous echymosis, hepato-splenomegaly and ascites. Case 2 was a diagnosed case of Systemic Lupus Erythematosus (SLE) presented with only persistent raised of serum ALT. Both were diagnosed as autoimmune hepatitis on the basis of positive auto antibodies, histopathology of liver tissues and exclusion of all other causes of acute and chronic hepatitis.

Keywords: *Autoimmune hepatitis, children, auto antibodies*

INTRODUCTION

Autoimmune hepatitis (AIH) is one of the prototype of autoimmune liver disease, it was first described in the 1950.[1-3] AIH is characterized by progressive inflammatory tissue damage as a result of the loss of self-tolerance.[4] AIH is more common in women; ratio of 3.6/1.0.[5] The prevalence of AIH is in Scandinavia is 1 to 2 cases /100,000 populations / year with a point prevalence of 11 to 17 cases / year.[6,7] In Canadian cohort, an annual incidence of pediatric AIH of 0.23 case /100,000 children.[8] In Bangladesh, Benzamin et al found that, about 8% of children with chronic liver disease with hepatomegaly and or splenomegaly are due to AIH. [9]

Autoimmune hepatitis (AIH) is characterized biochemically by increased transaminase levels, and serologically by circulating autoantibodies and high immunoglobulin G (IgG) levels, histologically by interface hepatitis, in absence of known etiology. Autoimmune hepatitis can present at any age and in all ethnic groups, the peak incidence occurs at the ages of 16 to 30 years. [5-7,10,11]

On the basis of autoantibody AIH classified as type 1 and type 2.

a. Type 1: Antinuclear antibody (ANA) and or anti Smooth muscle antibody (SMA). It presents at puberty & accounts for two third of cases.

b. Type 2: Anti liver kidney microsomal (LKM1) and or anti liver cytosol 1(LC1) antibody. It usually occurs in younger age & during infancy. [12,13]

Autoimmune hepatitis always suspected when all cause of acute and chronic hepatitis is excluded.[14]

CASE REPORTS

Case 1

Choity, 8½ years old immunized girl, 1st issue of non-consanguineous parents, presented with jaundice for 1 month along with anorexia, nausea, weakness and gradual abdominal distension. She also developed bleeding from nose for last 7days. There was no H/O abdominal pain, altered sleep pattern, abnormal behavior, any GI bleeding, rash, arthralgia, H/O of blood transfusion, any surgical procedure, any autoimmune diseases or family history of such type of illness and no H/O offending drug exposure. She had past H/O jaundice and ascites 1 ½ years back. On examination, she was moderately pale, icteric (fig 1), skin survey revealed multiple echymosis. Vitals were within

1. *Md. Benzamin, Resident (phase-B), Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka,
   Email: drmd.benzamin@yahoo.com, Cell: 01719183948
2. Zannatul Ferdous Sonia, Resident (phase-B), Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka, Bangladesh.
3. Md Rukunuzzaman, Professor, Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka.
4. Khan Lamia Nahid, Assistant Professor, Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka.
5. Bishnu Pada Dey, Assistant Professor, Department of Pathology, BSMMU, Dhaka.
6. Kamal Hossen, Medical Officer, Department of Pediatrics, Dhaka Medical College, Dhaka.
7. Kaniz Fathema, Resident (phase-B), Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka.
8. Mukesh Khadga, Resident (phase-B), Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka.
9. Mohammad Majharul Islam, Assistant Professor, Department of Pediatrics, Patuakhali Medical College, Patuakhai.

For Correspondence

normal limit. Anthropometrically she was well thriving. Abdominal exam revealed, hepato-splenomegaly and ascites evidenced by shifting dullness. Other systemic examinations revealed normal findings.

Investigation showed- moderate anaemia (Hb 9.6 gm/dl), Leucopenia (WBC 3400/mm^3), Thrombocytopenia (53000/mm3), serum bilirubin increased (6mg/dl), prolong prothrombin time (26.6 sec, INR: 2.38), serum ALT was mildly raised (102 U/L), hypoalbuminemia (20 gm/l), ultrasonography of whole abdomen showed hepatomegaly with coarse parenchyma with increased parenchymal echogenicity and splenomegaly and moderate ascites. Investigations for HBV, HCV and Wilson disease were negative. For Autoimmune hepatitis, ANA was negative, Anti- LKM1 was positive, Total IgG: 28 g/l increase (normal 7-16 g/l), Tissue Trans-glutaminase- Ig A was negative, thyroid function test was normal and anti -Thyroglobulin Ab were negative. Endoscopy of upper GIT showed Grade III esophageal varices and histopathology of liver tissue revealed moderate chronic hepatitis, consistent with autoimmune hepatitis (table 1). So finally we diagnosed the case as chronic liver disease with portal hypertension with coagulopathy due to autoimmune hepatitis with grade III esophageal varices. We treated the child with Tab. Prednisolone 2 mg/kg /day and tab. Azathioprine (1-2mg/kg/day) added 2 weeks later of prednisolone started. Tablet. Propranolol (1mg/kg/day) was given as primary prophylaxis for portal hypertension.

Case 2

Bristy, a 10 ½ years old immunized girl, 3rd issue of non consanguineous parents, diagnosed case of Systemic Lupus Erythematosus (SLE) for last 1 year and on treatment with tab. prednisolone (0.6 mg/kg/day) along with tab. hydroxychloroquine. She was referred to us with the complaints of persistent raised S.ALT for last six months. She had no H/O anorexia, nausea, vomiting, abdominal pain, headache, weight loss, any gastrointestinal bleeding, H/O of blood transfusion, any surgical procedure, family history of such type of illness and no H/O offending drug exposure. She had H/O jaundice 2 years back. On examination she was anicteric, mildly pale, vital signs were within normal limit, anthropometrically well thriving, no feature of steroid toxicity, bed side urine albumin (BSUA) was nil and abdominal examination revealed no organomegaly. Investigation shows- mildly anaemic (Hb 11.4 gm/dl), S. bilirubin and prothrombin time normal, S. ALT raised (1027 U/L), Investigations for HBV, HCV, HAV, HEV and Wilson disease were negative. For Autoimmune hepatitis- Anti- LKM1: positive, anti SMA: positive, comb's test (direct and indirect) : negative. Histopathology of liver tissue was highly suggestive of autoimmune hepatitis. (table 1) So finally we diagnosed the case as Systemic Lupus Erythematosus (SLE) with Autoimmune hepatitis. We treated the child with tab. Prednisolone 2 mg/kg /day, tab. hydroxychloroquine and tab. Azathioprine (1-2mg/kg/day) added 2 weeks later of prednisolone started.

Table 1 : Investigation profile of case-1 (Choity) and case-2 (Bristy)

Investigations	Case 1	Case 2
Hb	9.6 gm/dl	11.4 gm/dl
WBC	3600/mm3	9000/mm3
Platelate	53000/mm3	2,20000/mm3
S. bilirubin	6mg/dl ↑	0.6mg/dl
PT	26.6 sec↑	13.4 sec
INR	2.38 ↑	1.04
S. ALT	102 U/L ↑	1027 U/L ↑
S. Albumin	20 gm/L ↓	43gm/L
USG of whole abdomen	Liver- enlarged. Coarse parenchyma with parenchymal echogenicity increased and splenomegaly. vascular dilatations around splenic hilar region. Moderate Ascites present.	Mild hepatomegaly with heterogenous echogenicity and splenomegaly.

Table 1

Investigations	Case 1	Case 2
HBs Ag-	Negative	Negative
Anti HCV	Negative	Negative
Anti HAV IgM	Not done	Negative
Anti HEV IgM	Not done	Negative
S. Ceruloplasmin:	22mg/dl	41 mg/dl
24 h urinary copper	58.5 µgm / day	42.77 µgm / day
Slit lamp examination of eye	No K-F ring found	No K-F ring found
ANA	Negative	Positive
Anti- LKM1	Positive	Positive
Total IgG	28 g/l ↑	Not done
Anti SMA	Not done	Positive
S.F T4	9.94 µg/dl (N)	7.4 µg/dl (N)
TSH	0.81µIU/mL (N)	2.1µIU/mL (N)
Thyroglobulin Ab	<20.0 IU/ml (N)	<20.0 IU/ml (N)
Endoscopy of upper	Grade III esophageal	Not done
GIT	varices seen	
Histopathology of Liver biopsy tissue	Portal area revealed a moderate number of chronic inflammatory cells. Marked piecemeal necrosis and mild lobular necrosis present. Bridging fibrosis is also seen. Comments- Moderate chronic hepatitis in consistent with autoimmune Hepatitis.	Portal area show moderate fibrosis and many number of chronic inflammatory cells. Marked interface hepatitis and mild lobular degeneration are present. Bridging fibrosis is also seen. Comments- highly suggestive of autoimmune hepatitis. (fig 2)

Fig.-1: Jaundice (case 1)

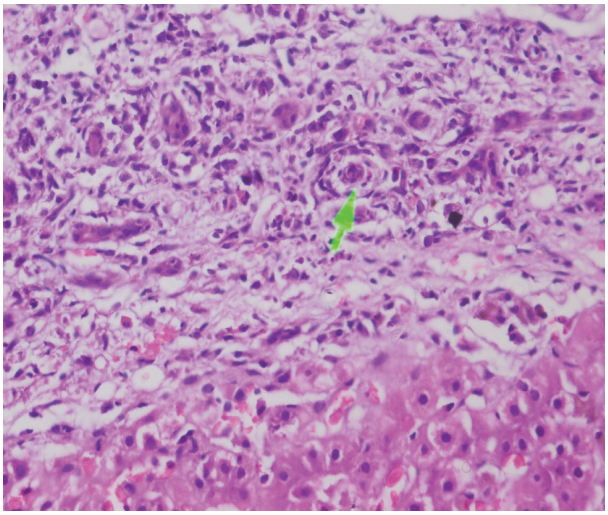


Fig.-2: H&E, 200x: Section of liver tissue showing plasma cell rich Portal inflammation, Interface hepatitis and Hepatocyte rosette formation (Marked with arrow).

DISCUSSION

AIH has variable clinical presentation which include followings- acute presentation like viral hepatitis with malaise, nausea, anorexia, vomiting, joint pain, abdominal pain, followed by jaundice, dark urine, pale stool

(40-50%), fulminant hepatic failure or chronic liver disease, complication of cirrhosis and portal hypertension without history of previous liver disease and jaundice. Non specific symptoms like progressive fatigue, relapsing jaundice, amenorrhea, headache, anorexia, joint pain, abdominal pain, diarrhea, weight loss, this symptom may last for 6 month to few years before diagnosis. Incidental finding of raised ALT without sign symptoms is another presentation of AIH. [8,15-20] Our case 1 presented with jaundice, anorexia, nausea, weakness and hepato-splenomegaly, ascites and bleeding manifestation in the form of epistaxis and echymosis. Case 2 presented with raised ALT without sign symptom.

AIH can present at any age and in all ethnic groups, but it has female predominance. [5,6,10,11] Our both cases are female.

Family history of autoimmune disease (40%) is frequent in AIH.[14] But in our both case there is no family history of autoimmune disease.

Diagnosis of AIH is made by combination of clinical, biochemical, immunological and histological features and exclusion of other liver diseases (like hepatitis B, C, E, Wilson disease, non alcoholic steatohepatitis (NASH) and drug induced liver disease. [5,14,21]

The key of diagnosis of AIH is the presence of auto antibody. Following are consider for diagnosis of AIH- Raised IgG level and auto antibody found like Antinuclear antibody (ANA), anti Smooth muscle antibody (SMA), anti liver kidney microsomal (LKM1) antibody, anti liver cytosol (LC1) antibody, anti mitochondrial antibody (AMA). [12-14] Our case 1 also had Anti- LKM1- positive, raised Total IgG and case 2 had ANA positive, Anti-LKM1: positive, anti SMA positive.

Histological features of AIH consist of: Interface hepatitis characterized by infiltration of lymphocytes, plasma cells; which cross the limiting plate and invade the surrounding parenchyma. Connective tissue collapse resulting from hepatocyte death and expanding from the portal area into the lobule ("bridging collapse"). Hepatic regeneration with "rosette" formation.[22-27] Our case 1's histtopathology of liver tissue showed portal area with a moderate number of chronic inflammatory cells, marked piecemeal necrosis and mild lobular necrosis and bridging fibrosis present. Case 2's histtopathology of liver tissue showed portal area with moderate fibrosis and many number of chronic inflammatory cells, marked interface hepatitis, mild lobular degeneration and bridging fibrosis present.

Twenty percent (20%) of AIH patients have other autoimmune diseases at diagnosis or developed during follow up. Autoimmune thyroiditis with hypothyroidism (8-23%), inflammatory bowel disease (18%), celiac disease (5-10%), hemolytic anemia, vitiligo, diabetes mellitus, urticaria pigmentosa, sjogren syndrome (SJS), SLE, glomerulonephritis, idiopathic thrombocytopenia, addison disease.[14,15,17,28] Our case 1 had no autoimmune disease but case 2 was a diagnosed case of Systemic Lupus Erythematosus (SLE).

Final diagnosis of AIH was done after exclusion of liver disease (like hepatitis B, C, E, Wilson disease, NASH and drug induced liver disease) that may share serological and histological features with autoimmune hepatitis.[14] We exclude HAV,HBV,HCV , Wilson disease, NASH in both case 1& 2.

After diagnosis, prompt treatment should be started. AIH is responsive to immunosuppressive drug. Treatment consists of two parts- induction of remission and maintenance phase.

Conventional treatment include prednisolone 2mg/kg/day (maximum 60 mg/day) and azathioprine. Prednisolone dose decreases in parallel to decline of ALT over a period of 4 to 8 weeks, maintenance dose of prednisolone will be 2.5 to 5 gm/day. For adjustment of prednisolone dose, liver function tests should be done frequently, preferably weekly. Azathioprine (AZ) is added 0.5 to 2 mg/kg/day, 2 weeks after starting prednisolone.[5,14,21,29-31] In both case we started treatment with prednisolone 2mg/kg/day. Azathioprine (AZ) is added 0.5 to 2 mg/kg/day, 2 weeks after starting prednisolone. Azathioprine will be continued in maintenance phase.

CONCLUSIONS

AIH has various spectrum of clinical manifestations like asymptomatic raised ALT to jaundice, ascites, hepato-splenomegaly etc. So AIH should be put in differential diagnosis of any liver disease in children. Auto antibodies and liver biopsy are the gold standard for diagnosis of AIH. Other autoimmune diseases may be associated with AIH. Long term treatment and meticulous follow up is needed for preventing disease progression.

REFERENCES

1. Mackay IR, Taft LI, Cowling DC. Lupoid hepatitis. Lancet 1956; ii: 1323–6.

2. Joske RA, King WE. The L.E.-cell phenomenon in active chronic viral hepatitis. Lancet 1955; 269: 477–80

3. Mackay IR. Chronic active hepatitides. Front Gastrointest Res. 1975;1:142–187.

4. Fernández MIC, Hernández DR, Eugenio DEC, Palanca W, Guridi ZD, Fabián LG.Diagnosis and Treatment of Autoimmune Liver Diseases in a Tertiary Referral Center in Cuba. Current Theraputic Research. 2017; 85: 8–14.

5. Manns MP, Czaja AJ, Gorham JD, Krawitt EL, Mieli-Vergani G, Vergani D, et al.Diagnosis and management of autoimmune hepatitis. Hepatology 2010;51:2193-13.

6. Werner M, Prytz H, Ohlsson B, Almer S, Bj€ornsson E, Bergquist A, et al. Epi-demiology and the initial presentation of autoimmune hepatitis in Sweden: anationwide study. Scand J Gastroenterol 2008;43: 1232-1240.

7. Miele-Vergani G. Autoimmune hepatitis in childhood. Clin Liver Dis 2014;3:6-8.

8. Jimenez-Rivera C, Ling SC, Ahmed N, Yap J, Aglipay M, Barrowman N, et al. Incidence and characteristics of autoimmune hepatitis. Pediatrics 2015;136 :e1237–48.

9. Md. Benzamin, Maimuna Sayeed, Md.Saidul Islam, Rubaiyat Alam, Md. Rukunuzzaman, Md Wahiduzzaman Mazumder, et al. Study of etiological profile of children presented with hepatomegaly and/or splenomegaly: An experience from Pediatric Gastroenterology Department, Bangabandhu Sheikh Mujib Medical University. Paed. Neph. J. Bang. 2018: 3(1): 9-17.

10. Boberg KM, Aadland E, Jahnsen J, Raknerud N, Stiris M, Bell H. Incidence and prevalence of primary biliary cirrhosis, primary sclerosing cholangitis, and autoimmune hepatitis in a Norwegian population. Scand J Gastroenterol 1998; 33:99.

11. Al-Chalabi T, Boccato S, Portmann BC, McFarlane IG, Heneghan MA. Autoimmune hepatitis (AIH) in the elderly: a systematic retrospective analysis of a large group of consecutive patients with definite AIH followed at a tertiary referral centre. J Hepatol 2006; 45:575.

12. Vergani D, Alvarez F, Bianchi FB, Cançado EL, Mackay IR, Manns MP, et al. Liver autoimmune serology: a consensus statement fromthe committee for autoimmune serology of the International Autoimmune Hepatitis Group. J Hepatol 2004;41: 677–83.

13. Villalta D, Girolami E, Alessio MG, Sorrentino MC, Tampoia M, Brusca I, et al. Autoantibody profiling in a cohort of pediatric and adult patients with autoimmune hepatitis. J Clin Lab Anal 2016;30:41–6.

14. Mieli-Vergani G, Vergani D, Baumann U, Czubkowski P, Debray D, Dezsofi A, et al. Diagnosis and Management of Pediatric Autoimmune Liver Disease: ESPGHAN Hepatology Committee Position Statement. JPGN 2018;66: 345–360.

15. Gregorio GV, Portmann B, Karani J, Harrison P, Donaldson PT, Vergani V, et al. Autoimmune hepatitis/sclerosing cholangitis overlap syndrome in childhood: a 16-year prospective study. Hepatology 2001;33:544–53.

16. Di Giorgio A, Bravi M, Bonanomi E, Alessio, G, Sonzogni, A, Zen Y, et al. Fulminant hepatic failure of autoimmune aetiology in children. J Pediatr Gastroenterol Nutr 2015;60:159–64.

17. Gregorio GV, Portmann B, Reid F, Donaldson PT, Doherty DG, McCartney M, et al. Autoimmune hepatitis in childhood: a 20-year experience. Hepatology 1997;25:541–7.

18. MieliVergani G, Heller S, Jara P, Vergani D, Chang MH, Fujisawa T, et al. Autoimmune hepatitis. J Pediatr Gastroenterol Nutr 2009;49:158–64.

19. Ramachandran J, Sajith KG, Pal S, Rasak JV, Prakash JA, Ramakrishna B, et al. Clinicopathological profile and management of severe autoimmune hepatitis. Trop Gastroenterol. 2014;35:25–31.

20. Brissos J, Carrusca C, Correia M, Cabral J. Autoimmune hepatitis: trust in transaminases. BMJ Case Rep 20142014.

21. European Association for the Study of the L. EASL Clinical Practice Guidelines: Autoimmune hepatitis. J Hepatol 2015;63:971–1004.

22. Czaja AJ, Carpenter HA. Autoimmune hepatitis. In: Macsween RNM, Burt AD, Portmann BC, eds.

Pathology of the Liver. 4th Edition Churchill Livingstone; 2001:415–34.

23. Miao Q, Bian Z, Tang R, Zhang H, Wang Q, Huang S, et al. Emperipolesis mediated by CD8 T cells is a characteristic histopathologic feature of autoimmune hepatitis. Clin Rev Allergy Immunol 2015;48: 226–35.

24. de Boer YS, van Nieuwkerk CM, Witte BI, Mulder CJJ, Bouma G, et al. Assessment of the histopathological key features in autoimmune hepatitis. Histopathology 2015;66:351–62.

25. Kumari N, Kathuria R, Srivastav A, Narendra K, Ujjal P, Surender K Y. Significance of histopathological features in differentiating autoimmune liver disease from nonautoimmune chronic liver disease in children. Eur J Gastroenterol Hepatol 2013;25: 333–7.

26. Tucker SM, Jonas MM, Perez-Atayde AR. Hyaline droplets in Kupffer cells: a novel diagnostic clue for autoimmune hepatitis. Am J Surg Pathol 2015;39: 772–8.

27. Tiniakos DG, Brain JG, Bury YA. Role of histopathology in autoimmune hepatitis. Dig Dis 2015; 33(suppl 2):53–64.

28. Wong GW, Heneghan MA. Association of extrahepatic manifestations with autoimmune hepatitis. Dig Dis 2015;33(suppl 2):25–35

29. Mieli-Vergani G, Vergani D. Paediatric autoimmune liver disease. Arch Dis Child 2013;98:1012–7.

30. Floreani A, Liberal R, Vergani D, Mieli-Vergani G. Autoimmune hepatitis: contrasts and comparisons in children and adults - a comprehensive review. J Autoimmun 2013;46:7–16.

31. Czaja AJ, Bianchi FB, Carpenter HA, Krawitt EL, Lohse AW, Manns MP, et al. Treatment challenges and investigational opportunities in autoimmune hepatitis. Hepatology 2005;41:207–15.

Case Report

A 30-Year-Old Male Patient of Miliary Tuberculosis Presented with Pancytopenia and Intracerebral Haemorrhage Mimicking Brain Tumor in MRI

Ahmed QMU[1], *Hasan MN[2]

Abstract

Unlike to fever, pancytopenia is a rare hematological manifestations of tuberculosis and intracranial haemorrhage as well. Here we report a case of disseminated tuberculosis presented with pancytopenia and intracranial haemorrhage. The patient presented with prolonged pyrexia, weight loss and subsequently unconsciousness and convulsion. After the diagnosis of tuberculosis with pancytopenia and intracerebral haemorrhage flowed by convulsion, he was treated with category-1 standard anti-tubercular therapy and anticonvulsant. After completion of the anti-tubercular drug his fever completely subsided and gained weight and pancytopenia was improved. But he is still on anti-convulsant medication with good control of seizure.

Keywords: *Tuberculosis, pancytopenia, intracerebral haemorrhage*

INTRODUCTION

Tuberculosis (TB) has a protean clinical manifestations. Hematologic abnormalities associated with extrapulmonary TB include anemia of different types, leucopenia, leukocytosis, leukemoid reaction, thrombocytosis, thrombocytopenia, and rarely pancytopenia.[1] Complications due to pancytopenia, especially cerebral hemorrhage is even rare.[2] We describe the case of an immunocompetent patient who presented with fever of unknown origin (FUO) with pancytopenia and subsequently developed cerebral hemorrhage. Subsequent clinical course is also discussed. We report the case to correlate the uncommon presentations of a commonly encountered disease to emphasize the need for early diagnosis and treatment, otherwise fatal condition.

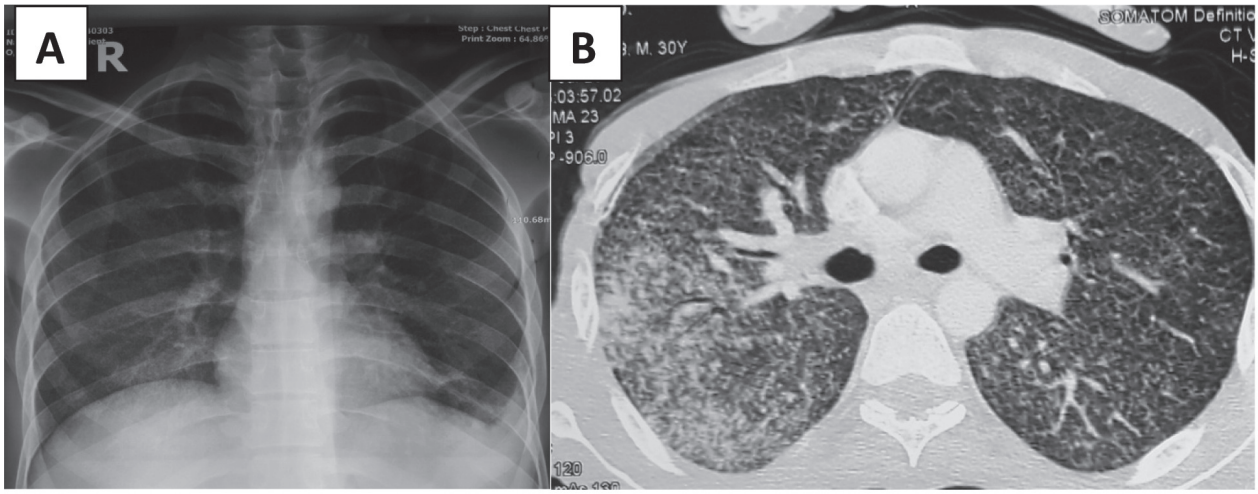
1. Dr. Quazi Mamtaz Uddin Ahmed, Associate professor, Deaprtment of internal medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka.

*2. Dr. Md. Nazmul Hasan, Assistant professor, Department of Internal Medicine, BSMMU, Shahbagh, Dhaka. Email-nazmul_31st@yahoo.com

*Correspondence

CASE REPORT

A 30-year-old male went to Saudi Arabia with a job. But after staying there for two weeks, he developed fever. There was no improvement after treatment for three weeks in Saudi Arabia. So, he returned to Bangladesh with fever and cachexia (FIGURE-3A) and was admitted at Dhaka Medical College Hospital (DMCH). At DMCH, some tests were run which included complete blood count (CBC), Blood for culture and sensitivity, Serum Electrolyes, C-reactive protein (CRP), chest X-ray, Urine routine examination and culture, Bone marrow examination (table-1). Except for raised CRP (82 mg), all investigations were normal. He was treated with meropenem 1 gm IV 8 hourly for 14 days. But still there was no improvement of fever, which continued with a range from 101^0 F to 104^0F. The patient decided to go to another hospital and got himself admitted in department of Internal Medicne at Bangabandhu Sheikh Mujib Medical University (BSMMU). On admission, his CBC showed pancytopenia (WBC-1080/µL, Hb- 9.9 gm/dl, Platelet- 19000/µL). Although his CXR was normal (figure-1A), we did high resolution CT (HRCT) scan of the chest. HRCT showed miliary mottling consistent with military tuberculosis (Figure-1B). Anti-tuberculous treatment (ATT) were started and fever began to subside after six days. But on the ninth day of ATT, he developed aphasia. MRI was advised which was done after five days of onset of aphasia due to financial constraints of the patient. MRI of brain with T2 weighted image showed large mixed intensity lesion in the left fronto-parietal region with perilesional oedema and effacement of the lateral ventricle (figure-2A). Radiological differential diagnosis was either intracerebral haemorrhage or glioblastoma multiforme. He was treated with IV dexamethasone along with ATT. Although, the ATT patient got rid of fever by this time, his consciousness deteriorated and he became unconscious. After four days, he regained his consciousness with slight



Chest X-ray PA view HRCT of chest

Fig-1: A) Chest X-ray showing no detectable abnormalities B) HRCT chest revealed multiple bilateral miliary shadows.

recovery of speech. He was hospitalized at BSMMU for forty days and regained his speech completely. He was discharged and asked to come for follow up visit. He came after completion of ATT with follow-up MRI of brain which showed complete resolution of the brain lesion with evidence of gliosis. Four months after completion of ATT, he developed generalized tonic clonic seizures several times. He was prescribed carbamazepine with the advice to continue the drug. One year on, he is still free from seizure and active in his daily life. He improved after treatment with anti-tubercular drug except convulsion which probably due to gliosis of brain (figure-3)

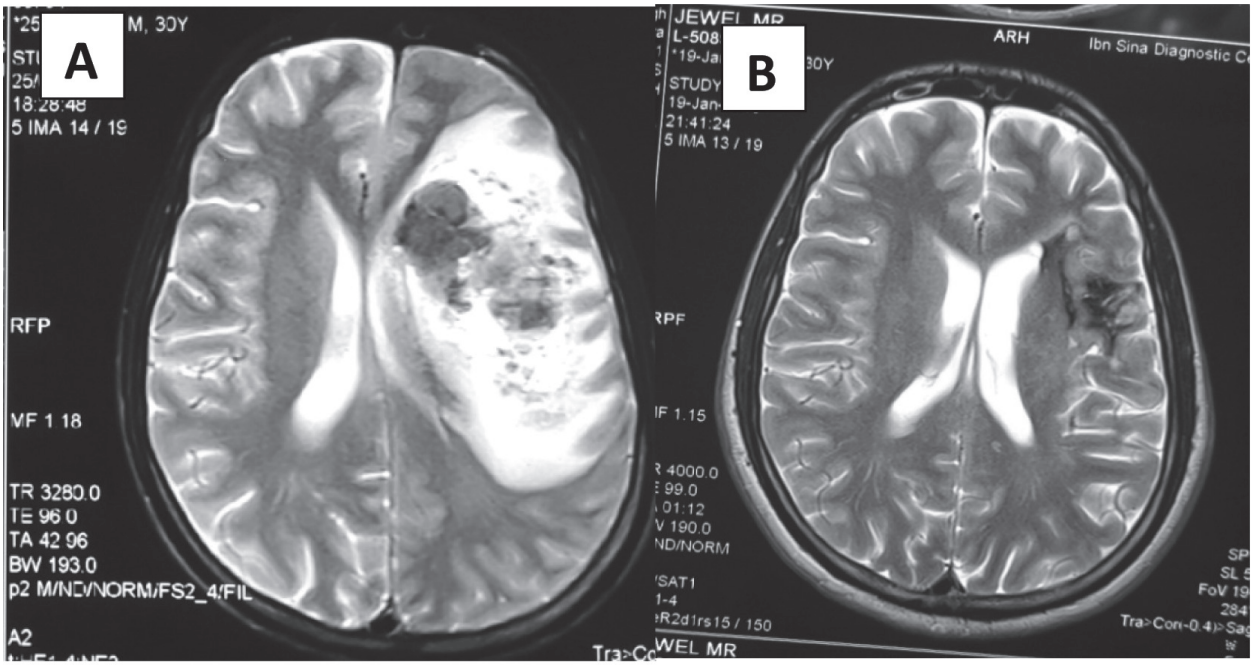


Fig-2: MRI of brain: A) Showing large mixed intensity lesion in left fronto-parietal region with peri-lesional edema and midline shifting and effacement of the lateral ventricle. B) Showing a small hypo-intense area with complete resolution of the previous lesion.

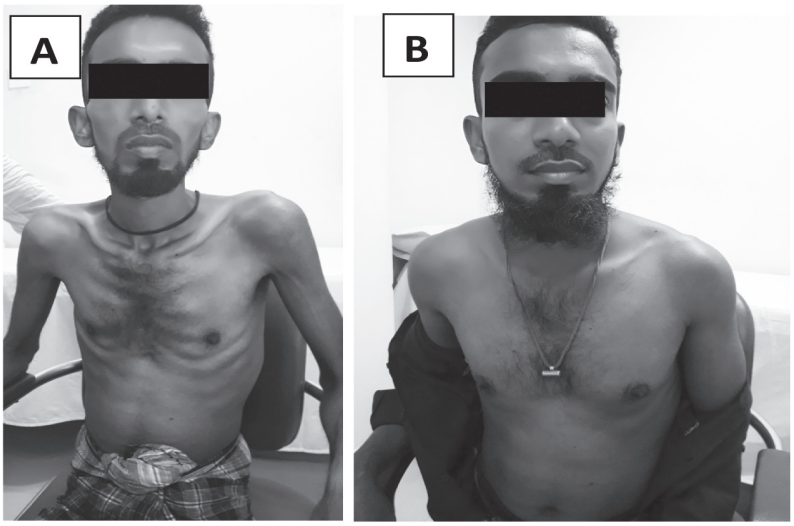


Fig -3: General condition of the patient before (A) and after(B) treatmemt with anti-tubercular drugs.

Table- I: Results of the investigation reports

Name of the investigations		Results
1.	**CBC**	
	Haemoglobin WBC- Platelet- **ESR**	9.9 gm/dl 1080/µL 19000/µL **30 mm in the first hour**
2.	CRP	82 mg/dl
3.	Serum creatinine	0.9 mg/dl
4.	SGPT	40 IU/L
5.	Chest X-ray	Normal
6.	HRCT chest	Multiple military mottling in the both lung field
7.	MT	NEGATIVE
8.	Blood culture and sensitivity	No growth
9.	Urine R/M/E and culture and sensitivity	**Normal**
10.	**Bone marrow examination**	**Reactive marrow**
11.	**MRI of the brain**	Showing large mixed intensity lesion in left fronto-parietal region with peri-lesional edema and midline shifting and effacement of the lateral ventricle

DISCUSSION

Tuberculosis is a common problem in Bangladesh. Most of the cases are diagnosed with relative ease. But sometimes, it is very difficult to diagnose, especially when presented with fever of unknown origin(FUO). Moreover, complications like pancytopenia and cerebral hemorrhage make the situation worse. Our patient presented with all these features**.** In a patient with FUO, where the CXR is normal, we should do HRCT of chest. In neutropenic patients upto 50% of the cases may have normal chest X-ray but HRCT chest may show evidence of pneumonia.[3] Unfortunately, HRCT is still underperformed in a patient with FUO. Our

patient highlighted the importance of this test. Pancytopenia is a rare manifestation of tuberculosis. Patients with miliary tuberculosis accompanied by a pancytopenia rarely survive their disease.[2] Pancytopenia may be due to temporary suppression of bone marrow by the cytokines or due to direct invasion of the bone marrow by the acid fast bacilli as evident by granulomas with or without caseous necrosis in bone marrow trephine biopsy.[4]

Cerebral hemorrhage is an uncommon finding in pancytopenic patients. Bleeding from other body sites are more common. The cause of cerebral bleeding in our patient is not obvious. It could be due to pancytopenia or it could be due to intracerebral tuberculoma. Cerebral tuberculosis can cause mycotic aneurysm or it may weaken the cerebral vessel walls.[5,6] Both may lead to rupture of cerebral vessels with resultant intracerebral, intraventricular and subarachnoid hemorrhages5,6 There are case reports supporting tuberculosis as a cause of intracranial bleedings. On many occasions diagnosis is made at autopsy.[5,6] Also the timing of intracerebral hemorrhage can vary in intracerebral tuberculosis. It can be the presentation of the disease or it can happen anytime during ATT.[7,8] Our patient developed intracerebral bleeds after first week of ATT. Tuberculosis affecting the central nervous system and bone marrow should be treated early. Otherwise, it is likely to be fatal. Our patient is lucky to get rid of his ordeal and lead a normal life.

CONCLUSIONS

A immucompetent patients presented with fever of unknown origin and pancytopania whose MRI of brain showed cerebral haemorrhage and also found bilateral miliary shadows by HRCT was treated with category-1 anti-tubercular therapy (ATT). The response of ATT and other symptomatic therapy was good and prognosis was also good. Early diagnosis and treatment can save the TB patients from fatal condition

REFERENCES

1. R.Avasthi, S.C. Chaudhary, D.Mohanty, and K Mishra,"Disseminated tuberculosis: interesting hematological observations", Journal of Association of Physicians of India, vol.58, no. 4, pp.243-244,2010.
2. Escourt LJ, Stanworth SJ, Collet D,Murphy MF.Intracranual haemorrhage in a thrombocytopenic haematologic patients-a nested case control study:the InCiTe study protocol. BMJ open 2014; 4:e004199
3. Heussel CP,Kauczor HU,Heusel G,Fischer B,Mildenberger P, et.al. Early detection of pneumoniain febrile neutropenic patients:use of thin section CT.AJR Am J Roentgenil 1997;169:1347-53
4. B. J. Hunt, V. Andrews and K.W. Pettingale. The significance of pancytopenia in miliary tuberculosis. Postgraduate Medical Journal. 1987 Sep; 63(743): 801-804
5. Hai Zou, Ke Hua Pan, Hong-Ying Pan, Dong-Sheng Huang: Cerebral hemorrhage due to tuberculosis meningitis: a rare case report and literature review. Oncotarget.2015 Dec 29;6(42): 45005- 45009.
6. BN Panda, RS Shah and RRK Nair. Tuberculosis of brain presenting with recurrent stroke and intracranial haemorrhage. Med J Armed Forces India. 1995 Apr;51(2):139-141.
7. Shuangshoti S, Phisitbutr M. Fatal haemorrhage in tuberculosis of brain. J Med Assoc Thai 1979; 62: 639-645.
8. Nakayama Y, Tanaka A, Nagasaka S. Ikui H. Intracerebral haemorrhage in a patient with moyamoya phenomenon caused by tubercular arteritis: a case report. No Shinkei Geka 1999; 27: 751-755.

Obituary News January-2020

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

Sl.No.	Name & Address	Age	Date of Death
1	Dr. Md. Roushan Ali Life Member, BMA, Rangpur Branch	62	06/9/2019
2	Dr. Md. A Q Ruhul Amin Ex- President BMA, Chandpur Branch	70	07/09/2019
3	Dr. Shamchuddin Ahmed Ex- President BMA, Moulvibazar Branch	82	20/09/2019
4	Dr. Kazi Abdul Majid Father of Prof. Dr. Md. Atiqur Rahman (Treasurer of BSMMU)	78	23/09/2019
5	Dr. Golam Mohiuddin Dipu Life Member, BMA, Comilla Branch And Ex- Secretary, BMA Comilla Branch	55	30/09/2019
6	Dr. Animesh Majumder Life Member, BMA Rangpur Branch And Ex- Secretary, BMA, Rangpur Branch	62	03/10/2019
7	Dr. Abdul Latif Father of Nilima Akhter Lili, Publicity Secretary, Bangladesh Mohila Awami League	80	15/10/2019
8	Dr. Abrar Ahmed Life Member, BMA, Barishal Branch	68	20/10/2019
9	Dr. Md. Yunus Ali Sarkar MP Ex- Joint Secretary, Bangladesh Medical Association (BMA)	66	27/012/2019

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.

Call for paper

To reach the doctors throughout the country and ensure their participation as author, contents and presentation of the Bangladesh Medical Journal have been updated & changed to some extent. In addition to original articles, review articles and case reports; we are going to publish following sections regularly.

Letters to the editor
With a view to increase the bondage with the readers, we encourage to write letters to the editor. Letters may include original research presented in a research letter format or case reports or series. Alternatively, readers may express their ideas, opinions on important national or international issues related to doctors, medical science or medical profession.

On being a doctor
Doctors are encouraged and advised to share their sweet, bitter, sad, memorable & illuminating experiences as a professional doctor in the hospital and private chamber.

Medical news
Important recent updated inventions and ideas that may change the knowledge, attitude & practice of a doctor and courses of the medical sciences, both at home and abroad; may be written to us for publication in Bangladesh Medical Journal.

Medical jokes/poems
Meaningful jokes or poem writing related to medical profession and submitting to us by soft copies are encouraged. There is no deadline of submission.

Please send your writings to the e-mail address of Bangladesh Medical Association Journal : info@bmaj.org

Published by: Dr. Md. Ehteshamul Huq Choudhury on behalf of the Bangladesh Medical Association, BMA Bhaban, 15/2, Topkhana Road, Dhaka-1000, Bangladesh. Phone: +88-02-9568714, Fax: +88-02-9562527, +88-02-6566060, e-mail: info@bmaj.org, website: www.bmaj.org. Subscription: Local-Tk. 15 for single and Tk. 60 for annual. Overseas-$5 for single and $20 for annual.
Printed by: Asian Colour Printing, 130, D.I.T. Extension Road, Fakirerpool, Dhaka-1000, Bangladesh. Tel: 49357726, 58313186, E-mail: asianclr@gmail.com. web: www.acp1980.com