JAMCCu
https://www.amccomilla.edu.bd/jamcu

JOURNAL
ARMY MEDICAL COLLEGE CUMILLA

ISSN: 2663-158X
eISSN: 2663-1598

Vol 02 No 02 July 2019

Army Medical College Cumilla Journal

Vol-02. No-2, July-2019

An official Journal of Army Medical College Cumilla, Cumilla Cantonment, Cumilla, Bangladesh

Editorial Board

Address of Correspondence
Dr. Mohammad Shakil
Mobile:01612711572, Phone:0818-0121
e-mail: amccjornal@gmail.com

Army Medical College Cumilla Journal

Vol-02. No-2, July-2019

Contents

Editorial

The Role of SGLT2 inhibitors in Heart Failure

Prof. (Dr.) Md. Khairul Alam

Sodium glucose co-transporter 2 (SGLT2) inhibitors are the latest class of anti diabetic drugs[1]. These agents prevent 90% reabsorption of filtered glucose in the early S1 segment of proximal tubule by inhibiting SGLT2 proteins[2]. At present the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) approved four SGLT2 inhibitors such as dapagliflozin (Dapa), canagliflozin (Cana), empagliflozin (Empa) and ertugliflozin (Ertu) for the treatment of type 2 diabetes mellitus (T2DM)[3]. Most of them are currently commercially available in many countries including Bangladesh.

In 2008 FDA and in 2012 EMA issued guidance to the pharmaceutical industry for all new antidiabetic medication for type 2 diabetes. This guidance focused specifically for the requirements of long-term cardiovascular (CV) safety trial to approval of new antidiabetic drugs[4]. But while doing research on CV safety of SGLT2 inhibitors some unprecedented good results have been found in terms of heart safety.

In EMPA-REG Outcome trial examined the CV safety of Empa, published in 2015[5]. A total 7020 patients with T2DM and established CV disease received two different doses of Empa (10 & 25mg daily) or placebo for a median observation period of 3.1 years. Among the patients who received Empa the investigator found a significant reduction in primary composite outcome 3P-MACE (death from CV causes, nonfatal myocardial infarction, nonfatal stroke) compared to patients treated with placebo. Regarding the secondary outcomes treatment with Empa resulted reduction of death from CV causes 38%, death from any causes 32%, and hospitalization for heart failure (HHF) 35%[5].

Another study the CANVAS published in 2017 to assess the CV safety of Cana[6]. A total 10142 patients with T2DM and established CV disease or ≥ 2 CV risk factors were randomly assigned to receive Cana (100 mg & 300 mg daily) or placebo. The study demonstrated significant reduction of the primary composite outcome of 3P-MACE and in addition reduced the incidence of HHF those who receiving Cana compared to patients treated with placebo but with a greater risk of amputation and bone fracture.

Later many CV outcomes trials of other SGLT2 inhibitors have confirmed the various benefits that seen in EMPA-REG Outcome and CANVAS. But clinical trials involving patients with T2DM have shown that SGLT2 inhibitors were consistent with reduce HHF[7]. These observations gave rise to the questions whether the benefit of SGLT2 inhibitors in patients with HF independent of the presence of diabetes.

A positive answer to this question has been found after the publication of the DAPA-HF trial in 2019[8]. In this phase 3 trial 4744 patients with class ll/lll/lV HF and left ventricular ejection fraction (LVEF) $\leq 40\%$ were randomly recruited to receive either Dapa (10 mg once daily) or placebo in addition to standard HF therapy in 20 countries[8]. About 42 % of study patients had T2DM. Over a median 18.2 months the primary composite outcome of worsening heart failure or death from CV causes was significantly lower in the Dapa group than in the placebo group (16.3% vs 21.2%, hazard ratio [HR], 0.74; 95% of confidence interval [CI], 0.65 to 0.85; $P < 0.001$). Secondary outcomes were also significant, including a lower occurrence of the composite of CV death or HHF and fewer symptoms of HF (16.1% vs. 20.9%, HR 0.75; 95%CI, 0.65-0.85; $P < 0.001$) and were as effective in the patients without T2DM as in those with diabetes. DAPA-HF study helped to use this drug for a patient with heart failure. The FDA approved Dapa on May 2020 for the treatment of patients with heart failure and a reduced ejection fraction (HFrEF) in adults with or without T2DM.

In Augest 2020, the EMPEROR-Reduced trial was published where the effective benefits of Empa on CV and HFrEF with or without diabetes have been examined[9]. In this phase 3 double-blind placebo-controlled trial total 3730 patients with class ll/lll/lV heart failure and LVEF $\leq 40\%$ with elevated N-terminal prohormone of brain natriureetic peptide (NT-proBNP) randomly assigned to receive Empa (10mg once daily) or placebo in addition to recommended HF therapy. The trial was performed in 20 countries for a median follow up period ~24 months. Compare to DAPA-HF, the patients in EMPEROR-

Reduced trial had more severe HF, 50% of them were diabetics. The primary outcome of CV death or HHF was significantly lower with Empa than with placebo (HR 0.75; 95% CI, 0.65 to 0.85; P < 0.001). The results of this trial indicate the Empa is superior to placebo in improving HF irrespective of diabetes status. This is a very important study patients with severe HF appeared to benefit.

The results of the EMPEROR-Reduced trials established the findings of DAPA-HF and created a reasonable ground to use SGLT2 inhibitors. The Canadian cardiovascular Society and the Canadian Heart Failure Society already have done this they recommended the use of SGLT2 inhibitors in patients with mild or moderate heart failure who have HFrEF ≤ 40% to improve symptoms and quality of life and to reduce the hospitalization and CV mortality[10].

Although the SGLT2 inhibitors were introduced as treatment of T2DM the results of the EMPA-REG outcome and others trials conclusively shows a clear common benefit in HHF irrespective of diabetes status. But in terms of CV death, all-cause mortality and adverse effects certain differences exist between them. When new heart failure drugs are investigated it is important to consider whether they provide benefit in addition to established therapies which has been adopted gradually in clinical practice. There by head-to-head randomized clinical trials, well-designed observational studies and real-world data are needed to clarify the differences between them. Then the physicians who prescribe antidiabetic drugs would know better which one to use in every day clinical practice.

Prof. (Dr.) Md. Khairul Alam
Vice Principal and Head, Dept. of physiology
Army Medical College Cumilla
Mobile: 01733716133
Email: dr.khairulalam@gmail.com

References

1. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of medical care in diabetes-2020. Diabetes Care 2020; 43(Suppl.1):S98–S110
2. Ghezzi C, Loo, D.D.F, Wright, E.M. Physiology of renal glucose handling via SGLT1, SGLT2 and GLUT2. Diabetologia 2018; 61: 2087-97.
3. Choi, C.I. Sodium-Glucose Co transporter 2 (SGLT2) Inhibitors from natural products: Discovery of next-generation antihyperglycemic agents. Molecules 2016; 21
4. Eleftheriadou, I Grigoropoulou, P Liberopoulos, E Liatis, S Kokkinos, A Tentolouris N. Update on cardiovascular effects of older and newer anti-diabetic medications. Curr. Med. Chem. 2018; 25: 1549-66
5. Zinman B, Wanner C, Lachin J M, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen O E, Woerle H J, et al. Empagliflozin, cardiovascular outcomes and mortality in type 2 diabetes. N Engl J Med 2015; 373:2117-28
6. Neal B, Perkovic V, Mahaffey, K W, de Zeeuw D, Fulcher G. Erondu N, Shaw W, Law G, Desai M, Matthews D R, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl Med 2017; 37: 644-57
7. Zelniker TA, WiviottSD, Raz I, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet 2019; 393: 31-9
8. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019; 381:1995-2008
9. Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med 2020;383: 1413-24
10. O'Meara E, McDonald M, Chan M, et al. CCS/CHFS heart failure guidelines: clinical trial update on functional mitral regurgitation, SGLT2 inhibitors, ARNI in HFpEF, and tafamidis in amyloidosis. Can J Cardiol 2020; 36:159-69

Prevalence of Chronic Suppurative Otitis Media amongst under Eighteen Population of a Selected Slum in Dhaka City

Abu Hena Md. Mustafijur Rahman[1], Mohammad Shakil[2], Shahara Begum[3]

Abstract

Background: Chronic suppurative otitis media is a major public health problem in our country. Serious complications may arise from it. **Objective**: This study was aimed to find out the prevalence of chronic suppurative otitis media (CSOM) amongst the children of a selected slum of Dhaka city. **Method**: It was a descriptive cross-sectional study. A total of 403 samples were examined and mother of all sample units were interviewed with preformed questionnaire and ear swab were collected from CSOM cases for laboratory examination. **Results**: Out of 403 children, 36 CSOM cases were identified, prevalence rate was 89/1000. Out of 36 CSOM cases about half 17(47.2%) were in 1-4 years age group. Majority of children 27(75.0%) of CSOM cases were illiterate and equal number 27(75.0%) had illiterate parents. About two-third 22(61.1%) had a poor monthly family income (TK. 3000-3999). Two-third 23(63.9%) had large family members of 5 to 6 persons. More than half 20(55.6%) took bath in pond, canal or ditch. The proportion of CSOM was high 16(44.4%) among the children with history of ear cleaning using chicken feather. In 36 CSOM cases, about half 20(55.6%) of CSOM cases received some treatment, but only 5(13.9%) received treatment from a qualified doctor. **Conclusion**: The findings of the study suggest that chronic suppurative otitis media is still a major health problem in our country. A systematic through nationwide population based study of CSOM should be conducted to get a national picture for understanding the magnitude of the problem. This is necessary for strengthening of intervention programmes for prevention of CSOM.

Keywards:Chronic Suppurative Otitis Media

J Ar M Coll Cu. 2019, July; 2 (2): 3-9
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Chronic suppurative otitis media (CSOM) is the result of an initial episode of acute otitis media and is characterized by a persistent discharge from the middle ear through a tympanic perforation. It is an important cause of preventable hearing loss, particularly in the developing world. [1] It is, defined as a chronic inflammation of the middle ear and mastoid cavity, which present with recurrent ear discharges or othorrhoea through a tympanic perforation for 3 months or more.[1.2] The disease usually begins in childhood as a spontaneous tympanic perforation due to an acute infection of the middle ear, known as acute otitis media (AOM), or as a sequel of less severe forms of otitis media (e.g. secretory OM). The infection may occur during the first 6 years of a child's life, with a peak around 2 years, the point in time when AOM become CSOM is still controversial. Generally, patients with tympanic perforations, which continue to discharge mucoid material for periods of from 6 weeks to 3 months, despite medical treatment, are recognized as CSOM cases. The WHO definition requires only 2 weeks of otorrhoea, but otolaryngologists tend to adopt a longer duration, e.g. more than 3 months of active disease. Different terms are used to define CSOM time to time by different researchers.[1] CSOM has been an important cause of middle ear disease. CSOM is a major health problem in many populations around the world. High rates of chronic otitis media have been attributed to overcrowding, inadequate housing, poor hygiene, lack of breast feeding, poor nutrition, passive smoking, high rates of naso-pharyngeal colonization with potentially pathogenic bacteria and inadequate or unavailable health care. Poverty is a major risk factor in developing countries and certain neglected populations. Since chronic suppurative otitis media begins with an acute onset of otitits media either acute otitis media or otitis media with effusion, risk factors associated with acute otitis media also be initially involved viral and bacterial infection, Eustachian tube dysfunction, young age and immature or impaired immunologic status, upper respiratory allergy, familial predisposition, presence of older siblings, male sex, bottle feeding, day-care attendance, passive smoking.[3.] CSOM is a significant cause of morbidity and mortality. In 1990, about 28000 deaths all over the world and largely among developing countries were due to otitis media. Mortality and disabilities due to otitis media are

Received May 2019 Accepted August 2019

primary related to the complications of CSOM particularly abscess. In 1993 world development report estimated that about 5.12 million disability adjusted life years (DALYs) were lost from otitis media, 91% of which comes from the developing countries. This was later scaled down in 1996 to 2.163 million DALYs, 94% of which comes from developing world. India and sub-Saharan Africa (SSA) account for most death and years of life lost and DALYs from otitis media. The disease and its squeal produce substantial social and economic cost. It is particularly common amongst poor communities in developing countries, and also in certain disadvantaged groups in developed countries.[1,2] CSOM is a major cause of hearing impairment, and this effect is a matter of serious concern, particularly in children, because it may have long- term effects on early communication, language development, auditory processing, psychological and cognitive development, and educational progress and achievements[1,4]. The global burden of illness from CSOM involves 65-60 million individuals with draining ears, 60% of whom (39-200 million) suffer from significant hearing impairment. Over 90% of the burden is borne by countries in the South- east Asia and Western Pacific regions, Africa, and several ethnic minorities in the Pacific Rim. CSOM is uncommon in the Americas, Europe, the Middle East, and Australia.[1,2] The prevalence of CSOM is less than one percent in USA and UK.[3]The exact prevalence of CSOM in Bangladesh is not available. But Chronic suppurative otitis media and its complications are a major health problem in Bangladesh. Several hospital and rural studies found prevalence of CSOM in12.7% to 39.50% of study population.[5,6,7] Here in this country, due to unawareness and lack of facility the people usually take less care of CSOM. On the other hand low socio-economic condition; poor housing and poor environmental sanitation influence the higher incidence of the disease. Without improving the socio-economic status, medical care and education level it would be very difficult to control the disease in our community.[8] This study conducted in a low socio-economic group is aimed to find out prevalence of CSOM. This information might be very much helpful for the policy makers for prevention and control of the disease.

Methods

This descriptive type of cross-sectional study was carried out in 2005, from January to June among the children under eighteen years of age of the selected slum with an objective to determine the prevalence of CSOM. The study population comprised of children of age below 18 years irrespective of the sex and religion residing in the stated area. Considering the validity, practical situation and length of study period as many as 403 samples were interviewed and examined for the study. Systematic random sampling technique was used for data collection. Total number of the household of the slum was collected from ward commissioner's office. The total families (households) were approximately 1800 and total population of children under eighteen years were approximately 3600. By systematic random sampling method I have selected 150 houses.Keeping in mind the study objectives a draft data collection instrument was prepared. It was an interview schedule with an observational checklist, which was a structured one to minimize time. The interview schedule was pre-tested in a non- sampling area of similar situation of Mirpur slum and was revised on the basis of the findings of pre-testing.For the collection of relevant data three methods were followed- Interviewing, filling up the observational checklist and collection of ear swab for laboratory test. All collected data were checked and verified thoroughly to reduce the inconsistency. The data were edited, coded and entered into the computer for analysis. Analysis was done according to the objectives of the study using suitable statistical package SPSS. Results were presented in tables and figures.

Results

This was a cross sectional study conducted in a selected slum of Dhaka City among the under eighteen population (Children) of both sexes with a view to assess the prevalence of chronic suppurative otitis media. A total of 403 children were examined and their responsible guardians were interviewed. The mean age of the children was 7.7 years, SD $\pm$ 4.7 years ranging from 1 to 17. The highest percentage was in age group 5-9 years followed by 1-4 years. Among the study children 208(51.6%) were boys and most 392(97.3%) of the children were Muslim. More than half of the children were illiterate followed by one-third of them had education between class I-V. Family size ranges from 3 to 7. Half of the children had family size 5-6, followed by 3-4 members (29.8%). It was found that two-third of the households were katcha followed by semipucca (19.1%).Two- third children had used tap water followed by ditch water (18.9%), pond (10.9%) and tube well water (5%).(Table 1).Out of 36 cases of CSOM, only 20(55.6%) received treatment for ear discharge. Most frequently, they received their treatment from salesman of pharmacy 6(16.7%), followed by 5(13.9%) each from homeopath and qualified physician Table 2. Out

of 403 children, 36(8.9%) war diagnosed as chronic suppurative otitis media (Table 3). The pattern of bacterial growth indicated that more than half 20(55.6%) were pseudomonas aeruginosa followed by 11(30.6%) staphylococcus aureus and 3(8.3%) Proteus vulgaris. (Table 4).The mean age of the children with CSOM was 5.1 years with a standard deviation ± 3.4 years and in non-CSOM mean was 8.0 years with standard devition± 4.7 years. Analysis found that mean age of the children with CSOM was significantly lower than the children with non-CSOM ($p<0.01$). This indicated that the CSOM was higher among the children with age group 1-4 years 17(47.2%) followed by 4-5 years 14(38.9%), 10-14 years 4(11.1%)(Table 5).The cases of CSOM was higher 27 (75%) among the illiterate children compared to literate children 9(25%) and the association was highly significant ($p<0.01$) & parental literacy identified as one of the important factors for CSOM. Analysis found that the CSOM was higher 27(75%) among the children having both father and mother illiterate compared to literate father and mother and the association was statistically significant ($p<0.01$).(Table 6).Analysis revealed that the SCOM was higher among the children of families having low monthly income (Taka 3583.33) compared to monthly income Taka4209.08 and this was statistically significant ($p<0.01$). This indicated that the cases of CSOM were higher 22(61.1%) among the children with monthly family income Taka 3000-3999, followed by 8(22.2%) in Taka 4000-4999, 5(13.9%) in Taka 5000-5999 and 1(2.8%) Taka 6000 and above (Table 7). The mean family size for the children having CSOM was 5.7 with SD ±1.2 and that of the children without CSOM was 5.2 with ±1.3 and this was statistically significant ($p<0.05$). As many as 23(63.9%) of CSOM were found among the children with family size 5-6, followed by 9(25.0%) in family member 7 and lowest 4(11.1%) among the children having family members 3-4. (Table 8)Bathing in pond, canal or ditch water identified as one of the important factors for CSOM. It was evident that the proportion of CSOM was higher among the children habituated to bath in the pond or canal or ditch water 20(55.6%) compared to tap or tube well water 16(44.4%). This showed a statistically significant ($p<0.01$) association between source of bathing water and CSOM.(Table 9).It was observed that the cases of CSOM were high among the children with history of ear cleaning using chicken feather 16(44.4%), followed by using match stick 11(30.6%), cloth and stick 4(11.1%), cotton bud 4(11.1%).(Table 10)

Table 1: Distribution of children by Socio demographic variables (n=403)

Characteristics	Group	Frequency	Percent (%)
Age	1-4	118	29.3
	5-9	141	35.0
	10-14	95	23.6
	>15	49	12.2
	Mean ± SD 7.7 ± 4.7 Range=1-17 yrs		
Gender	Boys	208	51.6
	Girls	195	48.4
Religion	Muslim	392	97.3
	Hinduism	11	2.7
Educational qualification	Illiterate	206	51.0
	Non-formal education	17	04.2
	Class I-V	156	38.7
	Class VI-X	16	04.0
	SSC-HSC	8	02.0
Family size	3-4	120	29.8
	5-6	202	50.1
	7	81	20.1
	Mean ± SD 5.2 ±1.3 Range=3-7 yrs		
Type of residence	Pucca	12	3.0
	Semipacca	77	19.1
	Jhupri	36	8.9
	Katcha	278	69.0
Source of bathing water	Tap water	259	64.3
	Tube well	20	5.0
	Pond	44	10.9
	Canal	4	1.0
	Ditch	76	18.9
	Total	403	100.0

Table 2: Distribution of children by pattern of treatment received for chronic suppurative otitis media

Pattern of treatment	Frequency	Percent (%)
No treatment	16	44.4
Traditional healer	4	11.1
Homeopath	5	13.9
Salesman of pharmacy	6	16.7
Qualified physician	5	13.9

Table 3: Distribution of children by presence of CSOM (n=403)

Presence of CSOM	Frequency	Percent (%)
Yes	36	8.9
No	367	91.1

Table 4: Distribution of children by pattern of bacterial growth (n=36)

Bacterial growth	Frequency	Percent (%)
Pseudomonas aeruginosa	20	55.6
Staphylococcus aureus	11	30.6
Proteus	3	8.3
No growth	2	5.6

Table 5: Distribution of children by chronic suppurative otitis media and age (n=403)

Age in years	Chronic suppurative otitis media			
	Present (n=36)		Absent (n=367)	
	Count	%	Count	%
1-4	17	47.2	101	27.5
5-9	14	38.9	127	34.6
10-14	4	11.1	91	24.8
15+	1	2.8	48	13.1
Total	36	100.0	367	100.0

Table 6: Distribution of children by CSOM and level of education of children and parents

Level of education of Children	Chronic suppurative otitis media			
	Present		Absent	
	No	%	No	%
Illiterate	27	75.0	179	48.8
Literate	9	25.0	188	51.2
Total	36	100.0	367	100.0
x^2=9.02:df=1:p<0.01				
Education of father				
Illiterate	27	75.0	187	51.0
Literate	9	25.0	180	49.0
Total	36	100.0	367	100.0
x^2=7.61:df=1:p<0.01				
Education of mother				
Illiterate	27	75.0	207	56.4
Literate	9	25.0	160	43.6
Total	36	100.0	367	100.0
x^2=4.66:df=1:p<0.01				

Table 7: Distribution of children by chronic suppurative otitis media and monthly income

Monthly family income (Taka)	Chronic suppurative otitis media			
	Present		Absent	
	No	%	No	%
3000-3999	22	61.1	98	26.7
4000-4999	8	22.2	134	36.5
5000-5999	5	13.9	95	25.9
≥ 6000	1	2.8	40	10.9
Total	36	100.0	367	100.0
t=3.777, p<0.01.				

Table 8: Distribution of children by chronic suppurative otitis media and family size

Family size	Chronic suppurative otitis media			
	Present		Absent	
	No	%	No	%
3-4	4	11.1	116	30.5
5-6	23	63.9	179	49.9
7	9	25	72	19.6
Total	36	100.0	367	100.0
t=2.403, p<0.05.				

Table 9: Distribution of children by chronic suppurative otitis media and source of bathing water

Sourcesof bathing water	Chronic suppurative otitis media			
	Present		Absent	
	No	%	No	%
Tap water & tube well	16	44.4	263	71.6
Others (Pond, Canal, Ditch)	20	55.6	104	28.4
Total	36	100.0	367	100.0
X^2=11:40; df=1; p<0.01.				

Table 10: Distribution of children by chronic suppurative otitis media and ear cleaning habit

Ear cleaning habit	Chronic suppurative otitis media	
	Present	
	Frequency	%
Chicken feather	16	44.4
Road side unskilled cleaners	1	2.8
Cloth and stick	4	11.1
Match stick	11	30.6
Cotton bud	4	11.1

Discussion

CSOM is a common health problem of our country, especially among the low socio-economic group of people. It has already been studied within and outside the country and the various factors for the development have been identified. The present study showed that the prevalence of CSOM among the study population was 89/1000 children. Out of the 403 children studied, 36 children (8.9%) were found to have CSOM. In a prevalence study in southeast Asia region, WHO found the prevalence of CSOM 7.8%.[1] Rupa et al (1999) found the prevalence of CSOM as 6% in India.[9] Ologe and Nwawolo (2002) conducted a study on "Prevalence of CSOM among school children in a rural community in Nigeria" and found 7.3%.[10] Similar result (9.44%) also found by Minja and Machembo (1996) in Tanzania.[11] However the present finding is less than the prevalence shown in some Bangladeshi studies. Majed (1977) found CSOM 15.06% in hospital based study.[5] Amin et al (1985) found 18.46%-38.58% in four rural ENT camps.[7] Haque (1994) found 31.25% in Rangpur Medical College Hospital.[6] Another

study done by Siddique and Khan (1994) at Rajbari district found 12.07%.[12]Sabur et al (1987) showed that the prevalence rate of CSOM 35.71% in a study in rural ENT camp.[13] Some other studies higher prevalence (12%-36%)[14,15,16,17]. The low prevalence of CSOM in the present study can be explained by the fact that with the passage of time the socio economic status of the country has improved. The increase in awareness among the mothers and improvement in health care facilities may have some positive impact in decreasing the incidence of CSOM.Low incidence (1.1%) of CSOM was stated in Kenya in 1992[18] and in some developed countries like United States of America and United Kingdom below 1%.[20] In this study the age distribution shows that highest 17 (47.2%) cases of CSOM were found in 1-4 years group; and 14 (38.9%) cases in 5-9 years group and 4 (11.1%) in 10-14 years age group. This is in accordance with the view of Browning GG (1989), as incidence of otitis media remains high in first five years of life, but thereafter tails off to become relatively in teenagers.[21] Hockelaman (1977) also found the prevalence high (32.9%) in early age. Reason behind this is, 1-4 years group is more vulnerable to develop RTI and anatomical arrangement of eustachian tube i.e shortness and direction makes journey easy for the organism from the nasal cavity and helps to develop otitis media. Sabur et al (1987) found in their study the cases of CSOM in infant, children and adult were 40%, 36% and 24% respectively.[22] It is consistent with the present study in regards to age distribution of the disease i.e. prevalence is decreasing with the increase of age. Similar result was also seen in study conducted by Karim (1983). The CSOM cases on that were 51% in 2-12 years age group, 27% in 13-20 years age group and 10% in 21-30 years age group. Rahman et al (1992), Yagi Hi (1990), Ologe and Nwawolo (2002), Obi et al (1995), Ahmed and Kudi (2003) also found CSOM are more prevalent in early age.[10,15,16,23,24] Educational status of children and parents were found inversely proportional to the prevalence of CSOM. In CSOM cases, 27 (75.0%) children were illiterate compared to literate children 9 (25.0%). The highest incidences of CSOM in illiterate children in present study depict that illiteracy has an important relation with the incidence of CSOM. In this study the association was highly significant. ($p<0.01$). Kamal (2001) found in her study 80% of the CSOM cases were illiterate.[8]Parental illiteracy was identified as one of the important factor for CSOM. CSOM was significantly higher among the children were both father and mother illiterate. Out of 169 children with literate mothers had 9 (5.6%) CSOM in present study. Where as in 234 children with illiterate mothers had 27 (11.5%) CSOM. An Indian study (1995) expressed higher figures of CSOM in relative frequencies of 15.7% in illiterate mothers and 12.9% in literate mothers.[14]The relatively higher incidence of CSOM among the children of illiterate mothers revealed that these mothers are ignorant about the disease and its treatment. CSOM was significantly higher among children of illiterate parents compared to literate parents ($p<0.01$). Chowdhury and Salauddin (1982) also found the higher prevalence of CSOM in illiterate children compared to literate.[25] Cases of CSOM were higher among the children having low monthly family income compared to high monthly income and the difference was significant. ($p<0.01$). The cases of CSOM were found higher 22 (61.1%) in taka 3000-3999, followed by 8 (22.2%) in taka 4000-4999, 5 (13.9%) in taka 5000-5999 monthly family income group in the present study done among slum dwellers. Cases of CSOM are generally found to be more prevalent in lower socioeconomic conditions, Siddiquee (1994) also found majority CSOM in poor and very poor family. In a rural based survey he found CSOM 19% in poor and 54% in very poor class. CSOM in middle and affluent classes were found in 25% and 2% families.[12] Higher the mean family size, higher the cases of CSOM were seen in this study. The children belonging to small family size (3-4) constituted less 4 (11.1%) compared to large family size (5-6) were 23 (63.9%). The relationship was statistically significant ($p<0.05$). Large family size is responsible for overcrowding and poverty, which in turn facilitates infection of ear. This finding is supported in WHO/ CIBA Foundation Workshop of 1996 where overcrowding has been recognized as a risk factor for CSOM.[2] Dulla and Banerjee (1991), Murray (2003) also recognized overcrowding as a risk factor in their study.[17,26] Bathing in ponds, canals or ditch water identified as one of the important factors for CSOM. The present study revealed that the proportion of CSOM was higher among the children habituated to bath in the pond, canal or ditch water 20(55.6%) compared to tap or tube well water 16(44.4%) and the association was statistically significant. ($p<0.01$). Khan and Hossain (1998) reported in their study that innate habit of Bangladeshi of bathing and dipping in ponds and river may be factors contributing to the high incidence of inflammatory middle ear disease in this country. The present study findings are consistent with above study findings.[25] Some other authors also recognized it.[13,27] It was observed that the proportion of CSOM was high among children with history of ear cleaning using unhygienic materials. Maximum patients 16(44.4%) cleaned their ear by chicken feather, 11(30.6%) cases used matchstick, 4(11.1%)

cases used cloth with stick and cotton buds 4(11.1%). This result is consistent with the study of Ahsan (2001)[28], he found the cases of CSOM was higher in those who had the habit of ear cleaning with chicken feather (44.4%) followed by cotton bud (12.5%). Chowdhury (1982) and Amin et al(1988) also found cleaning of ear with unhygienic material as a risk factor of CSOM.[25,,27] Altogether about half 20(55.6%) of the CSOM cases received treatment. Only 13.9% of cases received it from qualified doctor and 16.7%,13.9% and 11.1% received it from salesman of pharmacy, homeopathy doctor and traditional healers respectively. The picture of treatment seeking from competent professionals in our community is not very encouraging. One study in rural area of Rajbari district (1994) showed that only 8.49% of CSOM cases attended hospital.[29]This is similar to this study as only 13.9% received treatment from a qualified doctor. Karmi (1983) in his study found that 46% of patients got no treatment for their first attack, 37%were treated at different hospitals and rest were treated by traditional healers and at home[30]. CSOM is a common problem in developing countries and it is necessary to determine the local epidemiology for adequate treatment. It was found that out of 36 CSOM cases 34 showed culture positive. The pattern of bacterial growth indicate that 20(55.5%) were Pseudomonas aeruginosa followed by 11(30.6%) Staphylococcus aureus. It was also noted that 2(5.6%) did not show bacterial growth. The cases of no growth of bacteria may be due to use of antibiotics or may be due to non-bacterial causes. A retrospective study on 206 patient with CSOM in Gombe, Nigeria had done by Ahmed and Kudi (2003) 87.4% of patient had positive bacterial culture. These were Staphylococcus aureaus 37.8%, Pseudomonas aeruginosa 28.9% and Proteus species 18.3%.[24] Staphylococcus aureaus, Pseudomonas aeruginosa and Proteus species were found common organism in other studies also.[15,16,18,20,21,22,27,30]

Conclusion

From this study it can be concluded that prevalence of CSOM is still high in Bangladesh. Majority of the patient were in the age group 1-4 years and CSOM was more common in children of low socioeconomic condition. There is also some relationship between CSOM with habit of bathing in polluted water. Most of this patient had the habit of cleaning ear with unhygienic materials like chicken feathers. About half of the patients did not received any treatment and among them who received treatment, most of them received it from unskilled person. Among the organism isolated in present study Pseudomonas aeroginosa formed the predominate isolate. Based on this result, reviewing relevant literatures and subsequent discussion, it can be said that the findings of the study can be useful for future research and planning for the prevention of mortality and morbidity of chronic suppurative otitis in our country.

Authors Affiliation

1. *Col Dr. Abu Hena Md. MustafijurRahman,MPH, MPhil ADMS, 33 INF DIV, Cumilla Cantonment.
2. Dr. Mohammad Shakil, MPH, Associated Professor, Dept. of Community Medicine, Army Medical CollegeCumilla.
3. Dr. Shahara Begum, M Phil, Asst Prof Biochemistry dept. Sheikh Hasina Medical College, Tangail

* For Correspondence

Reference

1. Acuin J, Berman S, Moris P, et al. Chronic suppurative otitis media burden of illness and management options, child and adolescent health and development, prevention of blindness and deafness. World Health Organization, Geneva, Switzerland. 2004; 1-33.
2. Acuin J.Chronic suppurative otitis media. Clinical evidence. BMJ. 2003;1-9.

   https://apps.who.int/iris/bitstream/handle/10665/63870/WHO_PDH_98.4.pdf?sequence=1&isAllowed=y
3. Smith AW, Bluestone c, Alberti P, et al. Prevention of hearing impairment from chronic otitis media. WHO/CIBA foundation workshop report. London, UK. 19-21 Nov 1996; 1-12.
4. Telle DW. Otitis media in infancy and intellectual ability, school achievement, speech and language, J Infect Dis. 1990;162(3): 685-694
5. Majed MA. EMT problems in Bangladesh, Bangladesh medical journal. 1979; 8(2): 53-59
6. Haque GHM, Joarder MAH, Amin AHA, Islam MA, Ahsan MZ, Akaiduzzaman DGM. Pattern of EMT disease; An out patient based study in Rangpur Medical College Hospital. Northern medical college journal. 1996; 5(1): 52-55
7. Amin MN, Chowdhury WA, Sheik MS, Abdullah M. Pattern of ENT disease in rural Bangladesh. J Bangladesh college of phys & surgs. 1989; 7: 23-27
8. Kamal N. Prevelance of chronic suppurative otitis media among the children of two selected slum dwellers

in Dhaka city (Dissertation). Dhaka: NIPSOM; 2001:3-5

9. Rupa V. Jacob A. Joseph A. Chronic suppurative Otitis media : prevalence and practices among rural South Indian children. Interntional journal of paediatricotorhinolaryngol. 1999; 48(3): 217-221.
10. Ologe FE, Nwawolu CC, Prevalence of chronic suppurativeotits media among school children in a rural corner in Nigeria. Nigeria postgraduate medical journal. 2002 ; 9(2): 63-66.
11. Minja BM, Machembo A, Prebalence of otitis media, hearing impairment and cerumenimpection among school children in rural and urban Dares Salam, Tanzania. International journal paediatric otorhinolaryngol. 1996; 37(1): 29-34.
12. Siddique BH, Khan AH. Chronic suppurative otitis media a rural area based study, Sir Salimullah Medical College Journal. 1995; 3(1): 31-33
13. Sabur MA, Hafiz MM, Haroon AA. A study of pattern of ENT disease in rural Bangladesh, Bangladesh Journal of otorhino laryngology. 1987; 1(2): 15-17
14. Verma AK, Vohra A, Maitra A, Banarjee M, Singh R, Mittal SK, Epidemiology of chronic suppurative Otitis media and deafness in a rural area and developing an intervention strategy. Indian journal of paediatric. 1995; 62(6): 725-729.
15. Yasi HI, Chronic suppurative otitis media in Sudanese patients, East African medical journal, 1990 Jan; 67(1): 4-8.
16. Obi LL, Enweani IB, Giwa JO, Bacterial agent causing chronic suppurative otitis media, East African medical journal. 1995; 72(6): 370-372.
17. Murray Richard. Prescribing issues for Aboriginal people. Australian prescriber. 2003; 26(5): 106-109.
18. Hatcher J, Smith A, Mackenzie I, Thompson S, Bal I Macharia I. A prevalence study of ear problems in school children in Kiambu district, Kenya. International journal of paediatric otorhinolaryngol. 1995; 33(3): 197-205.
19. Muhaimeid H, Zakzouk S, Bafaqeeh S. Epidemiology of chronic suppurative otitis media in Saudi Arabia. International journal paediatric otorhinolaryngol. 1993;26(2): 101-8
20. Huebner E, Wasas Ad, Hackman MJM, Klugman P Klith. Bacterial activity of non- responding otitis media in South African children. The Journal of laryngology otology. 2003;117: 169-172
21. David P, Peter SR, Middle ear, chronic suppurative otitis media. Medical treatment. 2005;8: 1-10.
22. Faruque MN, Jesmin A, Abedin SAMA. Bacteriological study of chronic suppurative otitis media (CSOM), Northern medical journal. 1995;2(1): 20-22
23. Rahman M, Ahmed S, Occurrence of otitis media as a cause of tetanus amongst the patients of infections disease hospital. JOPSOM. 1992; 11(2): 59-62
24. Ahmed Bm, Kudi MT, Chronic suppurative otitis media in Gombe, Nigeria. Nigerian journal of surgical research. 2003; 5(122): 120-123.
25. Chowdhury MSN, Salauddin AKM. A note on a survey of CSOM amongst school children at Narayangong, Journal of preventive and sockal medicine. 1982;1(2): 63-66
26. Datt PK, Banarjee A. An epidemiological study of hearing loss in a slum in Pune. Indian journal of public health. 1991;35(4): 108-112.
27. Amin MN, Chowdhury WA. Bacteriological study of chronic suppurative otitis media and their sensitivity to antibiotics. Journal of Bangladesh college of physician and surgeons. 1988;5(2): 8-9
28. Ahsan AKMM, A study on prevalence of chronic suppurative otitis media under twelve years of children in a selected slum of Dhaka city (Dissertation), Dhaka: AFMI; 2001: 43.
29. Siddique BH. Khan AH. Chronic suppurative otitis media a rural area based study. Sir Salimullah medical college journal. 1995; 3(1): 31-33
30. Bafaqeeh SA, Zakzouk SM, Muhammad H, Essa A. Relevant demographic factors and hearing impairment in Saudi children. Epidemiology. 1994;108(4): 294-298.

Impact of Mastalgia In Women's Quality of Life

Abu Daud Md Shariful Islam[1], Julia Akhter Nira[2], Ahmed Rafi[3], Mizanur Rahman Molla[4], Tahmina Akhter[5]

Abstract

Background: Mastalgia is pain arising in the breast tissue, and can be cyclic or non-cyclic, intermittent or continuous. The aim of this study was to evaluate the relationship of mastalgia with depression and anxiety, and to examine its effects on the quality of life. **Materials and methods:** This cross-sectional study was conducted between July 2018 and March 2019 at combined military hospital, Cumilla. Total 30 pre-menopausal women with mastalgia were selected as study group and compared with 30 healthy women without any breast pathology, previous breast surgery or psychiatric illness. Patients investigated with Short Form-36, Hamilton Depression Scale and Hamilton Anxiety Rating Scale. **Results:** Between the two groups, there were no statistically significant difference for Physical role difficulty (P=0.38), Social functionalism (P=0.12), and Emotional role difficulty (P=0.16), but significant differences were observed for Physical functionalism (P=0.03), Body pain (P=0.04), and general health (P=0.01). The level of energy parameter was lower in patient group (P=0.01), but mental health level difference was not significant (P=0.10). **Conclusion:** Mastalgia in patients without any pathology is associated with depression and anxiety, and can affect patients quality of life.

Keywords: Mastalgia, Quality of life

J Ar M Coll Cu. 2019, July; 2 (2): 10-13
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Mastalgia is pain arising in the breast tissue. It is defined as tension, discomfort and pain in one or both breasts[1]. The pain is usually experienced bilaterally and in the upper quadrant[2]. Mastalgia could stem from breast tissue itself, extra mammary tissues or psychological reasons. Some of these are macromastia, diet or life style changes, Hormone Replacement Therapy (HRT), ductal ectasia, mastitis, increased water and salt retention, and high dose caffeine intake[1]. As the most common breast symptoms causing women to consult physicians, it may affect up to70% of women in their life time [3,4]. The high-level public awareness about breast cancer and the concern that mastalgia may indicate disease contribution to this trend[5]. Mastalgia can be cyclic or non-cyclic, intermittent or continuous, and localized or widespread. Non-cyclic Mastalgia may either originate from breast tissue or chest wall, or there can be intermittent or continuous Mastalgia, and in general no cause originating from chest wall is found. Cyclic Mastalgia is characterized with exacerbation of pain at the premenstrual period[6]. In most of the cases, no physical causes are determined and very little response is obtained from given medical treatment. In spite of all radiologic and medical developments, the etiology of mastalgia is not fully enlightened. There is a relationship determined between mastalgia with depression, anxiety, and psychological symptoms of somatization disorder, especially in treatment-resistant mastalgia; besides, mastalgia has been found to be related to high stress level[7,8,9]. Our aims in this study were to evaluate the relationship of the complaint of mastalgia with depression and anxiety, and to examine its effect on the quality of life.

Received July 2019 Accepted January 2020

Materials and Methods

This cross-sectional study was conducted prospectively between July 2018 and March 2019 at combined military hospital Cumilla. Ethical clearance was obtained from competent authority. Total 30 pre-menopausal women with mastalgia was selected as study group and compared with 30 healthy volunteers with same characteristics. In the patient selection, the following were excluded from the study: Those

diagnosed with breast cancer , those with history of psychiatric illness or use of any anti-depressant medication, those who had undergone previous medical procedures on the breast such as breast surgery, biopsy, etc. those with history of trauma to the chest region within the previous 1 month, those with mastalgia persisting for less than 6 months, those with benign events such as breast cysts, pregnant women and breast feeding women, those with an inflammatory event such as breast abscess. The exclusion criteria that had been applied to the patient group were applied to control group also. All the patients underwent a physical examination and ultrasound evaluation. The patients without any breast pathology were investigated with the Short Form 36 (SF-36), Hamilton Depression Scale, and Hamilton Anxiety Rating Scale[10,11,12]. The control underwent the same procedure. The SPSS 19 program was used in order to assess the data statistically, and the t test was applied. A p value of <0.05 was accepted as statistically significant.

Results

The mean age of the patients group was 33.05±2.16 years and control group 31.21±3.58 years without any statistically significant difference (P>0.05). When the two groups were compared for the SF-36 quality of life, the patients group was observed to be lower than that of control group. The difference between the two groups was not statistically significant when examined for physical role difficulty (P>0.05), social functionalism (P>0.05), and emotional role difficulty (P>0.05). On the other hand, there was significant difference between the groups for physical functionalism (P<0.05), body pain (P<0.05), and general health (P<0.05). In particular, the level of energy parameter was seen to be lower with patients group than that in the control group. In terms of this parameter, there was a highly significant difference between the groups (P<0.05). No statistically significant difference was detected in terms of mental health level (P>0.05). The mean values of the patient and the control groups in the SF-36 quality of life scale measurements have been presented in (Table 1). When the anxiety and the depression tests' values of the groups were compared, the anxiety level was observed to be higher in the patient group, and this difference was statistically significant (P < 0.05). The depression level was also found to be higher in the patient group, and although there was no significant difference between the two groups statistically, the difference was valuable (P > 0.05). The mean anxiety and depression level values of the groups have been presented in (Table 2).

Table 1: Assessment of the groups in terms of quality of life

SF-36	Mastalgia group (n=30)	Control group (n=30)	P value
Physical Function	69.15±4.28	75.28±3.16	0.03
Physical Role	55.06±1.82	64.19±5.16	0.38
Body Pain	54.79±3.20	66.13±3.81	0.04
General Health	53.14±1.57	59.11±2.06	0.01
Social Functionalism	62.29±3.20	69.47±3.21	0.12
Energy	41.36±2.18	55.39±4.18	0.01
Emotional Role	52.69±1.32	58.03±1.18	0.16
Mental Health	47.50±6.21	59.96±4.72	0.10

Table 2: Comparison of the depression and anxiety scale scores of the group

Scale	Mastalgia group (n=30)	Control group (n=30)	P value
HAM-D	12.60±1.16	10.06±0.18	0.06
HAM-A	11.26±1.28	7.40±0.51	0.03

Discussions

In this study, the mean age of study group was 33.05±2.16 years. In a series of 1219 patients, Johnson et al[7] reported that the age of women complaining of breast pain was 35 and 55 years. Although mastalgia is the most common reason of breast related symptoms patients consult with general surgery outpatient clinics and primary physicians with, its etiology has not yet been clarified[16,17]. Some factors such as caffeine, cigarette smoking, high plasma fatty acids, prolactin and acute stress have been demonstrated to possibly be effective on the etiology[18]. The relationship of caffeine consumption and smoking with breast pain is controversial[19,20]. In their series of 874 cases, Ader et al reported that increased caffeine consumption and smoking were corelated with mastalgia[4].There are numerous studies demonstrating a relationship between mastalgia and psychological stress[8,9,21], and it reduces women's quality of life considerably[16,17]. It has also been demonstrated that there are some psychological disorders in individuals with mastalgia such as loss of self-esteem, helplessness, depression[22]. In this study, the anxiety value was found to be significantly higher in patient group in comparison to control group. Similarly, the depression level was found to be higher too, but not statistically significant. However, significant difference in depression levels have been found in other studies[23]. Mastalgia in the daily life of women can be related to the increase of fear of breast cancer, and when the

suggestion and assurance are given that the symptoms are not related to cancer, successful treatment is achieved in 70 % of the patients[24]. It has been demonstrated in a large-scale study that cyclic mastalgia affects the sleeping status by 10, 6, and 13 %, the physical activity by 36 %, and the sexual activity by 48 %[25]. However, those with benign breast diseases had also been included in this study. Besides, unlike our study, patients with cyclic mastalgia had been included in the study and there was no control group formed. According to our study, significant decreases were detected in the four scales of the total eight SF-36 scales (physical functioning, corporal pain, general health, and energy) in the patient group. In terms of quality of life, mastalgia mostly affects the energy status, in other words, vitality. According to this, mastalgia has been found to be related to constant feeling of fatigue and exhaustion. At the same time, the anxiety due to the thought of poor health and thinking that it will get worse can cause limitations of all physical activities including bathing and dressing and the daily activities of the patient.

Conclusion

In patients who present with the complaint of mastalgia, when there is no detection of an underlying organic pathology, it should be kept in mind that this status can be related to depression and anxiety, and the treatment should be planned taking into consideration that mastalgia can affect the patient's quality of life significantly.

Authors affiliation

1. *Col Abu Daud Md Shariful Islam, Professor and Head, Department of Surgery, Army Medical College, Cumilla, and Senior Surgeon, CMH, Cumilla.
2. Lt Col Julia Akhter Nira, Classified Spl in Gynae and Infertility, CMH Dhaka.
3. Col Ahmed Rafi, Healthcare Management Specialist and Commandant, CMH Cumilla.
4. Lt Col Mizanur Rahman Molla, Dept of ophthalmology, CMH, Cumilla.
5. Dr Tahmina Akhter, Assistant Professor, Dept of Anatomy, Army Medical College, Cumilla.

*For correspondence

References

1. Yıldırım AC, Yıldız P, Yıldız M, Kahramanca Ş, Kargıcı H. Mastalgia-cancer relationship: a prospective study. J Breast Health. 2015; 11: 88-91.
2. Madlon-Kay J. Meme Kitleleri ve Diğer Meme Hastalıkları. In: Mengel MB, Schwiebert LP, editors. Lange Aile Hekimliği Ayak- tan Tedavi ve Korunma. Ankara: Güneş Tıp; 2013. p.44-47.
3. Preece PE, Baum M, Mansel RE, et al.: Importance of mastalgia in operable breast cancer. Br Med J. 1982; 284: 1299–1300.
4. Ader DN, South-Paul J, Adera T, et al.: Cyclical mastalgia: Prevalence and associated health and behavioral factors. J Psychosom Obstet Gynaecol. 2001;22: 71–76.
5. Morrow M: The evaluation of common breast problems. Am Fam Physician. 2000; 61: 2371–2378.
6. Tejwani PL, Srivastava A, Nerkar H, Dhar A, Hari S, Thulkar S, Chumber S, Kumar S. Centchroman regresses mastalgia: a randomized comparison with danazol. Indian J Surg. 2011;73(3): 199–205.
7. Johnson KM, Bradley KA, Bush K, Gardella C, Dobie DJ, Laya MB. Frequency of mastalgia among women veterans. Association with psychiatric conditions and unexplained pain syndromes. J Gen Intern Med. 2006;21(3): S70–5.
8. Preece PE, Mansel RE, Hughes LE. Mastalgia: psychoneurosis or organic disease? Br Med J. 1978;1: 29–30.
9. Colegrave S, Holcombe C, Salmon P. Psychological characteristics of women presenting with breast pain. J Psychosom Res. 2001; 50: 303–307.
10. Kabra N, Nadkarni A. Prevalence of depression and anxiety in irritable bowel syndrome: a clinic-based study from India. Indian J Psychiatry.2013; 55(1): 77–80.
11. Guloksuz S, Wichers M, Kenis G, Russel MG, Wauters A, Verkerk R, Arts B, van Os J (2013) Depressive symptoms in Crohn's disease: relationship with immune activation and tryptophan availability.

    https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0060435
12. Saeidi M, Mostafavi S, Heidari H, Masoudi S. Effects of a comprehensive cardiac rehabilitation program on quality of life in patients with coronary artery disease. ARYA Atheroscler. 2013; 9(3): 179– 85.
13. Ware JE. SF-36 health survey update. In: Maruish ME

planning and out- comes assessment, 3rd edn. Lawrence Erlbaum Associates, USA 2004; pp 693–718.

14. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960; 23: 56–62.
15. Bruss GS, Gruenberg AM, Goldstein RD, Barber JP. Hamilton anxiety rating scale interview guide: joint interview and test-retest methods for interrater reliability. Psychiatry Res. 1994; 53: 191– 202.
16. Hocaoglu Ç. What is mastalgia? J Breast Health. 2007; 3: 49-52.
17. Dinc T, Dikmen K, Coşkun F. The Importance of Breast Ultraso- nography and Risk Factors in Patients Admitted with Mastalgia. GMJ. 2013; 24: 127-129.
18. Cakir T, Cingi A, Fistikci N, Bez Y, Topcuoglu V, Gulluoglu BM. Organýkbýrnedenebaglýolmayanmastaljiyakýnmasýolanhastalardate-lkininyeri. Prospektifkesitselçalýşma. Meme sagligi Dergisi. 2006; 2: 96–99.
19. Goyal A, Mansel RE: Mastalgia; in Jatoi I, Kaufmann M (eds): Management of breast disease. Springer-Ver- lag, Berlin, 2010, pp. 69–76.
20. Iddon J: Mastalgia; in Dixon JM (ed): ABC of breast disease, 3rd ed. Blackwell Publishing, Edinburgh, UK, 2006, pp. 15–18.
21. Jenkins PL, Januil N, Gateley C, et al. Psychiatric illness in patients with severe treatment-resistant mastalgia. Gen Hosp Psychiatry. 1993; 15: 55–57.
22. Preece PE, Mansel RE et al. Clinical syndromes of mastalgia. Lancet. 1976;308(7987): 670-673.
23. Ramirez AJ, Jarrett SR, Hamed H, Smith P, Fentiman IS. Psychosocial adjustment of women with mastalgia. Breast. 1995; 4: 48–51.
24. Barros AC, Mottola J, Ruiz CA, Borges MN, Pinotti JA. Reassurance in the treatment of mastalgia. Breast J. 1999; 5: 162–165.
25. Ader ND, Browne WM. Prevalence and impact of cyclic mastalgia in a Unýted States clinic-based sample. Am Obstet Gynecol. 1997; 177(1): 126–132.
26. Kowalski C, Steffen P, Ernstmann N, Wuerstlein R, Harbeck N, Pfaff H. Health-related quality of life in male breast cancer patients. Breast Cancer Res Treat. 2012; 133(2): 753–7.

Microalbuminuria Among the Diabetic Patients at an Urban Diabetic Center, Bangladesh: A Prevalence Study

Sarker Hafiz Mahmud[1], Nasrin Akter[2], Wahida Khanam Chowdhury[3], Tahera Khanom[4], Ripon Chundra Majumder[5]

Abstract

Background: Microalbuminuria is one of the early markers not only of diabetic nephropathy but also cardiovascular diseases with diabetes. Detection and prevention of microalbuminuria in early stage may delay the progression of microalbuminuria to diabetic nephropathy, which may increase the life expectancy in diabetic patients. **Objective:** This study was conducted to determine the prevalence of microalbuminuria and associated factors among patients with type 2 DM in an urban diabetic center at north-east region of Bangladesh. **Materials and Method:** Total number of 305 people with type 2 diabetes mellitus were included our study. Urine microalbumin was measured by U-Albumin (Nycocard, Axis-Shield, Norway) solid phage, sandwich-format, immunometric method on spot sample. Measuring range of albumin was (Microalbuminuria present) 20-200 mg/L, equivalent to 30-300 mg/24 hours or 20-200 µgm/min. **Result:** Among the study population there were 208(68.2%) male subject, where 97(31.8%) were female. Among the total population in normoalbuminuric group 144 were male and 52 were female. In microalbuminuric group, male subject were 64 and female were 45. Chi-Square (X^2) tests shows no significant difference, in terms of gender distribution between normoalbuminuric group and microalbuminuric group. According to Albumin Creatinine Ratio (ACR) measurement among those 305 study subject, 196 (64.27%) people were normoalbuminuric and 109 (35.73%) people were detected as microalbuminuric. So in our study group the number of patient with microalbuminuria is 35.73% with the confidence interval 32.88% to 37.67%. **Conclusion:** The prevalence of microalbuminuria in a divisional city at north-east region of Bangladesh is 36.7%, which is a clinic based study. The risk factors are similar to that reported among Europeans. Fasting blood glucose, Systolic blood pressure, Diastolic blood pressure, Serum creatinine and number subject with HTN between normoalbuminuric group and microalbuminuric group of our study shows significant difference statistically.

Keywords: microalbuminuria; Prevalence; diabetes; type 2 diabetes; north-east Bangladesh.

J Ar M Coll Cu. 2019, July; 2 (2): 14-19
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Type 2 diabetes mellitus (DM) has emerged as the new pandemic of the 21st century and it is estimated that 80% of people with diabetes live in low and middle income countries. It is also estimated that there were 415 million people with DM worldwide in the year 2015 and this number is expected to increase to 640 million people by 2040.[1] In Africa, the number of people with DM is expected to increase by 162.5% by the year 2045.[1] The World Health Organization (WHO) estimated that diabetic nephropathy is the leading cause of end stage renal disease worldwide.[2] Microalbuminuria is considered to be an early stage of diabetic nephropathy.[3] Microalbuminuria is also considered to be a predictor for cardiovascular disease both among diabetic and nondiabetic subjects,[4] and is one of the components of the metabolic syndrome (insulin resistance syndrome).[5] Recent statistics from the World Health Organisation (WHO) project an increase in the prevalence of diabetes worldwide particularly in developing countries.[6]

The early nephropathy stage when urinary albumin excretion (UAE) is 30–300 g/24 h, and/or 20–200 mg/min, is known as microalbuminuria, and patients with microalbuminuria are referred to as having incipient nephropathy.[7] Intervention at this stage can retard or reverse the progression of nephropathy. Microalbuminuria represents the simplest and most sensitive prognostic factor to evaluate the risk of overt nephropathy in diabetes, thus representing the first stage of the progressive diabetic renal disease. Diabetic nephropathy in patients with type 2 diabetes has a cumulative prevalence rate of 30–40%.[8] Although some studies in the Sub-Sahara African have been able to show prevalence as high as 57%.[7] However, in Nigeria, several studies have reported the

Received September 2019 Accepted February 2020

prevalence of Microalbuminuria in type 2 DM (T2DM), which varies widely (16.1–41.2%).[9] Microalbuminuria is one of the early markers not only of diabetic nephropathy but also of cardiovascular disease morbidity and mortality in patients with diabetes. Studies have shown that 20% to 40% of patients with type 2 DM ultimately develop nephropathy.[10] Microalbuminuria is defined as urinary albumin excretion (UAE) rate of 30–300 mg/day in a 24 hour collection or ACR of 3.0–30.0 mg/mmol in a spot collection.[11] Measurement of UAE in a 24 hour collection is the gold standard method to determine the presence of microalbuminuria because UAE follows a circadian rhythm. This, however, has been found to be cumbersome, expensive, and time consuming, hence more practical alternatives; measurement of urinary albumin concentration (UAC) or ACR has been used. These can be done on a first morning void or a spot (random) urine sample. In a systematic review and meta analysis of studies comparing ACR on a random urine specimen to albumin excretion rate from an overnight or 24 hour timed sample, Ewald and Attia found that ACR on a random specimen had a sensitivity of 90% and a specificity of 84%, and they suggested that ACR on a random urine specimen be used routinely as the initial test in screening diabetics or microalbuminuria.[12]

Material and Method

A descriptive cross-sectional study was conducted during the period from 1st July 2014 to 30th June 2015 at Sylhet diabetic hospital, Sylhet with the collaboration with the Department of Pharmacology and Therapeutics, Sylhet MAG Osmani Medical College, Sylhet. Sylhet is a divisional city at north-east region of Bangladesh. Patients who had a confirmed and documented diagnosis of type 2 DM were included in our study as a study population. The Data for our study were collected between July 2014 and December 2014. The exclusion criteria includes- Patients who are known to have chronic kidney disease (CKD) or end stage renal disease, congestive cardiac failure, critically ill patients requiring admission, patients having signs of urinary tract infection on urine dipstick (i.e., presence of urinary nitrites and leucocytes of at least 1+), overt proteinuria of more than 300 mg/day, and pregnant women were excluded from the study. The minimum required sample size of 305 patients with type 2 DM was calculated according to the formula for sample size calculations in cross-sectional studies.[13-14] Patients were enrolled followed by simple systematic random sampling pattern. Among the patients, each third one who fulfills the inclusion and exclusion criteria was included questionnaire was used to interview patients to collect sociodemographic data and record clinical variables. Blood pressure was measured with a mercury sphygmomanometer from the right arm in sitting position after taking at least 10 min rest. Two blood pressure measurements were taken 10 min apart and the average of the two readings was used as the patient's final blood pressure for the study. Patients who were known to be hypertensive and on antihypertensive therapy or had systolic blood pressure of >140 mmHg or diastolic pressure of >90 mmHg was considerd as hypertensive.

Laboratory analysis

Serum & urine creatinine was estimated by alkaline picrate method. Glomerular filtration rate (GFR) was calculated by Cock-Crof Gault formula. After selection, the patients were advised to come back on next morning. Patients were advised to collect the morning spot urine sample in a plastic container. After collection the urine samples were labeled for identification and urinary microalbumin was measured. Urine microalbumin was measured by U-Albumin (Nycocard, Axis-Shield, Norway) solid phage, sandwich-format, immunometric method on spot sample. Measuring range of albumin: 5-200 mg/L, Increased values (Microalbuminuria present): 20-200 mg/L, equivalent to 30-300 mg/24 hours or 20-200 µgm/min.[15] In spot urine sample albumin was measured quantitatively and adjusted to urine creatinine. Then interpreted as ACR. The ratio <3.4 mg albumin/mmol of creatinine as normal albuminuria, ≥3.4-33.9 mg albumin/mmol of creatinine as microalbuminuria, and >33.9 mg albumin/ mmol of creatinine as macroalbuminuria.[16] Microalbuminuria measurements in a random urine sample (spot collection) shows almost perfect accuracy. Screening of micro and macro albuminuria and urinary albumin concentration measured in an random urine sample is simpler and less expensive than 24 hour urine collection.[17] Studies also suggested that urinary albumin creatinine ratio in random sample is appropriate for quantitative assessment of microalbuminuria and can be used instead of using 24 hours UAC, with high sensitivity (84.9%) and specificity (95.8%) with positive predictive value of 90% and negative predictive value of 93%.[18]

Statistical analysis

All statistical analysis was done by SPSS (Statistical package for social science) for windows version 16.0. Quantitative data were expressed as mean and standard deviation and comparison were performed between two groups by paired t

between two groups by Chi-Square (X^2) test. A probability value (p) of <0.05 was considered as significant.

Result

Total noumber of 305 people with type 2 diabetes mellitus were included our study. Among the study population there were 208(68.2%) male subject, where 97(31.8%) were female. Among them in normoalbuminuric group 144 were male and 52 were female. In microalbuminuric group number of male subject were 64 and 45 were female. This distribution is presented in Table 1 where Chi-Square (X^2) tests shows no significant difference between normoalbuminuric group and microalbuminuric group. According to ACR measurement among those 305 study subject, 196 (64.27%) people were normoalbuminuric and 109 (35.73%) people were detected as microalbuminuric. So in our study group the number of patient with microalbuminuria is 35.73% with the Confidence interval 32.88% to 37.67%. This prevalence of microalbuminuria in a urban diabetic center, north east region of Bangladesh is presented graphically in figure no 1. Figure number 2 shows distribution of sex among this two groups. Table no 2 show mean age of the patients in normoalbuminuric group was 48.61 ± 9.28 years and in microalbuminuric group was 51.12 ± 7.56 years. There is no significant difference of age were found between normoalbuminuric group and microalbuminuric group. The mean duration of diabetes in normoalbuminuric group was 4.8 ± 2.79 years and in microalbuminuric group was 5.15 ± 3.5 years with no significant difference between this two groups statistically. The mean fasting blood sugar was 7.4 ± 2.81 mmol/L and 9.27 ± 3.9 mmol/L in two groups respectively, which was statistically significant. Avarage systolic blood pressure in normoalbuminuric and microalbuminuric patients were 138.45 ± 18.67 mm of Hg and 144.73 ± 21.39 mm of Hg respectively. There was significant diffrence between avarage systolic blood pressure in normoalbuminuric group and in microalbuminuric group. In other end, diastolic blood pressure also showed significant difference between normoalbuminuric group and microalbuminuric group where average was 81.2 ± 11.46mm of Hg and 87.65 ± 13.8mm of Hg respectively. The mean of serum creatinine was 80.4 ± 26.2 mmol/L in normoalbuminuric group and in microalbuminuric group was 86.36 ± 13.9 mmol/L with significant difference between these two groups statistically. Among 196 subjects in normoalbuminuric group there was 27% hypertensive patients and in microalbuminuric group there was 35% patient with hypertension. This result was also statistically significant.

Table 1: Gender based distribution of study subjects along with presents of micro albumin in urine

	Normoalbuminuric	Microalbuminuric	Total	P value
Male	144	64	208(68.2%)	
Female	52	45	97(31.8%)	0.157
	196(64.27%)	109(35.73%)	305(100%)	

* Chi-Square (X^2) test was performed to measure P value

Figure 1: Presentation of microalbuminuric patients. (N=305)

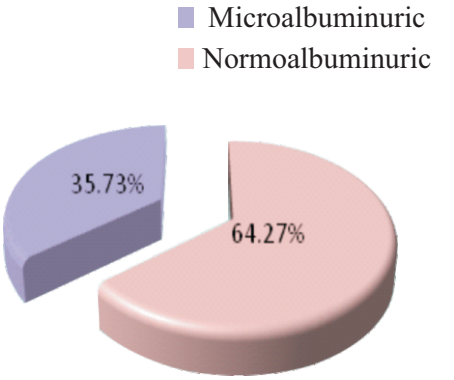


Figure 2: Total number of male and female presented in normo and microalbuminuric Group

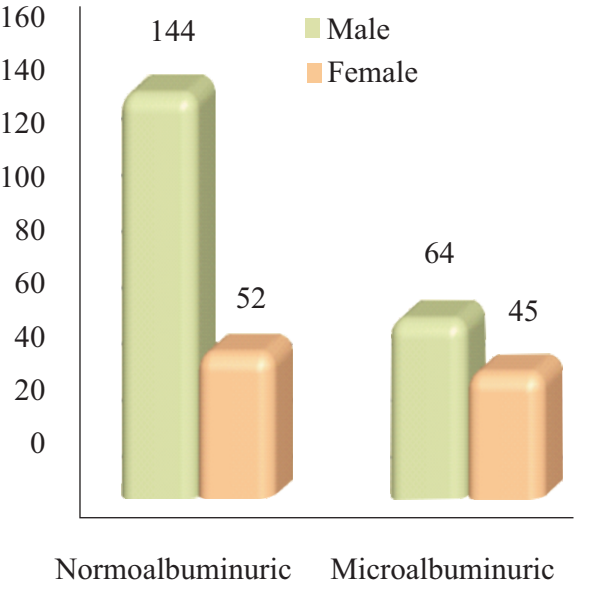


Table 2: Comparison of clinical variables between Normoalbuminuric and Microalbuminuric

Variables	Normoalbuminuric Group (n=196)	Microalbuminuric Group (n=109)	P Value
Age (Years)	48.61 ± 9.28	51.12 ± 7.56	0.15
Duration of Diabetes (Years)	4.8 ± 2.79	5.15 ± 3.5	0.08
Fasting Blood Glucose (mmol/L)	7.4 ± 2.81	9.27 ± 3.9	0.0002
Systolic Blood Pressure (mm of Hg)	138.45 ± 18.67	144.73 ± 21.39	0.01
Diastolic Blood Pressure (mm of Hg)	81.2 ± 11.46	87.65 ± 13.8	0.008
Serum Creatinine (mmol/L)	80.4 ± 26.2	86.36 ± 13.9	0.01
History of HTN	53 (27%)	39 (35%)	0.004

*P<0.05 is statistically significant. *Statistically significant using the Student's t-test

Discussion

Incidence of diabetes mellitus has increased drastically over past decade. Various epidemiological and cross sectional studies have reported marked variation in the prevalence of microalbuminuria. In our study group the number of microalbuminuric patient was 35.73% with confidence interval 32.88% to 37.67%. A descriptive cross-sectional study with 200 diabetic patients at Chitradurga showed prevalence of normoalbuminuria 71% and microalbuminuria 29%, this increased prevalence was due to increased in duration of type 2 diabetes mallitus.[19] In another study, a diabetes centre in southern India showed the prevalence of microalbuminuria 36.3% (95% confidence interval 33.8 to 38.9). The prevalence of microalbuminuria increased with the increase in duration of diabetes. Multivariate regression analysis revealed age, diastolic blood pressure, glycated haemoglobin (HbA1C), fasting plasma glucose, and duration of diabetes to be associated with microalbuminuria.[20] Gupta et al reported prevalence of microalbuminuria 26.6% in north Indian type 2 non-proteinuric Diabetic patients,[21] while John et al. reported a prevalence of 19.7% from a tertiary hospital in Vellore, south India[22]. Vijay et al. studied among 600 type 2 diabetic patients at a diabetic centre in Chennai city. In their study they reported that 15.7% of study polulation had proteinuria.[23] Studies in the white UK population revealed a prevalence of microalbuminuria of 7%–9%,[24-25] while in Mexican Americans, it was 31%,[26] Pima Indians 26%[27] and Hispanic Americans 35%.[28] In our study age, sex and duration of diabetes showed no significant difference between normoalbuminuric group and microalbuminuric group. But fasting blood glucose, systolic blood pressure, diastolic blood pressure, serum creatinine and patients with HTN showed significant difference between two groups. Vijay et al have reported duration of diabetes, systolic and diastolic BP, age and serum creatinine levels to be associated with proteinuria.[29] According to John et al male gender, increasing age, duration of diabetes, poor glycaemic control and raised blood pressure was associated with microalbuminuria.[30] One of the limitations of our study was that, it was a clinic based study. This could have introduced some degree of referral bias. However the prevalence of microalbuminuria is similar to that reported in other studies.

Conclusion

The prevalence of microalbuminuria in a divisional city at north-east region of Bangladesh was 36.7%, which was a clinic based study. The risk factors are similar to that reported among Europeans. Fasting blood glucose, systolic blood pressure, diastolic blood pressure, serum creatinine and patients with HTN between normoalbuminuric group and microalbuminuric group showed significant difference statistically. The prevalence of diabetes and its complication (micro and macrovascular) among Bangladeshis are increasing day by day and by the year 2025, this may place considerable burden on the health budgets of this country. This call for early detection and good control of diabetes should consider reducing the burden of diabetic kidney disease and its complication in future.

Authors Affiliation

1. *Dr. Sarker Hafiz Mahmud, Assistant Professor, Department of Pharmacology & Therapeutics, Army Medical College Cumilla, Cumilla Cantonment, Bangladesh.
2. Dr. Nasrin Akter, Assistant Professor, Department of Pharmacology & Therapeutics, North East Medical College, Sylhet, Bangladesh.
3. Dr. Wahida Khanam Chowdhury, Pharmacist, Department of Pharmacology & Therapeutics, Cumilla Medical College, Cumilla, Bangladesh.
4. Dr. Tahera Khanom, Assistant professor, Deptartment of Microbiology, Army Medical College, Cumilla
5. Dr. Ripon Chundra Majumder, Assistant Professor. Department of Nephrology, Eastern Medical College Cumilla & Hospital, Cumilla

* For Correspondence

References

1. IDF Diabetes Atlas. 7th ed. Brussels, Belgium: International Diabetes Federation; 2015. Available from:https://www.idf.org/e_library/epidemiology_research/diabetes_atlas/13_diabetes_atlas_seventh_edition.html.
2. Varghese A, Deepa R, Rema M et al. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Postgraduate Med Journal. 2001;77: 399-402
3. Mogensen CE, SteVesMW,Deckert T, et al. Functional and morphological renal manifestations in diabetes mellitus. Diabetologia. 1981;21: 89–93
4. Damsgaard EM, Froland A, Jorhgensen OD, et al. Microalbuminuria as a predictor of increased mortality in elderly people. BMJ. 1990;300: 297–00
5. Groop L, Ekstrand A, Forsblom C, et al. Insulin resistance, hypertension and microalbuminuria in patients with type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia. 1993;36: 642–7
6. King H, Auberti RE, Herman WH. Global burden of diabetes, 1995–2025. Prevalence, numerical estimated and projections. Diabetes Care. 1998;2: 1414–31
7. Bouhanick B, Berrut G, Chameau AM, Hallar M, Bled F,Chevet B, et al. Predictive value of testing random urine sample to detect microalbuminuria in diabetic patients on outpatient basis. Diabete Metab. 1992;18: 54-8
8. Parving HH, Lewis JB, Ravid M, Remuzzi G, Hunsicker LG, DEMAND Investigators. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: A global perspective. Kidney Int. 2006;69: 2057-63
9. Agaba EI, Agaba PA, Puepet FH. Prevalence of microalbuminuria in newly diagnosed type 2 diabetic patients in Jos Nigeria. Afr J Med Sci. 2004; 33: 19-22
10. American Diabetes Association. Standards of medical care in diabetes 2012. Diabetes Care. 2012;35(1): S11-63
11. KDIGO 2012. Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;3: 1-150
12. Ewald B, Attia J. Which test to detect microalbuminuria in diabetic patients? A systematic review. Aust Family Phys. 2004;33: 565-71
13. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. Gastroenterol Hepatol Bed Bench. 2013;6: 14-7
14. Ufuoma C, Ngozi JC, Kester AD et al. Prevalence and risk factor of microalbuminuria among type 2 diabetes mellitus : A hospital based study from warri, Nigeria. Sahel Medical Journal. 2016;19(1): 16-20
15. Karim A, Das D, Salahuddin M, Marjan GA, Islam MN, Shaha AK, Gupta RD, Islam SM, Amin R AND Rashid HU. Prevalence Of Microalbuminuria And Overt Proteinuria In Hypertension And Their Relations With Renal Function In A Rural Population Of Bangladesh. Bangladesh Journal of Medicine. 2013;24: 59-64
16. Poudel B, Yadav BK, Nepal, AK, Jha B and Raut KB. Prevalence and Association of Microalbuminuria in Essential Hypertensive Patients. North American Journal of Medical Science. 2012;4: 331–335
17. Zelmanovitz T, Gross JL, Oliveira JR, Paggi A, Tatsch M and Azevedo MJ. The receiver operating characteristics curve in the evaluation of a random urine specimen as a screening test for diabetic nephropathy. Diabetes Care, 1997;20: 516-519
18. Pathania M, Rathaur VK, Yadav N, Jayara A and Chaturvedi A. Quantitative Micro-albuminuria Assessment from 'Random Voided Urinary Albumin: Creatinine Ratio' Versus '24 hours Urinary Albumin Concentration' for Screening of Diabetic Nephropathy. Journal of Clinical and Diagnostic Research. 2013;7: 2828–2831
19. Girish I, Vijeth SB, Nandini HV. A cross sectional study to assess the prevalence of microalbuminuria in patients with type 2 diabetes mellitus. Int J Res Med Sci. 2018; 6(1): 117-120
20. Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Post grad Med J. 2001; 77: 399–402
21. Gupta DK, Verma LK, Khosla PK, et al. The prevalence of microalbuminuria in diabetes: a study from north India. Diabetes Res Clin Pract. 1991;12: 125–8
22. John L, Rao PS, Kanagasabapathy AS. Prevalence of diabetic nephropathy in non insulin dependent diabetes. Indian J Med Res. 1991;94: 24–9
23. Vijay V, Snehalatha C, Ramachandran A, et al. Prevalence of proteinuria in non-insulin dependent diabetes. J Assoc Physicians India. 1994;42: 792–4
24. Gatling W, Knight C, Mullee MA, et al. Microalbuminuria in diabetes: a population study of the prevalence and an assessment of three screening tests. Diabet Med. 1988;5: 343–7
25. Marshall SM, Alberti KGMM. Comparison of the prevalence and associated features of abnormal albumin excretion in insulin-dependent and non-insulin-dependent diabetes. Q J Med. 1989;70: 61–71

26. Haffner SM, Morales PA, Gruber MK, et al. Cardiovascular risk factors in non-insulin dependent diabetic subjects with microalbuminuria. Arterioscler Thromb. 1993;13: 205–10
27. Nelson RG, Kunzelman CL, Pettit DJ, et al. Albuminuria in type 2 (non-insulin-dependent) diabetes mellitus and impaired glucose tolerance in Pima Indians. Diabetologia 1989;32: 870–6.
28. Hamman RF, Franklin GA, Mayer EJ, et al. Microvascular complication of NIDDM in Hispanics and non-Hispanic whites. Diabetes Care. 1991;14: 655–63
29. Vijay V, Snehalatha C, Ramachandran A, Viswanathan M. The prevalence of proteinuria in non-insulin dependent diabetes. J Assoc Physicians India. 1994;42: 792-4
30. John L, Rao PS, Kanagasabapathy AS. Prevalence of diabetic nephropathy in non-insulin dependent diabetes. Ind J Med Res. 1991;94: 24-9

Item analysis of Multiple Choice Questions in Anatomy Examination

Tahmina Akhter[1], Mizanur Rahman Molla[2], Farjana Akhoond[3], Mohammad Shakil[4]

Abstract

Background: Multiple choice questions (MCQs) or Items forms an important part to assess students in different educational streams. The quality of MCQs is determined by two parameters such as difficulty index (DIF I) and discrimination index (DI). **Objectives:** Evaluation of items to develop a pool of valid items & to update question bank for designing question paper as per the need of assessment. **Materials and Methods**: Study was conducted on fifty (50) 1st year MBBS students of Army Medical College, Cumilla who appeared in first term Anatomy examination, May 2018. It comprised of twenty (20) Anatomy multiple "true/false response" type MCQs with no negative marking. Difficulty index (DIF I) and discrimination index (DI) of each item was analyzed. **Results and conclusions**: Maximum 14(70%) item have the DIF within the acceptable range (P =30–70%), and four (20%) item was too difficult (P <30%). Whereas DI of majority 9 (45%) items was excellent (d >0.35) and four (20%) of the items was poor (d < 0.20). No item had negative discriminative power. Item analysis is an important tool to discriminate good and bad test items. It helps to increase the need of skills in constructions of items and identifies the specific area which need more focus to discard or clarity.

Keywords: Multiple choice questions, item analysis, difficulty index, discrimination index.

J Ar M Coll Cu. 2019, July; 2 (2): 20-23
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Appropriate use of assessment strategies is a challenge to educators. Assessment, integral to learning involves an appraisal of student learning and feedback for improving teaching-learning experiences.Carefully constructed tests by educators will enhance educational functions[1]. A wide range written assessment tool is used now a days, short answer question (SAQ), modified essay question (MEQ), essay question (EQ), problem based question (PBQ), structured essay question (SEQ), multiple choice question (MCQ).Multiple choice questions (MCQs)/items are the most common method of assessing the knowledge capabilities of undergraduate, graduate, and postgraduate students in medical colleges. These can be used for both formative and summative assessments. It is said that appropriately constructed MCQs result in objective testing that can measure knowledge, comprehension, application, analysis, and evaluation. MCQ is an assessment tool that requires examinees to identify the correct answers of a question and it consists of a stem that directly or indirectly poses questions and distracters from which the answer is selected[2]. Typically students select the correct answers by circling the associated number or letter, or filling in the associated circle on the machine-readable response sheet[3]. To maintain the objectivity and consistency, MCQ is a good assessment tool, and it can cover a large amount of knowledge from the area of course contents to be tested. Student who practiced the past questions become adopt at choosing the correct option from a list without the in-depth understanding the topic was one of the disadvantage of MCQ claimed by Sam et al[4]. Hence, MCQs to be used must be of quality and they need to be tested for the standard or quality. Item analysis is one such tool that provides information regarding the reliability and validity of a test items. Item analysis examines the student responses to individual test items/MCQs to assess the quality of those items and test as a whole. In simple terms, it is a process of collecting, summarizing, and using information from students' responses to assess the quality of test items. In this studytwo parameters such as difficulty index (DIF I) and discrimination index (DI) are used to assess the quality of MCQs/items currently in used in Anatomy[5].

Received August 2019 Accepted February2020

Materials and Methods

The present research was a set of observational study. The data were collected from the first term final Anatomy MCQ examination held in May 2018, where fifty (50) 1st year MBBS students were appeared. It comprised of 20 multiple

true or false responses a MCQs. Total 20 mark was allotted for twenty (20) MCQs. Each MCQ have a single stem with five (5) responses or options. Total twenty (20) MCQ items were analyzed. A correct response was awarded 0.2 marks, and zero (0) marks for each incorrect response. The range of the score is being 0-1. There was no negative marking and the passed marks were 12 (60%). After evaluation of the examination, marks obtained by the students were arranged in descending order and entered in statistical package for social science (SPSS) version-20. The upper one-third students (16) were considered as high achievers (H) and lower one third (16) as low achievers (L). For computation purpose, marks obtained by middle one-third were discarded. Difficulty Index (DIF I) and Discriminatory index (DI) were analyzed for each item.

Difficulty index

Difficulty index DIF I of an item depicts the ease or difficulty of an item. It is the percentage of students in high and low achievers group who answered the item correctly. It ranges between 0% and 100%[9]**.** It was calculated using the formula DIF I or P = H + L × 100/N; where, H = number of students answering the item correctly in the high achieving group, L = number of students answering the item correctly in the low achieving group, and N = total number of students in the two groups (including nonresponses). Values between 30% and 70% are acceptable, with lower values reflecting the higher difficulty and vice versa.

Discrimination index or d value

DI is the ability of an item to differentiate between students of higher and lower abilities and ranges between 0 and 1.[9] Greater values indicate higher discrimination power. It was calculated using the formula DI = 2 × (H–L)/N where, the symbols H, L, and N represent the same values as mentioned above.

Results

Study was done with the fifty (50) 1st year MBBS students who had appeared in first term MCQs examination in Anatomy, in May 2108. Total twenty (20) MCQs were analyzed where each question contain highest value one (1) and lowest value zero (0). After statistical analysis, it was found out that mean score was 12.99 ± 1.71. Difficulty index of maximum 14 (70%) items was in the acceptable range (p= 30-70%), 2 (10%) items were too easy and only 4 (20%) item was too difficult. Interpretation of the results of DIF was shown in Table-I.

Table 1: Difficulty index (DIF I)found in MCQs of Anatomy

Cutoff point (%)	Number (% frequency of the items*)	Interpretation	Action
<30	4 (20%)	Too difficult	Revised/discard
30-70	14 (70%)	Good/acceptable	Store
>70	2 (10%)	Too easy	Revised/discard

*n= 20 MCQs were analyzed

Mean ± SD= 12.99 ± 1.71

Discrimination index of majority 9 (45%) of the items was excellent, 7 (35%) items was good and one-fourth (20%) of the items was poor (<0.20), and the percentage was not ignorable shown in table-II.

Discrimination index of majority 9 (45%) of the items was excellent, 7 (35%) items was good and four(20%) of the items was poor (<0.20), and the percentage was not ignorable shown in table-II (Figure 2).

Table 2: Discrimination index (DI) found in MCQs of anatomy

Cutoff point (%)	Number (% frequency of the items*)	Interpretation	Action
<0.20	4 (20%)	Poor	Revised/Discard
0.2-0.34	7 (35%)	Good	Store
≥0.35	9 (45%)	Excellent	Store

*n=20 MCQs were analyzed

Discussion

The assessments integrating MCQs are commonly used method of assessing the cognitive domain of learning, though psychomotor and affective domains cannot be assessed[6]. Still, it has an advantage of testing large number of students in a short time period with quick and easy marking. An appropriately constructed and framed MCQ needs to be tested for the standard or quality. Item analysis is one such tool which is a valuable yet relatively simple procedure performed after the examination that provides information regarding the reliability and validity of a test[7]. It is of great help in improving the quality of items and prepares a viable question bank for subsequent use. It is also helpful to both students and teachers as it provides feedback to the teacher to improve their method of teaching and encourage the learners to learn more effectively[8]. In a study conducted by Kaur M.et al.[9] on 150 MBBS students of Pharmacology for 50 MCQs,the P value of 38 (76%) items was in the acceptable range (30–70%), 11 (22%) items was too easy (P > 70%), and 1 (2%) items was too difficult (P < 30%). In another study on

item analysis done by Patel and Mahajan[10] on 150 MBBS students for MCQs test with 50 questions, 10 (20%) items were in unacceptable range (P < 30% or P > 70%) and 40 (80%) items were in acceptable range (P = 30–70%). Item analysis done by Mehta and Mokhasi[11] on 100 MBBS students for MCQs test comprising 50 questions in the subject of anatomy reported mean DIF I of 63.06 ± 18.95 with DIF I of 31 (62%) items in the acceptable range (P = 30–70%), 16 (32%) items were too easy (P > 70%), and 3 (6%) items were too difficult (P < 30%). Study conducted by Patil and Patil[12]on 100 MBBS students of medicine for 100 MCQs, mean DIF I of 48.90 ± 13.72 was reportedIn this study, the P value of 35 (22%) items was in the acceptable range (30–70%), 25 (25%) items was ideal (50–60%), 18 (18%) items was too easy (P > 70%), and 22 (35%) items was too difficult (P < 30%).Rao C et al[13] reported mean difficulty index (P) was 50.16 ± 16.15 , out of a total 40 items, difficulty indices of 5% MCQ items were easy (P > 70%), about 10% weredifficult (P < 30%) and the remaining 85% of the items were within an acceptable range (30–70%). Kolte[14] reported mean DIF I as 57.92 ± 19.58. In this study, the P value of 26 (65%) items was in acceptable range (30–70%), 10 (25%) items were easy (P > 70%), and 4 (10%) items were difficult (P < 30%). Another study conductedby Akhter B et al.[5]having a mean DIF I14.39 ± 1.75.OfThe P value of 11 (55%) items was in the acceptable range (P = 30–70%), 8 (45%) items were too easy (P > 70%), and 1 (5%) item was too difficult (P < 30%). Our findings corresponded with the study by Mehta and Akhter et al having a mean DIF I of 12.99 ± 1.71 The P value of 14(70%) items was in the acceptable range (P = 30–70%), 2(10%) items were too easy (P > 70%), and 4 (20%) item was too difficult (P < 30%). Too difficult items (DIF I ≤ 30%) can lead to deflated scores, while the easy items (DIF I > 70%) may result into the inflated scores and a decline in motivation[15]. Items with high DIF I (>70%) should be placed either at the start of the test as "warm-up" questions to boost the confidence of students or discarded, similarly items with low DIF I (<30%) should be either revised or removed altogether. Our study hazed four item which was too difficult and it was discarded. Items which were too easy were 14 and these were revised and kept for subsequent use along with items within acceptable range. DI is another important parameter of item analysis that helps in detecting the ability of items to discriminate between skilled and unskilled examinees. DI normally ranges from 0 and 1, but sometimes its value can be <0 when this index is called negative DI.[15]It is because of more number of students from lower achiever group able to answer the item correctly in comparison with students from high achiever group. The reason for this negative value is either due to ambiguous question or an answer key that was wrongly marked. Our study items did not show negative DI. In an item analysis study by Patil and Patil[12] out of total 100 items, 24 had DI < 0.2 (poor), 45 had DI ≥ 0.20 and ≤ 0.35 (good), and 31 had DI > 0.35 (excellent). A study by Singh et al[16]. on item analysis of 20 MCQs reported 6 items (30%) with DI < 0.2, 4 (20%) items with DI ≥ 0.20 and ≤ 0.35, and 10 (50%) items with DI >35.In another study by Patel and Mahajan[10]on item analysis of 50 items, 9 items had DI < 02, 21 items had DI ≥ 0.20, and ≤ 0.35 and 20 items had DI > 0.35. In a study by Mehta and Mokhasi[(11)]on item analysis, mean DI was 0.33 ± 0.18. Out of total 50 items, 15 (30%) items had DI < 0.2, 9 (18%) items was DI ≥ 0.20 and ≤ 0.35, and 26 (52%) items had DI > 0.35. Study by Akhter et al analyzed of 20 MCQs reported 4 items (20%) with DI < 0.2, 5(25%) items with DI ≥ 0.20 and ≤ 0.35, and 11 (55%) items with DI >35. Our study was in accordance with this study and showed 4 (20%) items had DI < 0.2, 7(35%) items had DI ≥ 0.20 and ≤0.35, and 9 (45%) items had DI > 0.35. Four items with DI < 0.2 were discarded altogether due to their poor discriminating power. Seven items with DI ≥ 0.20 and ≤0.35 were revised and kept for subsequent use along with items with high discriminating power (DI > 0.35).

Strength and Limitations

To the best of our knowledge, this is the first study conducted atArmy Medical College in Cumilla, to analyzed items of first term examination. The number of examinees on whom the test was administered was small in number. Further studies on larger student population will help to improve the assessment strategies in the undergraduate MBBS curriculum. The outcomes observed in this study is limited to one exam and does not reflect other academic courses. Results from this study highlight the importance of analyzing items after test administration and using the results to develop test banks.

Conclusion

It is concluded from the present study that majority of the test items were within the recommended values. Construction of good MCQs is not a simple task. However, some test items did not meet the requirement of well-designed question items. Hence, these items can be revised or discarded, and a viable question bank can be prepared.Faculty training in item generation will enhance the quality of the test items.

Ethical Clearance

Institutional Review Board approval was not sought because the study did not deal with human subject.

Authors affiliation

1. *Dr Tahmina Akhter, Assistant Professor, Dept of Anatomy, Army Medical College, Cumilla.
2. Lt Col Mizanur Rahman Molla, Dept of ophthalmology, CMH, Cumilla.
3. Dr. Farjana Akhoond, Assistant Professor, Dept of Anatomy, MH Samorita Medical College, Dhaka
4. Dr. Mohammad Shakil, Associate Professor, Department of Community Medicine, Army Medical College Cumilla.

*For correspondence

References

1. D'Sar JL, Dionaldo MLV. Analysis of Multiple Choice Questions: Item Difficulty, Discrimination Index and Distractor Efficiency. International Journal of Nursing Education. 2017; 9(3): 109-113
2. Wojtczak, A. (2002). Glossary of medical education terms, International Association for Medical Education. Available at: http://www.iime.org/glossary.htm
3. University of Waterloo, (2017). Exam questions: types characteristics and suggestions Centre for teaching excellence .Retrieved from:https://uwaterloo.ca/centre-forteachingfor teaching-excellence/teaching-resources/teachingtips/developing assignments/exams/questions-types-characteristics-suggestions
4. Sam AH, Hameed S, Harris J, Meeran, M.Validity of very short answer versus single best answer questions for undergraduate assessment, Biomedical Central Medical Education. 2016;16:266, https://doi.org/10.1186/s12909-016-0793-z
5. Akhter B, Mollika N, AkhoondF.Item analysis of used MCQS in undergraduate anatomy examination. International Journal of Scientific Research. 2018;7(12): 63-64
6. Singh T, Anshu. Principles of Assessment in Medical Education. New Delhi: Jaypee Brothers Medical Publishers; 2012. p. 89
7. Considine J, Botti M, Thomas S. Design, format, validity and reliability of multiple choice questions for use in nursing research and education. Collegian 2005;12(1): 19-24
8. Pande SS, Pande SR, ParateVR, Nikam AP, Agrekar SH. Correlation between difficulty & discrimination indices of MCQs in formative exam in physiology. South East Asian J Med Educ. 2013;7(1): 45-50
9. Kaur M, Singla S, Mahajan R. Item analysis of in use multiple choice questions in pharmacology. Int J App Basic Med Res. 2016;6(3): 170-3.
10. Patel KA, Mahajan NR. Itemized analysis of questions of multiple choice question exam. Int J Sci Res. 2013;2: 279-80.
11. Mehta G, Mokhasi V. Item analysis of multiple choice questions – An assessment of the assessment tool. Int J Health Sci Res. 2014;4: 197-202.
12. Patil VC, Patil HV. Item analysis of medicine multiple choice questions (MCQs) for under graduate (3rd year MBBS) students. Res J Pharm Biol Chem Sci. 2015;6: 1242-51.
13. Rao C, Kishan Prasad HL, Sajitha K, Permi H, Shetty J. Item analysis of multiple choice questions: Assessing an assessment tool in medical students. Int J Educ Psychol Res. 2016;2(4): 201-4.
14. Kolte V. Item analysis of multiple choice questions in physiology examination. Indian J Basic Appl Med Res. 2015;4(4): 320-6.
15. Gajjar S, Sharma R, Kumar P, Rana M. Item and test analysis to identify quality multiple choice questions (MCQs) from an assessment of medical students of Ahmedabad, Gujarat. Indian J Community Med. 2014;39(1): 17-20.
16. Singh JP, Kariwal P, Gupta SB, Shrotriya VP. Improving multiple choice questions (MCQs) through item analysis: An assessment of the assessment tool. Int J Sci Appl Res. 2012;1: 53-7.

Ebola Virus Disease - A Retrospective Study Amongst 149 Confirmed Cases of Ebola Treatment Unit, Bong County, Liberia

Nazmul Huda Khan[1], Sazzad Ahmed Abdul Kdaer Khan Zilani[2], Muhammed Alam[3]

Abstract

Introduction: Ebola is a great concern of global health today because of its high fatality rate. The case fatality rate for this infection was 59% to 88% in all outbreaks. Ebola virus can spread between humans by contact with blood, body fluids and excretions and tissues. Ebola treatment units are facilities prepared to receive and isolate a patient with possible Ebola until a diagnosis can be confirmed or ruled out and plan to care for and manage a patient with confirmed Ebola . **Methodology:** This retrospective descriptive study was carried out to find out the mode of spread, morbidity and mortality rates and ratio amongst the confirmed cases of Ebola viral disease (EVD), who received treatment from Ebola treatment unit (ETU), Bong County, Liberia. All 149 confirmed cases (n) were selected for this study from the aforementioned ETU. The questionnaire was setup keeping in mind the objectives of the study. **Results:** As many as 77 (52%) were female and 72(48%) were male amongst the study population. Among the cases, 92(56%) survived after treatment while 57(44%) expired. Direct contact was the main cause 74 (49.66%), followed by patient transport 24 (16%), contact with body fluid 19(13%), participants at funeral 12(8%) amongst other mode of spread. **Conclusion:** Direct physical contact, patient transport, contact with body fluid and participation at funerals were the major means of spread of EVD. Careful study and analysis definitely will explore new dimension to combat this devastating health burden of African countries and the world as a whole.

Keywords: Ebola virus, Spread of Ebola virus, Evola treatment unit.

J Ar M Coll Cu. 2019, July; 2 (2): 24-27
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Ebola is a great concern of global health today because of its high fatality rate. Ebola virus can spread between humans by contact with blood, body fluids and excretions and tissues. Large quantities of Ebola virus have been found in blood two days after the onset of symptoms. During the acute stage of the disease, Filo viruses are also found in many secretions and excretions those are not visibly contaminated with blood, including saliva, tears, breast milk, semen and feces. Aerosol transmission may be possible, but it does not seem to be a significant route of transmission between humans[1].Outbreak of Ebola hemorrhagic fever is reported periodically in Africa. The number of outbreaks have increased in the last ten years, either due to a higher incidence or better screening of the disease. In human populations, the African Filo viruses usually have high mortality rates. Zaire Ebola virus is the most pathogenic one. The case fatality rate was 59% to 88% in all outbreaks up to 2008. In five of seven epidemics, it was at least 78%. Sudan Ebola virus is less virulent, having case fatality rate 41-65%. Only one outbreak of Bundibugyo Ebola virus has been reported; the case fatality rate was 36%**.** Ivory Coast Ebola virus was reported only once in 1999[2]. Ebola treatment units are facilities prepared to receive and isolate patients with possible Ebola virus until a diagnosis can be confirmed or ruled out, and to manage the patients with confirmed Ebola until discharge or transfer is completed.

Materials and Methods This retrospective descriptive study was carried out to reveal the mode of spread, morbidity and mortality rates and ratio amongst the confirmed cases of Ebola viral disease (EVD), who received treatment from Ebola treatment unit (ETU), Bong County, Liberia (fig: 1). A total 1027 cases of EVD received treatment from the aforementioned ETU during the period of July-December 2015. Amongst them, all suspected and probable cases were excluded. The study populations were all confirmed cases both males and females of all ages. All 149 confirmed cases were selected as study population for this study. A check list was prepared to gather information from the documents

Received January 2019 Accepted August 2019

provided by the Bong county health authority. The questionnaire consisted of three parts. Part-I contained personal information, part-II - the pattern of contact and part-III about the mortality of the cases. The checklist filled with data was edited through checking and rechecking at the end of data compilation. An analysis plan was developed keeping in mind the objectives of the study.

Figure 1: Map of Liberia showing location of ETU

Results: In this study, the range of age of the study population was 10-80 years. About one fourth, 38 (26%) cases were in between 31-40 years, followed by 27 (18%), 26 (17%) and 21 (14%) in the age group between 21-30 years , 41-50 years and 51-60 years respectively (fig-2). As many as 77 (52%) were female and 72 (48%) were male amongst the study population. Among all cases, 92 (56%) survived after treatment while 57 (44%) expired which is shown in (Fig-3) below. Regarding the mode of spread, it is found that direct contact was responsible for the maximum 74 (49.66%), followed by patient transport 24 (16%), contact with body fluid 19 (13%) and participants at funeral 12 (8%) amongst others (fig-4). The highest number of cases were reported in the months of November 46 (31%), followed by September 40 (27%), August 35 (23%) and October 17 (11%) (fig-5).

Figure 2: Confirmed EVD cases by age/sex (n-149)

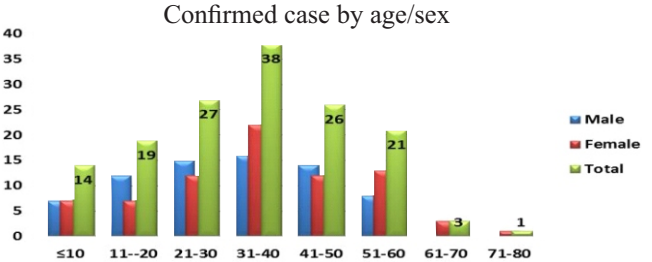


Figure 3: Survivors/ dead ratio amongst the Confirmed EVD cases (n-149)

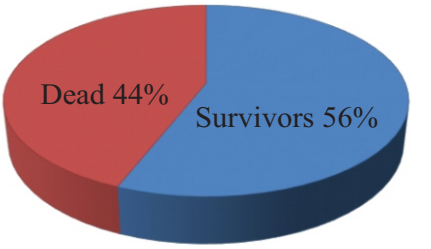


Figure 4: Mode of spread amongst the Confirmed EVD cases (n=149)

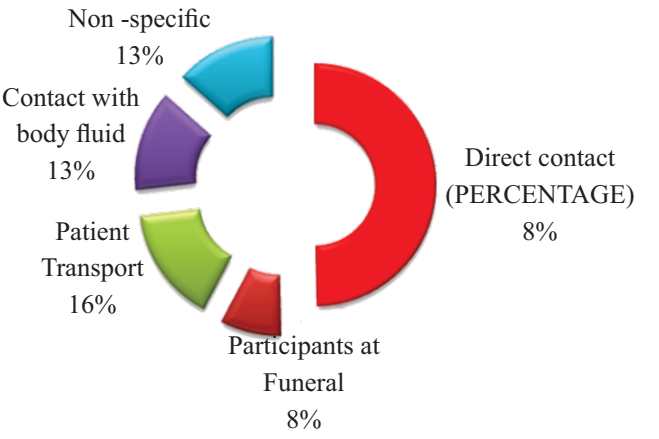
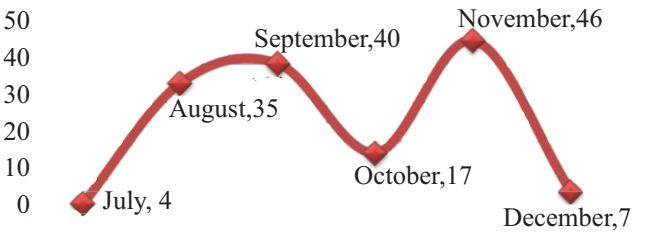


Figure 5: Epidemic curve of confirmed Ebola cases July-December 2014 (n=149)



Discussion

In this study, it was found that the incidence of confirmed EVD cases were maximum among the age group 31-40 years (26%) followed by 21-30 years (18%) and 41-50 years (17%). An epidemiological surveillance by Koffi Isidore Kouadio, Peter Clement et al in Lofa County, Liberia conducted from March-September, 2014 revealed that the age group 20-50 years were mostly affected. The children, adolescents and young adults (0-20 years old) affected more

than the age group ≤60 years. [3] In this study findings there were more female cases 77 (52%) than male 72 (48%). In their surveillance by Koffi Isidore Kouadio, Peter Clement et al. found that among their 619 cases, there were more female 326 (52.7%) than male 293 (47.3%). In both the researchers, the study findings are similar. This research revealed that the mortality rate was 77 (52%) in male and 72 (48%) amongst female. Koffi Isidore Kouadio, Peter Clement et al found more death among men (51.5%) than women (48. 5%) which is similar in term of rates and ratio.[3] In this study it is revealed that among all cases (n=149), 92 (56%) survived and 57(44%) expired after treatment at ETU. Various researchers between the year 1976 and 2012 since EVD outbreak, showed that the fatality percentage was highest 69% in case of Zaire virus followed by the Sudan virus a 53%. Overall fatality rate was 53.3% in their study conducted by Koffi Isidore Kouadio, Peter Clement et al[3]. In this study the mode of spread of EVD was found maximum through direct contact (49.66%) followed by patient transportation 24 (16%), contact with body fluid 19 (13%) and participants at funerals 12 (8%). In a survey conducted by the Ministry of health & welfare, Liberia found that 28 (16%) among 173 household contacts developed EVD. 28 (30%) out of 95 family members who had direct contact with a primary case were infected, none of 78 family members affected who did not have direct contact. [4] Another study conducted by Stefano Merler, MS, Marco A, Laura F et al on "Spatiotemporal spread of the 2014 outbreak of Ebola virus disease in Liberia" up to Aug 16, 2014, found the information that 38·3% cases were infected in hospitals, 30·7% in households and 8·6% at funerals.[5] In this research percentage of being infected through direct contact found little higher; reason may be due to the existing number of primary cases during contact.[1]

Conclusion

This retrospective descriptive study showed that the direct physical contact, patient transport, contact with body fluid and participation at funerals were the major mode of spread of EVD. Study finding also showed higher level of survival rate at ETU. This study revealed that there was marginal difference in the mortality rate amongst male and female. The people. The high fatality rate and substantial burden on the health care delivery system of EVD become great concern and public health issue globally. Careful study and analysis in this regard definitely will explore new dimension to combat this devastating health burden of African countries and the world as a whole.

Authors Affiliation

1. *Lt Col (Dr.) Nazmul Huda Khan, Commanding Officer, 35 Field Ambulance, Cumilla Cantonment
2. Colonel (Dr.) Sazzad Ahmed Abdul Kdaer Khan Zilani, SMO, Medical Squadron Base Bashar, Bangladesh Air Force
3. Lt Col (Dr.) Mohammed Alam, Department of Urology, CMH Dhaka

*For correspondence

References

1. World Health Organization. Ebola virus disease in West Africa-the first 9 months of the epidemic and forward projections. N Engl J Med. 2014; 371: 1481.

   https://www.nejm.org/doi/full/10.1056/NEJMoa1411100

2. Ministry of health and Social Welfare, Liberia Ebola situation report no 119-200, 2015

   https://apps.who.int/ebola/current-situation/ebola-situation-report-5-august-2015

3. Koffi I K, Peter C et al. Epidemiological and Surveillance Response to Ebola Virus Disease Outbreak in Lofa County, Liberia (March-September, 2014).

   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447624/

4. Government of Liberia Ministry of Health and Social Welfare. Liberia Operational Plan for Accelerated Response to Re-Occurrence of Ebola Epidemic, July – December 2014.

   https://reliefweb.int/sites/reliefweb.int/files/resources/evd-outbreak-response-plan-west-africa-2014-annex3.pdf

5. Stefano M, Marco A, Laura F et al. "Spatiotemporal spread of the 2014 outbreak of Ebola virus disease in Liberia" up to Aug 16, 2014

   https://www.researchgate.net/publication/270588629_Spatiotemporal_spread_of_the_2014_outbreak_of_Ebola_virus_disease_in_Liberia_and_the_effectiveness_of_nonpharmaceutical_interventions_A_computational_modelling_analysis

6. MSF.Ebola Expatriate Health Recommendation, draft 7, 2014.http://cdn.evaluation.msf.org/sites/evaluation/files/attachments/ocb_ebola_review_medop_final_2.pdf

7. MSF. Public Health Engineering in emergency situation, first edition 1994

https://medicalguidelines.msf.org/download/attachments/30544471/public_health_en.pdf?api=v2

8. World Health Organizationand Clintonhealthaccess.org.Training manual of cold training on clinical management of EVD organized jointly by in Liberia wef 2-6 February 2015.

9. United Mission for Ebola Emergency Response (UNMEER). Internal Situation Report 0600 Hours NYT – 13 March 2015 / No. 124

https://www.humanitarianresponse.info/en/operations/liberia/document/un-mission-ebola-emergency-response-unmeer-external-situation-report

10. District health organization, Bong County, Liberia. Monthly health report July 2114- May 2015,

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5515557/

Assessment of FT_3, FT_4 and TSH in Children with Autism Spectrum Disorder

S M Mahbubul Quadir[1], Mohammed Ali Chowdury[2], S M Suhrawardy[3], Md Imran Waheed[4]

Abstract

Background: There is increasing recognition that thyroid dysfunction is associated with neurological and psychiatric disease, including neurodevelopmental disorders such as intellectual disability and autism spectrum disorder. **Objective:** The aim of the study was to measure FT_3, FT_4, and TSH in children with autism spectrum disorder and to compare the results with healthy children. **Materials and Methods:** This descriptive type of cross-sectional study was conducted in the department of Physiology of Army Medical College Chattogram from May 2016 to April 2017**.** A total number of 100 subjects were selected in the current study. Among them 60 autistic children were selected from PROYASH Chattogram a specialized school for autistic children. Age matched 40 apparently healthy children were included in the control group for comparison. Data were collected in pre-designed structured questionnaire by the researcher himself. Biochemical assessment of thyroid function in the form of free triiodothyronine (FT_3), free tetraiodothyronine (FT_4) and thyroid-stimulating hormone (TSH) were done by using commercially available enzyme-linked immunosorbent assay (ELISA) kits. The statistical analyses were done by unpaired students "t" test. **Results:** Serum thyroid stimulating hormone (TSH) level was significantly high ($p \leq 0.05$) in children with autism spectrum disorder (ASD) and there was no significant difference ($p \geq 0.05$) of FT_4 and FT_3. **Conclusion:** Thyroid function test bears importance in clinical tests of the children with autism spectrum disorder.

Keywords: Autism spectrum disorder, thyroid function, FT_3, FT_4, TSH.

J Ar M Coll Cu. 2019, July; 2 (2): 28-32
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Autism Spectrum Disorder (ASD) is the fastest growing developmental disability, affecting more children than cancer, diabetes and AIDS combined[1]. Autistic disorder (historically called early infantile autism, childhood autism, or Kenner's autism) is characterized by symptoms from each of the following three categories: qualitative impairment in social interaction, impairment in communication and restricted, repetitive and stereotyped patterns of behavior or interests with onset before the age of 3 years[2]. It affects 1 out of every 68 children in the USA and it is more often found among boys than girls[3]. Worldwide prevalence of ASD is reported to be 3 to 6 per 1000 children with a familial incidence of 2% to 8% in siblings of affected children. Its prevalence differs by the region, but a higher prevalence of up to 1:88 children has been reported. In Bangladesh the current estimates of prevalence is nearly 10.5 lakhs[4]. The exact pathogenesis of autism is still unknown; however, genetic, neurologic, environmental and immunological factors may be involved[5]. It is clear that genetics alone do not determine the entire ASD phenotype. It is determined by genetic susceptibility but other non-genetic factors can modify it. So in most cases autism appear to be caused by a combination of autism risk genes and non-genetic factors that influence early brain development[6]. Studies indicate that non-genetic factors such as thyroid dysfunction due to endocrine disrupting toxins, teratogens, obstetric complications and prenatal infections such as rubella, cytomegalovirus are responsible for autistic cases[6,7]. There is no doubt that normal thyroid function is required for normal neurological development and thyroid dysfunction associated with many neurodevelopmental disorders including Autism Spectrum Disorder (ASD)[8]. Current diagnostic methods and screening tools are somewhat subjective and are difficult to assess in younger children, which can often result in missed opportunities for early intervention. A biological marker that could predict ASD risk, assist in early diagnosis or even identify potential therapeutic targets would have great clinical utility[9]. While biomarker research in ASD has greatly increased in recent years, progress has been limited by a number of factors, and no universal biological markers for ASD have yet been identified[10]. One of the biggest issues in developing biological markers for ASD is the heterogeneity of the

Received August 2019 Accepted March 2020

disorder. There is wide variation in symptoms among children with ASD and this is further complicated by a number of co-morbid factors associated with the disorder[11]. Research suggests that there are various types of neuroendocrinological abnormalities present in autistics and TSH could possibly serve as a biochemical parameter of the disease[12]. Several studies were undertaken in other countries to evaluate thyroid hormones as possible biochemical marker for ASD[12]. A recent study showed that children born with very low levels of thyroxine had a higher risk of developing an autism spectrum disorder[13]. Many researchers are beginning to appreciate that thyroid dysfunction may masquerade as autism. One study showed that 45 of 62 children diagnosed with autism were also hypothyroid[13]. Another showed that mothers of children with autism were most likely hypothyroid during pregnancy[14]. Some researchers concluded that "thyroid hormone deficiency in early development might cause nervous system damage such that autistic symptoms are likely to ensue." Thyroid hormones namely T_3 and T_4 all serve to regulate neuronal proliferation, myelination and differentiation in discrete regions of the brain during definitive time periods[14]. Deficiencies in any of these thyroid hormones during critical times especially the first two years of life can have significant deleterious behavioral and cognitive effects. Autism spectrum disorders are an increasingly important health concern in Bangladesh at present. The heightened awareness has been accompanied by a renewed interest to uncover the underlying pathophysiologic mechanisms and to find possible causes of the disorder at multiple levels. It has been hypothesized that disturbance in the thyroid hormone availability and metabolism during critical periods of neuronal development may lead to behavioral disturbances as noted in ASD[15]. The etiology of autism is a highly contemporary field of research in neuroscience and psychiatry and can be considered as a challenging issue as there is no direct mechanism that can simply explain the pathogenesis of autism. Deficiency of thyroid hormones may have a significant contribution to the causes of ASD but their exact relationship remains debatable. Hence, the present study was designed to evaluate serum free triiodothyronine (FT_3), free thyroxine (FT_4) and thyroid-stimulating hormone (TSH) levels in children with autism to explore the role of thyroid hormone deficiency as one of the risk factors associated with autism. The possible resulting correlations may Provide new insights on autism diagnosis and therapy.

Materials and Methods

This descriptive type of cross-sectional study was conducted in the Department of Physiology of Army Medical College Chattogram from May 2016 to April 2017. Ethical permission was taken from Ethical Review Committee of Army Medical College Chattogram. Sixty consecutive autistic children from PROYASH Chattogram a specialized school for autistic children with different symptoms of behavioral abnormalities, sensory processing abnormalities and impaired ability to communicate were included in the present study. Age matched 40 healthy children were used in this study including (20) male and (20) female as controls. All included patients were subjected to detailed history and thorough neuropsychiatric examination. Individual interviews were conducted with every included child and his/her parents for clinical assessment of autistic symptoms severity using Childhood Autism Rating Scale (CARS). Under aseptic precaution, 5 ml of venous blood was collected from antecubital vein of each subject of both groups for biochemical test. Serum free triiodothyronine (FT_3), tetraiodothyronine (FT_4) and thyroid stimulating hormone (TSH) level were estimated by Micro ELISA redder Biokit (U.S.A). These tests were carried out in the Biochemistry Laboratory of Army Medical College Chattogram. Data were expressed as mean ±SD (Standard deviation). Statistical analysis was done by using SPSS for windows version 17. Unpaired Student's't' test were used as the tests of significance and p value <0.05 was accepted as the level of significance.

Results

The demographic and clinical data of the studied patients regarding age, sex, Childhood Autism Rating Scale (CARS) degree and score are presented in Table 1 with significant male predominance in autistic children. The mean ages of the patients included in the current study was (7.03y±2.34y) with age range between (3-12) years. The mean serum levels of the studied biomarkers (FT3, FT4 and TSH) in children with autism are presented in Figure 1 and Table II. In this study significantly high levels ($p \leq 0.05$) of thyroid stimulating hormone (TSH) were found in autistic children, while non-significant differences ($p \geq 0.05$) in the levels of serum free thyroxine (FT4) and triiodothyronine (T3).

Table 1: Demographic data of the studied groups

Variables	Patients group				p-value
	Patients (total), (N=60)	Patients with mild to moderate autism (n=30)	Patients with severe autism (n=30)	Control group (n=40)	
Age, mean ± SD	7.03±2.34	6.8±2.08	27 (90.0)	7.91±3.21	0.236
Sex, n (%)					
Males	55 (92.6)	28 (93.3)	3 (10.0)	20 (50.0)	<0.001*
Females	5 (8.3)	2 (6.7)		20 (50.0)	
CARS score, mean ± SD	-	32.67±1.99	46.8±4.23	-	<0.001*

Figure 1: Comparisons between the mean levels of FT_3, FT_4 and TSH in patients with autism versus the control group.

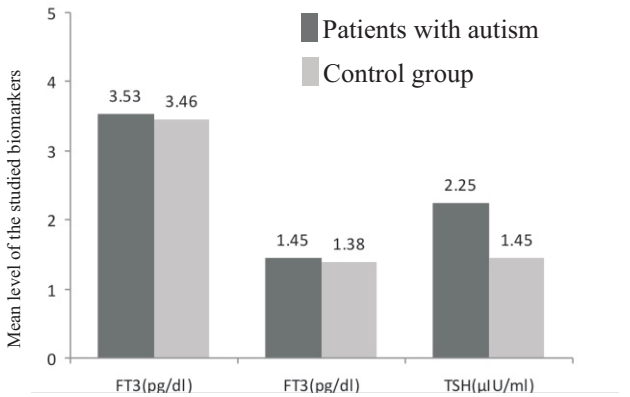


Table 2: Mean ± SEM of the serum levels of FT_3, FT_4 and TSH in children with autism compared with the control group.

Variables	Patients	Control	P-value
FT3 (pg/dL)	3.53±0.54	3.46±0.36	0.064
FFT4 (ng/dL)	1.45±0.13	1.38±0.09	0.580
TSH(µIU/ml)	2.25±1.05	1.45±0.96	<0.05*

Discussion

Autism spectrum disorder (ASD) is a severe disorder that affects the neurological development, characterized by disturbances in the social interaction and communication, in addition to stereotyped repetitive behaviors[16]. The true reason of these abnormalities is obscure, so this is a very interested area of research. Since the first reports describing childhood autism, there have been several attempts to find a common causes or biochemical marker among the children that display symptoms of autism[17]. Behavioral abnormalities and limitations, sensory processing abnormalities and impaired ability to communicate are the main issues in this manifaceted disorder[18]. Shelton et al. showed the susceptible gender ratio is 4-5 boys to 1 girl which is almost agreed with the ratio of the cases in the present study[19]. Thyroid hormone is essential for normal brain development during a critical period beginning in utero and extending through the first 2 years of post partum. It regulates neuronal proliferation, myelination and differentiation in discrete regions of the brain during definitive time periods[20]. Thyroid hormone also regulates development of cholinergic and dopaminergic neurons in the brain. Deficiencies in thyroid hormone during this critical time can have significant behavioral and cognitive effects[20]. Thyroid diseases in children and autism have many overlapping signs and symptoms. These include but are not limited to: Feeding problems, prolonged jaundice, poor muscle tone, gastrointestinal abnormalities [21]. Thyroid disease is a major contributor to the of causes of autism, it is not widely known because the routine thyroid blood tests frequently fail to detect the problem. There is increasing knowledge that normal thyroid function is required for normal neurological development and thyroid dysfunction associated with many neurodevelopmental disorders including ASD[25].The findings of the present study revealed significantly higher TSH serum levels with nonsignificant differences in the serum levels of FT_3 and FT_4 among children with autism when compared with the controls with significantly higher serum levels among children with severe degree of autism versus those having mild to moderate autism, suggesting the presence of subclinical hypothyroidism in autistic children. These findings were in agreement with the study of Khanwho reported a high rate of hypothyroidism in children with autism[22]. Nir et al. reported larger diurnal variation in TSH serum levels in comparison with controls explaining that thyroid dysfunction in ASD is probably related to hypothalamic–pituitary axis[23]. Although the exact mechanism between thyroid dysfunction and neuropsychiatric disorders is unclear, Frye et al. concluded that the presence of folate receptor α-autoantibodies (in up to 70% of autistic patients) contributes to the higher TSH levels and hence the occurrence of thyroid dysfunction in children with autism[24]. Folate is not a prominent cofactor in the synthesis of thyroid hormones, but it is an essential cofactor for phenylalanine hydroxylase in the form of tetrahydrobiopterin (derived from folate cycle) required for conversion of phenylalanine into tyrosine amino acid from which thyroid hormones are synthesized[24]. Hoshiko et al. reported an association between low thyroid hormones at

birth and the subsequent diagnosis of ASD, stating that compensatory mechanisms adopted to correct thyroid hormone deficiency may bring back hormone levels to normal or near-normal levels, but persistent neurodevelopmental impairment that arise due to this deficiency may persist even after the thyroid hormone levels themselves have returned to normal[25]. In contrast, some studies failed to confirm the occurrence of thyroid dysfunction and reported no differences in TSH, T_3 and T_4 in patients with autism versus the controls[26, 27]. In summary, our findings leads to the suggestion that impairment of mental and cognitive development found in autistic children may result from the subclinical hypothyroidism present in these special children.

Conclusion

Thyroid stimulating hormone (TSH) was significantly higher in children with autism spectrum disorder (ASD), but FT_3 and FT_4 was not significantly lower in children with ASD. Therefore thyroid function test bears importance in clinical tests of the children with ASD.

Authors Affiliation

1. *Major S M Mahbubul Quadir, Associate Professor, Department of Physiology, Army Medical College Chattogram, Chattogram.
2. Colonel Mohammed Ali Chowdury, Assistant Director of Medical Services, 24 Infantry Division, Chattogram.
3. Dr. S M Suhrawardy, Professor & Head, Department of Physiology, Army Medical College Chattogram, Chattogram.
4. Major Md Imran Wahed, Instructor, Army Medical Core Center & School (AMCC&S).

*For correspondence

References

1. Singh S, Yazdani U, Gadad B. Serum Thyroid-Stimulating hormone and interleukin-8 levels in boys with Autism Spectrum Disorder. J Neuroinflammation. 2017;14(4): 113-118.
2. Achkova M. "Diagnosis Autism – from Kanner 1- and Asperger to DSM-5". Intellectual Disability - Diagnosis and Treatment. 2014;2(2): 112-117.
3. CDC. Prevalence of autism spectrum disorder among children aged 8 years-autism and developmental disabilities monitoring network, 11 sites, United States. MMWR. 2014;63(SS-2): 1–21.
4. Rahman M. Autism Spectrum Disorder. J Bangladesh Coll Phys Surg. 2010;28: 143-44.
5. Elamin NE, Al-Ayadhi LY. Brain autoantibodies in autism spectrum disorder. Biomarks Med. 2014;8: 345-352.
6. Pardo CA, Eberhart G. The Neurobiology of Autism. J Brain Pathol. 2007;17: 434-47.
7. Muhle R, Trentacoste SV, Rapin I. The Genetics of Autism. J Pediatrics. 2004;113(5): 72-86.
8. Rovet JF. The role of thyroid hormones for brain development and cognitive function. Endocr Dev. 2014;26: 26-43.
9. Hewitson L. Scientific challenges in developing biological markers for autism. OA Autism. 2013;1(1): 1-7.
10. Amaral DG. The promise and the pitfalls of autism research: an introductory note for new autism researchers. Brain Res. 2011;1380: 3-9.
11. Schaafsma SM, Pfaff DW. Etiologies underlying sex differences in autism spectrum disorders. Front Neuroendocrinol. 2014;35(3): 255-71.
12. Bjorklund G, Saad K, Chirumbolo S. Immune dysfunction and neuroinflammation in autism spectrum disorder. Acta Neurobiol Exp (Wars). 2016;76(4): 257–268.
13. Vondra K, Stárka L, Hampl R. Vitamin D and thyroid diseases. Physiol Res. 2015;64(2): 95-100.
14. Morreale de Escobar G, Obregon MJ. Escobar del Rey F. Role of thyroid hormone during early brain development. Eur J Endocrinol. 2014;151 (3): 25-37.
15. Howdeshell KL. A model of the development of the brain as a construct of the thyroid system. Environ Health Perspect. 2013;110(3): 337-48.
16. Landa RJ. "Diagnosis of autism spectrum disorders in the first 3 years of life". Nature Clinical Practice Neurology. 2012;4: 138-147.
17. Al-Bazzaz A, Al-soufi R. "Measurement of some biochemical parameters autism in Jordan". Eur J Biochem. 2013;278: 78-99.
18. Coury DL, Paul A, Alessio F, George F. "Gastrointestinal Conditions in Children with Autism Spectrum Disorder: Developing a Research Agenda". Pediatrics. 2012;130(2): 160-168.

19. Shelton JF, Hertz-Picciotto I, Pessah IN. "Tipping the balance of autism risk: Potential mechanism linking pesticides and autism". Environ Health Perspective. 2012;120(7): 12-15.

20. Porterfiel D. "Thyroidal dysfunction and environmental chemicals--potential impact on brain development". Environ Health Perspect. 2013;108(3): 433-438.

21. Román GC. "Autism: transient in utero hypothyroxinemia related to maternal flavonoid ingestion during pregnancy and to other environmental anti-thyroid agents". J Neurol Sci. 2017;262(2): 15-26.

22. Khan AA. Thyroid dysfunction. Br Med J. 2016;4: 495.

23. Nir I, Meir D, Zilber N, Knobler H, Hadjez J, Lerner Y.

Brief report: circadian melatonin, thyroid-stimulating hormone, prolactin, and cortisol levels in serum of young adults with autism. J Autism Dev Disord. 2010;25(6): 641-654.

24. Frye RE, Wynne R, Rose S. Thyroid dysfunction in children with autism spectrum disorder is associated with folate receptor α autoimmune disorder. J Neuroendocrinol. 2017;29(3): 1-12.

25. Hoshiko S, Grether JK, Windham GC, Smith D, FesselK. Are thyroid hormone concentrations at birth associated with subsequent autism diagnosis? Autism Res. 2011;4(6): 456-463.

26. Abbassi V, Linscheid T, Coleman M. Triiodothyronine (T3) concentration and therapy in autistic children. J Autism Child Schizophr. 2012;8(4): 383-387.

27. Cohen DJ, Young JG, Lowe TL, Harcherik D. Thyroid hormone in autistic children. J Autism Dev Disord. 2013;10(4): 445-450.

Frequency of Depression Among Patients Admitted in Combined Military Hospital, Cumilla

Ahmed Rafi[1], Muhammad Abdul Kayum Shaikh[2], Afreen Ferdous[3], Imranul Hasan Murad[4]

Abstract:

Background: Depression is very common, it is affecting over 120 million people worldwide. Epidemiological surveys conducted recently in general populations have found that the lifetime prevalence of depression is in the range of 10% to 15%. It is natural to assume that prevalence of depression among the hospitalized patients is more, which may affect their recovery process. This study aims to find the level of depression in a tertiary care level hospital. **Methods:** This was a cross sectional descriptive study where purposive consecutive sampling method was implemented. Patients having previous or current history of psychiatric illness were excluded from the study. Total 95 patients who were admitted in the hospital were interviewed. After taking socio-demographic information, depression were assessed by Hamilton Depression Rating Scale (HAM-D) was used. **Results:** Total 95 patients were interviewed from 3 major departments of CMH, Cumilla. Among the patients 21.1% patients were found having significant (HAMD score >10) level of depression. 13.7% has mild depression; patients have moderate and severe depression are 3.2% and 4.2% respectively. **Conclusion:** Higher level of depression among the admitted patients point to the need of assessing mental health for their rapid and complete recovery.

Keywords: Depression, Hamilton Depression Rating Scale

J Ar M Coll Cu. 2019, July; 2 (2): 33-37
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Psychological element is an integral part of health, as it is defined as complete physical, mental and spiritual wellbeing and not merely an absence of disease. Among many psychological symptoms depression is one of the major symptom, which causes great burden. Depression is very common, it is affecting over 120 million people worldwide. Epidemiological surveys conducted recently in general populations have found that the lifetime prevalence of depression is in the range of 10% to 15%. Mood disorders as defined by the World Mental Health (WMH) and the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) have a 12-month prevalence which varies from 3% in Japan to over 9% in the US[1]. Although disorder severity correlates with the probability of treatment in almost all countries, 35.5% to 50.3% of serious cases in developed countries and 76.3% to 85.4% in less-developed countries received no treatment in the 12 months preceding the interview[2]. Depression can strike at any time, but on average, first appears during the late teens to mid-20s. The high female:male sex ratio in the prevalence of depression, especially during the reproductive years, is one of the most replicated findings in epidemiology[3]. Some studies show that one-third of women will experience a major depressive episode in their lifetime[4]. Using the DALY, unipolar MD was classed in 1990, as the fourth leading burden of disease or injury cause worldwide for both sexes, behind lower respiratory infections, diarrheal diseases, and perinatal disorders[5]. By 2004 it had moved up to third place and World Health Organization projections estimate that it will be the leading cause of disease burden worldwide by 2030[6]. As mentioned earlier, depression can affect anyone—even a person who appears to live in relatively ideal circumstances. Several factors can play a role in depression, like differences in certain chemicals in the brain, depression can run in families, people with low self-esteem or different environmental factors. So it is quite obvious that being physically ill of any kind have a chance of developing depression as a psychological reaction or part of the disease process. Depressive disorder alone causes great burden; even when successfully treated and remission is achieved, depressive disorders still impose a considerable burden on the patient. Remission is rarely accompanied by a total disappearance of all symptoms. Residual symptoms, especially cognitive impairment or social dysfunction, can continue to reduce performance and cause considerable distress. The ever-present risk of relapse and recurrence also weighs heavily generally reducing the quality of life[2]. It can

Received April 2019 Accepted June 2019

cause the affected person to suffer greatly and function poorly at work, at school and in the family. At its worst, depression can lead to suicide. The burden of depression and other mental health conditions is on the rise globally. Burden of depression can be grouped as classical burden (residual symptoms, cognitive impairment, decreased quality of life etc.), Mortality burden (suicide, cardio and cerebro-vascular), disability burden (psychosocial, work days lost), family burden and economic burden. General medical condition with depressive symptoms cause even greater burden. Presence of depressive symptoms is likely to impede their recovery with further complications. Depression among hospitalized patients with chronic health conditions has been well studied[7,8]. Psychological symptoms may arise from many sources after admission, like inadequate adjustment to the unfamiliar hospital environment, insufficient privacy, exposure to strange instruments, financial concerns, and disease stress[9]. In many cases it is also associated with a higher incidence of unsatisfactory treatment outcomes[10]. In some instances, anxiety and depression have been morbid enough to result in increased morbidity, readmission, and psychiatric diagnosis after discharge[7,11,12].In a large longitudinal population-based study from the United Kingdom, women and men with any level of depression were 17.2% and 15.4%, respectively. Moderate-to-severe depression was seen in 6.9 % women and men[13]. In a Pakistani study with tuberculosis patients, 46.3% were depressed and 47.2% were anxious on the HADS scale[14]. A study conducted in Pakistan on 50 Patients hospitalized for surgeries with chronic remitting health conditions was found to have severe depression among 74% of the patients[15]. The risk of cardiac mortality after an initial myocardial infarction is greater in patients with depression and this risk is related to the severity of the depressive episode. A study of 896 patients hospitalized for myocardial infarction found a direct relationship between the severity of the depressive symptoms as measured by the Beck Depression Inventory Score at hospitalization and the risk of cardiac death over the following 5 years[16]. Similarly, a meta-analysis of 20 studies has shown that clinical depression is a significant risk factor for mortality in patients with coronary heart disease both short-term (3–6 months; adjusted odds ratio 2.07) and long-term (6–24 months; adjusted odds ratio 2.61)[17]. Greater depressive symptoms were found to be associated with significantly higher risk of all causes mortality and a higher especially in elderly patient[19]. Depression in women during pregnancy is common. Prevalence rates have been reported to be 7.4%, 12.8%, and 12.0% for the first, second, and third trimesters, respectively[21]. Other studies have shown that 10% to 16% of pregnant women fulfil the diagnostic criteria for MD, and even more women experience sub-syndromal depressive symptoms[20]. As discussed, depression is greater among the medically ill individuals. This study aims at finding out depression along with their severity among the patient admitted in a tertiary care hospital.

Material and methods

This was a cross sectional descriptive study where purposive consecutive sampling method was implemented. Study was conducted in CMH, Cumilla from January to March 2019. Patients having previous or current history of psychiatric illness were excluded from the study. Total 95 patients who were admitted in the hospital were interviewed during this period. After taking verbal consent from the patients, first socio-demographic information were collected. Then to assess the level depression among the patients Hamilton Depression Rating Scale (HAM-D) was used. Score above 10 was considered as significant; 10-13, 14-17 and above 17 were labelled as having mild, moderate and significant level of depression respectively. All data were entered and analyzed using SPSS version 22. Mean and ±SD were calculated for descriptive variables including age, length of hospital stay, and anxiety and depression scores. Frequencies and percentages were calculated for stratified variables.

Results

Total 95 patients were interviewed from 3 major departments of CMH, Cumilla. 50, 26 and 19 patients from department of Medicine, Surgery and Gynecology were studied respectively. Average duration of hospital stay on the day of interview is 7.91 day (SD ±6.94). 18.95% (n=18) patients has multiple comorbidity, most of them is admitted in medical ward. Among the patients 20 individual (21.1%) was found having significant (HAMD score >10) level of depression. Mean age of the respondents is 38.98 years (SD±17.99) and maximum numbers of patients are between 21 years to 30 years (n=33). Depression is highest among the age group of above 60 years 37.5% (n=6) followed by age group of 51-60 years 27.3% (n=3) (Figurer- I). Among 95 patients 65 are male (68.42%) and 30 is female (31.57%). Depression is more frequent in female population 26.66% (n=8) than male

population 18.46% (n=12). Severe depression is also greater in female group 37.5% (n=3) (Figure-2). Among the patients, 64.21% (n=61) is from urban background, whereas 35.78% (n=31) is from rural area (Figure-3). Depression is more among the rural habitants (23.53%) than the urban counterpart (19.67%). Most of the patient is from HSC passed group 52.63% (n=50), followed by secondary school group, 18.95% (n=18) (Figure-4). Depression is most common in illiterate group 33.33%, followed by graduate group, 10%. Most of the patient is in service, 53.7% (n=51), followed by housewife 29.5% (28). Depression is most among the others (like retired etc.) group of participants is 41.67% (5 among 12) and followed by in housewife group 25% (7 among 28). Participants are mostly married individuals, 75.8% (n=72) and they are also highest with depressive symptoms, 26.39% (n=19). 9 patient has family history of psychiatric illness and depression among them is significantly higher (55.56%, $p<0.001$) than patient not having family history (17.44%). Most of patient's monthly income are in between 21-30 thousand taka, but depression is most in income group of below 20 thousand taka per month (24.39%). Mean Hamilton Depressive Rating Score is 6 ±SD Search Results Featured snippet from the web ±4.61). 13.7% has mild depression; patients have moderate and severe depression are 3.2% and 4.2% respectively. Depression among the patients having multiple comorbidity (more than one) was significantly higher, 63.63% ($p<0.006$).

Figure 1: Distribution of patients according to their age group and level of depression

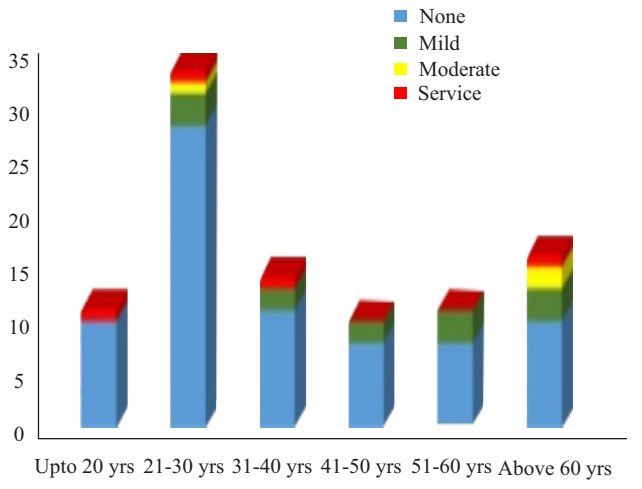


Figure 2: Distribution of participants according to gender and severity of depression

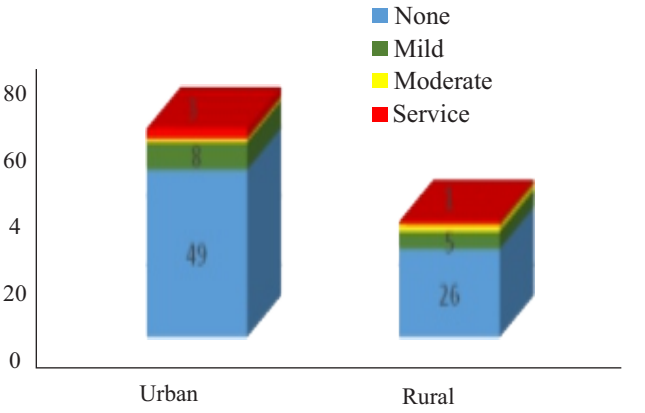


Figure 3: Distribution according to patients habitant (n=95)

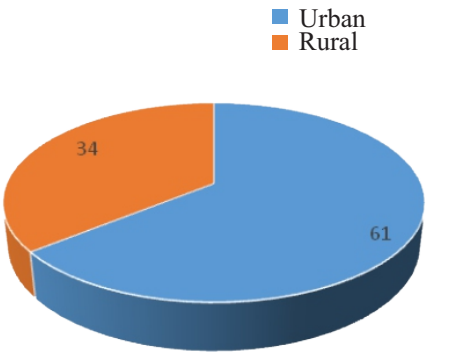
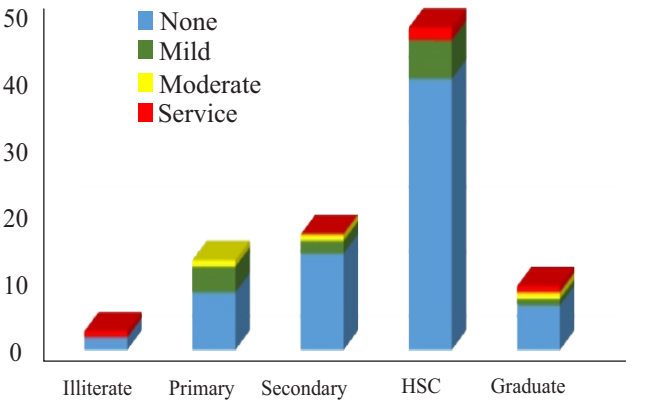


Figure 4: Distribution according to educational background and level of depression



Discussion

Frequency of significant depression among the patients was observed as 21.1%, which more than the general population (10-15%). It can be explained by two causes. One, the medical disease itself can depression. Other reason may be

external cause, like, psychological reaction of being ill, hospital admission, environment of the hospital, being separated from own environment etc. In this study, depression was found to be highest among the elder group of patients (37.5% among above 60 years group, followed by 27.3% among the 51-60 years group). Usually mean age of onset of depression is 27 years[21], this disparity may be explained as the participants of this study are special, having illness and admitted to hospital. Depression is common among female, about twice as high than male counterpart. In this study depression was found more among the female group (26.66%), even severe was more among the female patients (37.5%). Depression among the hospitalized patient is higher than general population. Depression among the medically ill, largely depends on the disease itself, number of comorbid disorder and their level of disability. 13.7% has mild depression; patients have moderate and severe depression are 3.2% and 4.2% respectively. Few of the limitations of this study were its small sample size, short duration and using the English version of Hamilton Depression Rating Scale (HAM-D).

Conclusion

Depression was found higher among the hospital admitted patient, mostly among older patients having family history of psychiatric illness and multiple comorbidity. Attention should be given to these patients for proper determination of level of depression, so their recuperation process takes shorter course.

Authors Affiliation

1. *Col Dr Ahmed Rafi, Commandant, CMH, Cumilla
2. Lt Col Dr Muhammad Abdul Kayum Shaikh, Classified Specialist in Psychiatry, CMH, Cumilla
3. Dr Afreen Ferdous, Associate Professor, Department of Physiology, East West Medical College, Uttara, Dhaka
4. Lt Col Dr Imranul Hasan Murad, ; Classified Specialist in Dermatology, CMH, Cumilla

*For correspondence

References

1. Demyttenaere K, Bruffaerts R, Posada-Villa J, et al. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. JAMA. 2004;291:2581–2590.
2. Lepine JP, Briley M. The increasing burden of depression. Neuropsychiatric Disease and Treatment. 2011;7 (1): 3–7.
3. Grigoriadis S, Robinson GE. Gender issues in depression. Ann Clin Psychiatry. 2007;19: 247–255.
4. Kessler, RC, et al. Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6): 593602.
5. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burdenof Disease Study. Lancet. 1997;349: 1436–1442.
6. World Health Organization. The global burden of disease: 2004 update. 2004.
7. Daratha KB, Barbosa-Leiker C, H Burley Mm, et al. Co-occurring mood disorders among hospitalized patients and risk for subsequent medical hospitalization. Gen Hosp Psychiatry. 2012;34: 500-505.
8. Elliott PC, Murphy BM, Oster KA, Le Grande MR, Higgins RO, Worcester MU: Changes in mood states after coronary artery bypass graft surgery. Eur J Cardiovasc Nurs. 2010;9: 188-194.
9. Chhari N, Mehta SC: Stress among patients during hospitalization: a study from Central India. Ntl J Community Med. 2016;7: 274-277.
10. Ghoneim MM, O'Hara MW: Depression and postoperative complications: an overview . BMC Surg. 2016;16: 5.
11. Gasse C, Laursen TM, Baune BT: Major depression and first-time hospitalization with ischemic heart disease, cardiac procedures and mortality in the general population: a retrospective Danish population-based cohort study. Eur J Prev Cardiol. 2014;21: 532-540.
12. Gerson S, Mistry R, Bastani R, et al. Symptoms of depression and anxiety (MHI) following acute medical/surgical hospitalization and post-discharge psychiatric diagnoses (DSM) in 839 geriatric US veterans. Int J Geriatr Psychiatry. 2004;19: 1155-1167.
13. Breeman S, Cotton S, Fielding S, Jones GT: Normative data for the hospital anxiety and depression scale. Qual Life Res. 2015;24: 391-398.
14. Husain MO, Dearman SP, Chaudhry IB, Rizvi N, Waheed W. The relationship between anxiety, depression and illness perception in tuberculosis patients in Pakistan. Clin Pract Epidemiol Ment Health. 2008;4: 4.
15. Mirani S H, Areja D, Gilani S, et al. Frequency of Depression and Anxiety Symptoms in Surgical

Hospitalized Patients. Cureus.2019;11 (2): e41 41 .

16. Lespérance F, Frasure-Smith N, Talajic M, Bourassa MG. Five-year risk of cardiac mortality in relation to initial severity and one-year changes in depression symptoms after myocardial infarction. Circulation.2002;105: 1049–1053.
17. Barth J, Schumacher M, Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. Psychosom Med. 2004;66: 802–813.
18. Gump BB, Matthews KA, Eberly LE, Chang YF; MRFIT Research Group. Depressive symptoms and mortality in men: results from the Multiple Risk Factor Intervention Trial. Stroke. 2005;36: 98–102.
19. Juurlink DN, Herrmann N, Szalai JP, Kopp A, Redelmeier DA. Medical illness and the risk of suicide in the elderly. Arch Intern Med. 2004;164(11): 1179– 84
20. Marcus SM, Heringhausen JE. Depression in childbearing women: when depression complicates pregnancy. Prim Care. 2009;36: 151–165.
21. Harrison p, Cowen P, Burns T. Shorter Oxford Textbook of Psychiatry. 7th Edition.2018; 203-4.

Behavioral and Life Style Risk Factors Analysis for Pre-hypertensive and Hypertensive Population in Urban Dhaka

Jannatul Ferdousi[1], Saidul Arefin[2], Md. Khairul Alam[3], Mohammad Shakil[4]

Abstract

Background: Prevalence of hypertension is on rise silently and slowly in Bangladesh. This quasi experimental type of interventional study was conducted aiming at evaluating reversible of blood pressure through reduction of body weight in overweight or obese, individual avoidance of table salt intake, increment of physical activity and cessation of smoking, changing of food habit in urban committee. The study also aimed at finding out the socio-economic and demographic profile for pre-hypertension and stage-I hypertension evaluating outcome of behavioral risk reduction contributing to maintenance of reversal of hypertension. **Objective:** This study was conducted to analyze if modification of life style and behavioral risk factor can reduce pre-hypertension and stage-I hypertension. **Methods:** This intervention study was done in old Dhaka City from August, 2013 to October 2015 on respondents aged 18 years or above including an intervention period of 6 months. Non-probably type of judgment sampling was used to collect 150 respondents with pre-hypertension and stage-I hypertension. **Results:** Mean systolic blood pressure was 130±7.09 mmHg and mean diastolic blood pressure was 83.5±17.39 mmHg. Among the study group normal blood pressure was found only 45% cases while 30.0% had pre-hypertension, 19% had stage-I hypertension and 6% had stage-II hypertension. After 6 months mean change of systolic blood pressure was -9.31.7 mmHg and mean change of diastolic blood pressure was -4.20±1.94 mm Hg. Both systolic and diastolic blood pressure was significantly reduced from baseline, after 6 months of behavioral risk reduction intervention ($p<.001$). At beginning 58.7% took extra salt. After 6 months intervention it was 1.4%. Avoidance of extra salt intake was significantly related to change of both systolic and diastolic blood pressure ($p<0.001$). There was no significant change of smokers with blood pressure. Mean BMI reduction -1.62±1.8 kg/m2 ($p<0.05$). At the baseline of the study mean physical activities were 230.80±224.90/minute week and 518±275.70 minutes/week respectively after 6 months. Significant correlation of both systolic and diastolic blood pressure increment of physical activities ($p<0.001$). **Conclusion:** Reversal of pre-hypertension and stage-I hypertension was possible by structural behavior risk reduction meaning intake of balance diet with exclusion of extra salt intake, increment of physical activity along with reduction of body weight. Combination of all these parameter recommending to be used by the physician while treating and caring patients with pre-hypertension.

Keywords: Hypertension, Pre-hypertension, BMI, Physical activity.

J Ar M Coll Cu. 2019, July; 2 (2): 38-42
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

High blood pressure exerts a major share in the global burden of disease, and it is unduly higher in low income countries than in the high income countries. More specifically elevated blood pressure is responsible for approximately 60% of stroke and over 50% of ischaemic heart disease[1]. Pre-hypertension is associated with CVD mortality, especially stroke mortality[2] and stroke morbidity[3]. Pre-hypertension is now recognized as a potential candidate for cardiovascular intervention or risk reduction. The people with high normal systolic blood pressure (SBP) from 120 to 139 mmHg and diastolic blood pressure (DBP) from 80 and 89 mmHg developed by hypertension faster and in an increased risk of cardiovascular disease[4,5]. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC7), introduced the new category of "pre-hypertension", defined as systolic BP of 120 to 139 mmHg and/or diastolic BP of 80 to 89 mmHg[6]. Recent studies found an association between pre-hypertension and increased risk of coronary artery disease (CAD)[7,8]. Follow up studies also reported that pre-hypertension is an independent risk factor for cardiovascular and cerebrovascular disease[9]. In USA, the prevalence of pre-hypertension range between 31%[10] to 48.2%[11]. In the neighbor country, India, the prevalence stretched from 32% to 44%[12,13]. In Bangladesh, few studies were done on pre-hypertension. In 2009, Alamgir AKM find prevalence of stage-I HTN was 20.1% and pre-hypertension

Received March 2019 Accepted August 2019

was 34.3% between 18-64 years of age group in Urban Dhaka[14]. Another study was done in 2015 in rural area. Here they reported prevalence of pre-hypertension was 31.9% and hypertension was 16.0% respectively[15]. On the basis of the 7th JNC, pre-hypertension necessitates daily life adjustments to prevent development to hypertension[6]. WHO, British Hypertension Society and Joint National Committee agreed upon non-pharmacological approaches of behavioral risk reduction intervention for first 6-12 month incase of pre-hypertension and uncomplicated stage-I hypertension patient having no second risk factor[16]. These studies indicated the substantially rising trend of pre-hypertension and stage-I hypertension in Bangladesh. Smoking tobacco, physical inactivity, increased salt intake and over weight or obesity were identified as important modifiable behavioral risk factors for high blood pressure such observations references created interest in possibility of the primordial or primary prevention of pre-hypertension through non-pharmacological intervention on factors related to the development of high blood pressure.

Materials & Methods

This intervention study was conducted during the period of August, 2013 to October, 2015 on respondents aged 18 years or above in Sutrapur than of Dhaka City including an intervention period of 6 months. Non-probability type of judgment sampling was used to collect 150 respondents with pre-hypertension and stage-I hypertension. The respondents had neither any complications nor any co-morbidity The intervention was given person to person. Intervention included physical activity enhancement, dietary advice, avoidance of extra table salt intake and smoking cessation. Global standard tools were used to collect data through person-to-person interview and clinical assessment. Data analysis and interpretation done through SPSS.

Results

The mean age of the respondents with PHTN was 30.94 and mode 30.4. Peak age group 45.6% respondents were 25-34 years. Male was more than female respondents with PHTN. Mean age of the study participants with stage-I HTN was 60.6 and mode 38.6. Peak age group 51.7% respondents were 35-44 years and 63.8% of respondents were male. Positive history of High Blood Pressure among first degree family member is found among 63% (94). Respondent with PHTN and stage-I HTN at baseline study where no relation is found among 24% (36) Respondents (Fig-2). 20 respondents (13%) significant (t=19.61, df=281), p>0.001 between positive and negative response for family history. Combined effect of risk factor on BP: Multiple regression analysis is done food testing individual role in physical activity expressed in METs, changes of body weight in kg, salt intake and change of smoking habit ,after removing the effect of age ,sex, level of education ,yearly expenditure and intake of beef .BP reduction of salt intake is found to be best prediction (paired t-test = 14.084, p<0.001).Role of the reduction of BMI is also found to have significant role(paired t-test = 1.979, p<0.05) and smoking contributing no significant reduction followed by increment of physical activity reduction best prediction (paired t-test = 4.048, p<0.001) followed by METs increment .

Test of significant for change of BP

Paired Sample T test shows significant change of both Systolic & Diastolic BP at the end of 6 months . Value of paired t-test is found 10.9, df 141 ,value p>0.001. These value for diastolic blood pressure are 5.5, df 141, respectively with p value >0.001. Mean change of blood pressure at the end of the study is -9.4/4.3 mm Hg .

Table 1: Distribution of PHTN by Age and Sex (n=92)

Age	Sex				Total	
	Male		Female			
	n	%	n	%	n	%
18-24	16	17.4	6	6.5	22	23.9
25-34	36	39.2	6	6.5	42	45.6
35-44	13	14.1	12	13	25	27.2
45-54	1	1.1	1	1.1	2	2.2
55-64	1	1.1	0	0	1	1.1
Total	67	72.9	25	27.1	92	100

Table 2: Distribution of stage-I HTN by Age and Sex (n=58) History of hypertension

Age	Sex				Total	
	Male		Female			
	n	%	n	%	n	%
18-24	2	3.5	3	5.3	5	8.6
25-34	9	15.2	6	10.3	15	25.8
35-44	21	36.3	9	15.5	30	51.7
45-54	2	3.5	1	1.6	3	5.3
55-64	3	5.3	2	3.5	5	8.6
Total	37	63.8	21	36.2	58	100

Figure 2: Distribution of PHTN and stage-I HTN by History of Hypertension n=150

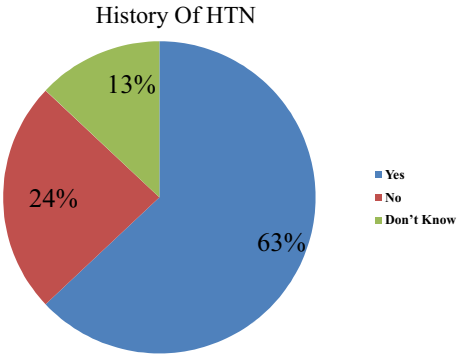


Table 3 : Combined effect of risk factor on BP

SL No	Description	t	p
1	Salt reduction	14.084	0.001
2	BMI	1.979	0.05
3	Physical activity	4.048	0.001

Table 4: Test of Significant for change of Blood Pressure after intervention

	Systolic Blood Pressure		Diastolic Blood Pressure	
	Baseline	After	Baseline	After
Sample	150	142	150	142
Mean Value	130+709	118.65+8.84	83.5+7.39	79.31+5.45
Change of BP		-9.35+1.75		-42+1.94
STD error	0.835	0.848	0.825	0.758
Paired T test		10.9		5.5
T value		141		141
P value		0.05		0.001

Discussion

Prevalence of pre-hypertension and stage-I hypertension (JNC-7 criteria) was found to be 30% and 19% at this urban study. This prevalence rate reflected a siminal finding by AKM[14] who studied in Mohammadpur area and also by Khanam et al (2015)[15]. However, the rate is higher in India 60%[17]. Pre-hypertension and stage-I hypertension was found to be more prevalent at the most productive age group (25-44 years). The prevalence of pre-hypertension was higher among the male than female. This finding is consistent with other finding[18,19]. Family history of hypertension, in first degree family members, was found positive among 63% people which is inconformity to other study[20]. One sample t-test result showed significant difference (t=19.61, df 281 p<0.001) between positive and negative response for family history. Dietary habit showed carbohydrate pre-hypertension and stage-I hypertension more common among fast food eaters. This is common food transition habit specially among the relatively younger population. Relation between use of extra salt and blood pressure was tested with multinominal regression analysis showing statistically significant association. This observation strongly indicated role of salt intake as causation of hypertension as was found in other studied[21]. This study also statistically proved that reduction of salt intake could significantly reduce both systolic and diastolic blood pressure. Salt was also found to be the best predictor for occurrence and reduction of both systolic and diastolic blood pressure (t=14.084, p=0.000). Extra salt intake was reduced from 58.7% at beginning of intervention to 1.4% at the end of 6 months intervention. In brief, salt intake is found significantly associated with causation of blood pressure and also reduction of salt intake significantly contributes to reversal of blood pressure. Increasing BMI is found to be an independent and important risk factor for respondents in this study. Relationship of higher BMI with pre-hypertension and stage-I hypertension was also observed in other studies[18-22]. Evidence exits that overweight and obesity are strongest predictor of pre-hypertension and stage-I hypertension[23,24]. BMI is the robust predictor (t=11.75, p>.001) in this study. Body weight is the balance between consumption and expenditure of energy. Only 4.3% respondents performed 60 min heavy physical activity in an average week and another 4.3% did 30 minutes only. This is a typical scenario for a middle class sedentary society[25]. Similar baseline study in 2002 among 25-64 years age group showed that only about 2.9% respondents perform heavy physical activity in an average week. The mean physical activity time in that study was 84 minute in an average week[26]. Moderate grade of physical activity influced more for reversal of hypertension (t=4.048, p<.001). Increment of physical activity was found to be an effective and efficient predictor for both systolic and diastolic blood pressure. Mean change of systolic blood pressure was 9.35±1.75 and diastolic blood pressure was 4.2±1.94 after 6 months intervention. This is consistent and comparable to study outcome of Apple (1997)[27,28,29] who could reduce BP by 11.4/-5.5 mmHg on 133 respondents in 3 weeks and -5.5/-3.0 mmHg on 459 respondents in 11 weeks by DASH plus intervention comparing to controlled diet. Hill studied on 309 hypertensive over a period of 24 months and could reduce BP -7.2/-14.3 mmHg by non-pharmacological

pharmacological approaches only[30]. Careful inclusion of the respondents at the beginning, routine follow up, quality information and holistic health care support to the respondents and their families made the drop-out to reduce at the present study. The total outcome of the study was statistically significant and consistent with other national or overseas studies in different perspectives.

Conclusion

Prevalence of pre-hypertension and stage-I hypertension in Bangladesh has been increasing silently but significantly. This study found association of elevated blood pressure with sedentary life style, increased intake of fat rich fast food and unhealthy behavioral pattern. After 6 months follow-up, important and significant determinants for reversal of blood pressure were found to be reduction of extra table salt intake, increment of physical activity and reduction of body weight through healthy balanced habit. People with pre-hypertension and stage-I hypertension can serve as a group of guide valuable interventions to control and prevent cardiovascular diseases.

Authors Affiliation

1. *Dr. Jannatul Ferdousi, Professor (c.c.), Department of Community Medicine, Dhaka National Medical College
2. Dr. Saidul Arefin, Professor, Institute of Nutrition and Food Science, University of Dhaka
3. Dr. Md. Khairul Alam, Professor & Head Department of Physiology, Army Medical College Cumilla.
4. Dr. Mohammad Shakil, Associate Professor, Department of Community Medicine, Army Medical College Cumilla.

*For correspondence

References

1. Lawes CM, Vander Hoorn S, Law MR, Elliottp, MacMahon S, Rodger A. Blood pressure and the global burden of disease 2000. Part II; estimates of attributable burden. J Hypertens. 2006; 24 (3): 423-30.
2. Huang Y, Su L, Cai X, Mai W, Wang S, Hu Y, et al. Association of all-cause and cardiovascular mortality with pre-hypertension: a meta-analysis. Am Heart J. 2014; 167 (2): 160-8. e161.
3. Huang Y, Cai X, Li Y, Su .L, Mai W, Wang S, et al. Pre-hypertension and the risk of stroke: a meta-analysis. Neurology. 2014; 82 (13): 1153-61.
4. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002; 360 (9349): 1903-13.
5. MacMahon S, Peto R, Culler J, Collin R, Neaton J, et al. Blood pressure, Stroke and coronary heart disease. Part-1, Prolonged differencesin regression dilution bias. Lancet. 1990; 335 (8692): 765-74.
6. Chobanian AV, Bakis GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, et al. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension. 2003; 42 (6): 1206-52.
7. Qureshi Al, Suri MF, Kimani JF, Divani AA, Mohammad Y. Is pre-hypertension a risk factor cardiovascular disease? Stroke. 2005; 36 (9): 1859-63
8. Shen L, Ma H, Xiang MX, Wang JA. Meta-analysis of cohort studies of baseline pre-hypertension and risk of coronary heart disease. Am J Cardiol. 2013; 111 (2): 266-71.
9. Wu S, Huang Z, Yang X, Lis, Zhao H, Ruan C, et al. Cardiovascular events in a pre-hypertensive chinese population: four-year follow up study. Int Cardiol. 2013; 167 (5): 2196-9.
10. Wang Y, Wang QJ. The prevalence of pre-hypertensionand hypertension among US adults according to the new joint national committee guidelines: new challenges of the old problem. Arch Intern. Med. 2004; 164 (19): 2126-34.
11. Zhang Y, Lee ET, Devereus RB, Yeh J, Best LG,FabsitzRR, et al. Pre-hypertension, diabetes and cardiovascular disease risk in a population-based sample: the strong Heart Study. Hypertension. 2006; 47 (3): 410-4.
12. Mohan V, Deepa M, Farooq S. Datta M, Deepa R. Prevalence, Awareness and control of hypertension in Chennai-The Chennai Urban Rural Epidemiology Study (CURES-52). J Assoc Physicians India. 2007; 55: 326-32.
13. Yadav S, Boddula R, Genitta G, Bhatia V, Bansal B, Kongata S, et al. Prevalence & risk factors of pre-hypertension & hypertension in an affluent north India population. Indian J Med Res. 2008; 128 (6): 712-20.
14. AKM Alamgir, MR Azad. Pre-hypertension - an Emerging Epidemic in Developing countries. J Dhaka Natl. Med. Coll. Hosp. 2009; 14 (1): 3-5.

16. World Health Organization (WHO), International Society of Hypertension (JSH) statement of management of hypertension. Journal of Hypertension 2003; 21: 1983-1992.

17. Yadav S, Boddula R, Genitta G, et al. Prevalence & risk factors of pre-hypertension and hypertension in an affluent North India population. India. J. Med. Res. 2008;128(6): 712-20

18. T Sai PS, Ke TL, Huang Cl, T Sai JC, Chen PL, Wang SY, et al. Prevalence and determinants of pre-hypertension status in the Taiwanese general population. J Hypens. 2005; 23 (7): 1355-60.

19. Wu Y, Huxley R, Li L, Anna V, Xie G, Yao C, et al. Prevalence, awareness, treatment an control of hypertension in China: data from the China National Nutrition and Health Survey 202. Circulation. 2008; 118 (25): 2679-86.

20. Mc Cusker ME, Yoon PW, Gwinn M, Malarcher AM,Neff, Khoury MJ. Family history of heart disease and cardiovascular disease risk-reducing behaviours. Genet Med. 2004;6 (3): 153-8.

21. Sacks FM, Svetkey LP, Vollmer WM, et al. The DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. N Engl J Med, 2001; 344 (1): 3-10.

22. Yu D, Huang J, Hu D, Chen J, Cao J, Li S, et al. Prevalence and risk factors of pre-hypertension among Chinese adults. J Cardiovasc Pharmacol. 2008; 52 (4): 363-8.

23. Koura MR, Al-Dabal BK, Rasheed P, Al-Sowielem LS,Makki SM. Pre-hypertension among young adult femals in Damman, Saudi Arabia. East Medlterr Health J. 2012; 18 (7): 728-34.

24. Rahmanian K, Shojhe M. The prevalence of pre-hypertension and its association to established cardiovascular risk factors in south of Iran. BMC Res Notes. 2012; (5): 386.

25. Lakka TA, Venelainen JM, Rauramaa R, Salonem R, Tuomilehto J, Salonem JT. Relation of leisure-time physical activity and cardiorespiratory fitness to the risk of acute myocardial infraction in men. New Eng. J. Med. 1994;330 (22): 1549-1554.

26. Rahman M, Meerjady SF, Akhter SFU, Hossain S, Mascie-Taylor CGN. Behavioral risk factors of non-communicable diseases in Bangladesh (STEPS Survey). http://www.who.int/infobase Ref 102410 accessed on 15-07-2014.

27. Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ, et al. Writing group of the PREMIER Collaborative Research Group. Effects of comprehensive life style modification on blood pressure control: main results of the PREMIER clinical trial. JAMA. 2003;289 (16): 2083-93.

28. Svetkey LP, Erlinger TP, Vollmer WM, Feldstein A, Cooper LS, Apple LJ, Ard JD, Elmer PJ, Harsha D, Stevens VJ. Effect of life style modifications on blood pressure by race, sex, hypertension status, andage. J Hum Hypertens. 2005;19(1): 21-31

29. Apple LJ, Moore TJ, Obarzan ek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. NEJM. 1997; 336: 1117-1124.

30. Hill MN. BHP Care: Comprehensive HBP care in young urban black men. Clin Cardiol. 2000; 23: 56-58.

Bile Duct Injuries Following Laparoscopic Cholecystectomy -Experience in Tertiary Care Hospital

Md. Mahfuzul Momen[1], Sonia Akter[2], Deb Prosad Paul[3], Ashok Kumar Sarker[4], Karina Rahman[5], S.M. Tauhidur Rahman[6]

Abstract

Background: The study was to improve surgical safety, reduce the incidence of bile duct injury (BDI) and determine the incidence of biliary injuries associated with LC and treatment plan. **Materials and Methods:** Patients of acute or chronic cholecystitis due to gallstones were included in this study while patients of obstructive jaundice and gallbladder mass were excluded. All patients were operated through laparoscopic cholecystectomy without On-table cholangiography. During procedure, bile duct injury was noted and evidences of bile duct injury were also collected postoperatively during hospitalization and follow-up visits. Data regarding complications in terms of bile duct injury were recorded and analyzed.The patients have been admitted before operation and classical LC was done. Monopolar electrocautery was used. The insertion of postoperative intraperitoneal drain or nasogastric tube depended on the surgeons' preference and opinion. The data was evaluated according to incidence and treatment of bile duct injury. **Results** :Results of this study suggest that 34.30% cases were male and 65.70%patients were female. During the three years (March 2016 and February 2019), 586 patients underwent LC. A total of 6 (1.02%) bile duct injuries were noted in this series. Among those who underwent LC, two (33.33%) cases of partial injury to the common hepatic duct out of which 1 was a case of Mirizzi's syndrome and another one occurred during an attempt to cauterize the avulse branch of cystic artery. In one (16.67%) patient's partial injury to common bile duct occurred due to tenting of common bile duct and short cystic duct. Complete transaction of common bile duct occurred in two (33.33%) cases due to difficult to define anatomy of Calot's triangle and excessive adhesion. one case was found Injury to accessory duct (Cholecystohepatic Duct). None of the patients in this study died as a result of LC. **Conclusion:** Bile duct injury is a major complication of LC and It can have devastating effects. They mainly result from anatomical anomalies, local pathology, and poor surgical techniques and errors of human judgment and are thus preventable to some extent.

Keywords: Laparoscopic, cholecystectomy, common bile duct, chronic cholecystitis, bile duct injury

J Ar M Coll Cu. 2019, July; 2 (2): 43-48
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Laparoscopic cholecystectomy is accepted as the gold standard in the surgical management of gallbladder disease.[1]The introduction of laparoscopic cholecystectomy has increased bile duct injuries by three to four folds.[2] Bile duct injury can lead to bile leakage, peritonitis, stricture formation, cholangitis, jaundice, chronic liver disease and septicemia. These injuries are frequently amenable to delayed recognition and difficult reoperations due to inflammation, infection and malnutrition[3]. The level of experience of the operating surgeon and the technical difficulties at operation are other factors that can add to the risk of bile duct injury. These injuries pose serious health and economic problems and aside from patient morbidity and mortality, they expose the surgeon to expensive medicolegal litigation. In addition, they increase substantially the economic burden to the patient, hospital and community, and some patients have needed hepatic transplantation for some patients have needed hepatic transplantation for survival[4]. A number of techniques have been devised to prevent such injuries and among these On-table cholangiography (OTC) is widely practiced. On-table cholangiography (OTC) was first recommended by Mirizzi[5] in 1931 on the basis of high incidence of common bile duct stones and thus reducing the incidence of unnecessary CBD exploration from 66% to < 5%.In cholecystectomy, the routine use of OTC is controversial as it is useful to map the anatomy of the biliary tree but on the other hand it increases the operation time, cost and unnecessary CBD exploration due to poor quality images and false-negative and false-positive results. The debate becomes further complicated with the advent of laparoscopic cholecystectomy which demands additional technical skills for OTC.[7] Numerous studies have shown that Laparoscopic cholecystectomy was performed safely with minimal use of OTC.[8,9] While others insist the routine use of OTC during laparoscopic

Received March 2019 Accepted December 2019

setup, On-table cholangiography is not performed routinely while doing laparoscopic cholecystectomy. It is mainly due to technical difficulty and non-availability of the equipment in most hospitals. In this study, we report the outcome of a series of patients undergone LC without On-table cholangiography.

Patients And Methods

This study was carried out in Enam Medical college & Hospital from March 2016 and February 2019. A total of 586 patients were included in this study. Patients of known gallstone disease without clinically and radiological proven complications (obstructive jaundice) were subjected to laparoscopic cholecystectomy. Patients were admitted through outpatient or emergency department. After proper history and examination, the gallstone diseases was diagnosed by ultrasonography and CT-scan where if needed. Patients with complications like obstructive jaundice or gallbladder mass were excluded from the study. All patients were operated as elective cases with laparoscopic procedure. Four ports laparoscopic cholecystectomy was performed in majority of the cases. Meticulous concentration was adopted for hepatobiliary anomalies. On-table cholangiography was performed in none of the cases. At the completion of procedure biliary tracts were examined carefully for evidence of evident or potential damage. They were observed for a day or two and then were discharged home. They were advised to attend the follow-up clinics at four to six weeks interval. During postoperative course and follow ups, they were looked for evidence of bile duct injury (peritonitis, biliary leakage through drain or biliary fistula). Thus, detected cases of bile duct injury were admitted for further work up. The data were entered into a proforma and was analyzed and results were drawn at the completion of study.

Results

Results of this study suggests that 34.30% cases were male and 65.70% patients were female. Out of the total 586 cases that underwent laparoscopic chole-cystectomy bile duct injury was observed in 6 (1.02%) six cases (Table 2).

Partial Injury to CHD: There were 2 (33.33%) cases of partial injury to the common Hepatic duct. One case was that of the "Mirizzi syndrome". The opening between the Hartman's pouch and CHD (common hepatic duct) became evident during dissection. Hence immediately laparoscopically repaired and T-tube placed. In the second case, a small spurt occurred from a vessel running over the CHD during dissection of dense adhesions in Calot's triangle, hence diathermy was used to coagulate the bleeder. After controlling the bleeding, bile was found. Immediately converted to laparotomy, showed a hole at the site where diathermy was used, a T tube was placed.

Partial Injury to CBD: In 1 (16.67%) patients, the partial injury to CBD occurred due to tenting and short cystic duct, these injury was detected per-operatively. The problem was solved by laparoscopically repaired and insertion of T-tube.

Complete Transaction of CBD: This occurred in 2 (33.33%) patients. In one, who had a very small gallbladder (hardly 2.5 cm), that was buried in the liver near porta hepatis. Besides the entire gallbladder was occupied by a large stone. Thus, CBD was mistaken for cystic duct, clipped and divided. The gallbladder which was densely adherent with the under surface of liver and was separated by blunt and sharp dissection using scissors and diathermy hook, and removed. After irrigation by Normal saline, bile was found in the operative field and injuries were detected. The problem was rectified by conversion to open. Laparotomy and hepatojejunostomy was performed and the patient ultimately recovered. Another one also results of the misidentification of the cystic duct related to the CBD due to adhesion. Laparotomy and suturing over T-tube insertion due to no segmental loss of CBD

Injury to Cholecystohepatic Duct: This was realized in a patient who returned on the 4th postoperative day with abdominal distension and pain. Ultrasound showed a huge collection under the liver and ultrasound guided drain was placed. As the leakage continued (around 1000 ml of bile daily), laparotomy was performed which revealed a cholecystohepatic duct which was ligated. The patient recovered uneventfully.

Table 1: Age distribution of study patients

Age in years	Male		Female	
	n	%	n	%
20-30	15	2.56	24	4.10
31-40	89	15.19	163	27.82
41-50	67	11.43	144	24.57
5160>	20	3.41	35	5.97
60	10	1.71	19	3.24
Total	201	34.30	385	65.70

Table 2: Reason For bile duct injury

Reason	No	%
Difficult to define the anatomy of Calot's triangle	2	33.33
Cystic artery bleeding	1	16.67
Mirizzi's syndrome	1	16.67
Tenting of common bile duct and short. cystic duct	1	16.67
Injury to accessory duct (Cholecystohepatic Duct)	1	16.67

Table 3: Management of Bile duct injury

Injury	N %	Action taken	Result
Partial injury to CHD	2(33.33%)	1) Laparoscopically repairand T-tube insertion 2) conversion to open surgery and insertion of T-tube.	No further complication
Partial injury to CBD	1(16.67%)	Laparoscopically repair and T-tube insertion	No further complication
Complete transection of CBD	2(33.33%)	1) Laparotomy and hepatojejunostomy (Segmental loss of CBD) 2) Laparotomy and suturing over T-tube insertion(No segmental loss of CBD)	Complete recovery after four weeks
Injury to accessory bileduct (cholecystohepatic Duct)	1(16.67%)	Laparotomy and ligate theCholecystohepatic Duct	Complete recovery after two weeks

Discussion

The Main Reasons for Intraoperative Bile Duct Injury:

Bile duct injury is a major complication of LC. Anatomical anomalies, local pathology, and poor surgical techniques are the main factors responsible.[13]Anatomic factors include bile duct variation, variation of the cystic duct, abnormal blood vessels, and hepatic portal rotation. Accessory hepatic duct variation was one of the important anatomical biliary damage factor.[14] Bile leak after laparoscopic cholecystectomy is uncommon but can occur in 0.3–2.7% of patients.[15,16,17] It has been previously suggested that the high rate of biliary injury associated with laparoscopic cholecystectomy is the result of the learning curve.[18,19] However, other authors have reported it an ongoing problem well beyond the learning period.[20,21] In our study, all the cases were performed by experienced laparoscopic surgeons who had already performed more than 100 LC, yet the bile duct injuries occurred in 1.02% of cases which indicates that no surgeon is immune from bile duct injuries during LC. Carroll BJ et al [18] also experienced that most of the injuries occurred from surgeons who were out of the learning curve. In 2 (33.33%) cases, these injuries were the result of misidentification of the anatomy due to inadequate dissection and undue tension, resulting in the tenting of CBD. While in one case (14.28%), injury occurred due to cauterization. Carroll BJ et[22] observed misidentification of anatomy in 48% cases and cautery injury in 11% of the cases. According to Hunter JG [23] these injuries can be avoided by the use of a 30° angle forward oblique viewing telescope, firm cephalic traction on the fundus and lateral traction on the infundibulum to place the cystic duct perpendicular to the common duct, dissection of the cystic duct where it joins the gallbladder, and routine fluoroscopic cholangiography. The variations of cystic duct include: short cystic duct, atrophic cholecystitis and abnormal position of the gallbladder.[14]In the study, one patient was found short cystic duct. One patient was found atrophic cholecystitis the variations of cystic duct. Another retrospective report also suggested that LC for acute cholecystitis and gallstone pancreatitis is associated with an increased risk of major bile duct injury.[24] The practical axiom is a simple one: if adequate exposure for a safe dissection cannot be obtained, the case should be converted. In some cases, a fundus-first dissection of the gallbladder may be required.[25] On-table cholangiography (OTC) reduces the chances of bile duct injuries, therefore some authors advocate routine while other selective cholangiography during LC. However, due to lack of facility and expertise we perform LC without OTC. Experience of laparoscopic cholecystectomy in the United States, where OTC is either a routine or selectively performed, showed the incidence of bile duct injury as 0.6%.MacFadyen BV et al observed the incidence of bile duct injury as 0.5%, while Calvete J et al.[26] experienced injuryrate of 1.3%. In our study, we found the rate of bile duct injuries as 1.02 % which is comparable with incidence of centers where OTC is routinely or selectively performed. Archer SB et al[27] in their study also reported better detection rate of bile duct injuries even without doing OTC.

Management of Bile Duct Injury: Immediate restoration for bile ducts or biliary-enteric drainage is crucial to the success of the surgery. The key to treatment is early

detection and correction. End to end anastomosis of the bile duct should be done to restore the anatomical integrity of the biliary tract and retain the function of the sphincter of Oddi. This manner have good blood supply, no anastomotic tension and will not cause any narrowing. Drainage near the anastomosis would prevent secondary infection.[28,29] The management of BDIs can be divided into non-operative and operative repair as well as into per-operative, early (<1week), intermediate (1 to 6 weeks), and delayed (>6 weeks) repair. The method and timing of the repair depends on several factors. The extent of injury, the expertise of the surgeon and his team, the amount of acute inflammation in the area, and the hemodynamic stability of the patient are the most important factors in achieving successful repair. It is necessary to have careful long-term postoperative monitoring of liver function and good interdisciplinary cooperation, especially with the suggestion of radiologist.[30,31]

There are several methods of the early treatment which include Conservative treatment, a simple repair, end to end bile duct anastomosis, Roux-en-Y biliary-enteric anastomosis, pedicle flap repair, peritoneal drainage and ERCP and nasal bile duct drainage.[32] The indications for conservative treatment include bile leakage is less than 300 ml, with no peritonitis. Ultrasonography should be done to rule out collections under the liver. Maintaining unobstructed drainage and preventing drainage tube slippage is crucial. After several weeks bile leakage would resolve. [33,34] End-to-endanastomosis of bile ducts has the advantage of maintaining the physiological function of the biliary tract. It is suitable for bile duct transaction which was found during the surgery and the defect length is less than 1.5 cm. The contraindication is defect greater than 1.5 cm, severe local inflammation, and poor general Condition. If the defect is larger than 1.5cm, the bile duct defect should be underwent Roux-en-Y anastomosed.[35,36] The choledochoenterostomy will not subject to restrictions due to the length of bile duct defect, and the indications are broader. The contraindications are severe peritonitis and when the diameter of the injured bile duct is less than 3mm. [37] In the study, the one patient who found injure underwent end-to-end anastomosis of bile ducts. Another patient underwent bile duct jejunum Roux-Y anastomosis and the prognosis were well.

Conclusion

Appropriate surgical indications, handling Calot triangle carefully and correctly, and conversion to open surgery at the right moment are the keys of prevention and treatment of bile duct injury during LC.

Authors affiliation

1. * Dr. Md. Mahfuzul Momen, Asst. Prof. Dept. Of Surgery Enam Medical College & Hospital
2. Dr. Sonia Akter Asst. Prof. Dept. Of Surgery Enam Medical College & Hospital
3. Dr. Deb Prosad Paul Prof. Dept. Of Surgery Enam Medical College & Hospital
4. Dr. Ashok Kumar Sarker Asst. Prof. Dept. Of Surgery Enam Medical College & Hospital
5. Dr. Karina Rahman, Asst. Professor, Dept of Surgery, EMCH.
6. Dr. S.M. Tauhidur Rahman, Associate Professor & Head Dept of Anesthesia, Eastern Medical College & Hospital.

*For correspondence

References

1. Strasberg SM, Hertl M, Soper NJ. An analysis of the problem of biliary injury during laparoscopic cholecystectomy. J Am Coll Surg. 1995;180:101–25.
2. Moosa AR, Easter DW, Van Sonnenberg E, Casola G,D'Agostino H. Laparoscopic injuries to the bile duct: A causefor concern. Ann Surg. 1992;215: 203-08.
3. Carroll BJ, Friedman RL, Liberman MA, Phillips EH. Routinecholangiography reduces sequelae of common bile duct injuries.Surg Endosc.1996;10: 1194-97.
4. Henry ML, Carey LC. Complications of cholecystectomy. Surg Clin North Am. 1983;63: 1191-1204.
5. Mirizzi PL. Operative cholangiography. Surg Gynecol Obstet1937;65:702-10.
6. Way LW, Admirand WH, Dunphy JE. Management ofcholedocholithiasis. Ann Surg. 1972;176: 347-59.
7. Vezakis A, Davides D, Ammori BJ, Martin IG, LarvinM,McMahon MJ. Intraoperative cholangiography duringlaparoscopic cholecystectomy. Surg Endosc.2000;14: 1118-22.
8. Morris JB, Margolis R, Rosato EF. Safe laparoscopiccholecystectomy without intraoperative cholangiography. Surg Laparosc Endosc.1993;3: 17-20.
9. Voyles CR, Sanders DL, Hogan R. Common bile duct evaluationin the era of laparoscopic cholecystectomy: 1050 cases later. Ann Surg. 1994;219: 744-52.
10. Barteau JA, Castro D, Arregui ME, Tetik C. A comparison ofintraoperative ultrasound versus

duct during laparoscopiccholecystectomy. Surg Endosc.1995;9: 490-96.

11. Cuschieri A, Shimi S, Banting S, Nathanson LK, PietrabissaA.Intraoperative cholangiography during laparoscopiccholecystectomy. Routine vs selective policy. Surg Endosc.1994;8: 302-05.
12. Kullman E, Borch K, Lindstrom E, Svanvik J, AnderbergB.Value of routine intraoperative cholangiography in detectingaberrant bile ducts and bile duct injuries during laparoscopiccholecystectomy. Br J Surg. 1996;83: 171-75.
13. Al-Kubati, W.R. Bile Duct Injuries Following Laparoscopic Cholecystectomy: A Clinical Study. Saudi Journal of Gastroenterology: Official Journal of the Saudi Gastroenterology Association. 2010;16: 100-104.
14. Buddingh,K.T., Nieuwenhuijs, V.B. , van Buuren,L., Hulscher, J.B. , de Jong, J.S. and van Dam, G.M. Intra-operative Assessment of Biliary Anatomy for Prevention of Bile Duct Injury: A Review of Current and Future Patient Safety Interventions. Surgical Endoscopy. 2011; 25(8): 2449-2461.
15. Vecchio R, MacFadyen BV, Latteri S. Laparoscopic cholecystectomy: an analysis of 114,005 cases of United States series. Int Surg. 1998;83: 215–9.
16. Merrie AE, Booth MW, Shah A, Pettigrew RA, McCall JL. Bile duct imaging and injury. A regional audit of laparoscopic cholecystectomy. Aust NZ J Surg. 1997;67: 706–11.
17. McMahon AJ, Fullarton G, Baxter JN, O'Dwyer PJ. Bile duct injury and bile leakage in laparoscopic cholecystectomy. Br J Surg. 1995;82: 307–13.
18. McMahon AJ, Fullarton G, Baxter JN, O'Dwyer PJ. Bile ductinjury and bile leakage in laparoscopic cholecystectomy. Br JSurg1995;82: 307-13.
19. Meyers WC, Club TS. A prospective analysis of 1518 laparos-copic cholecystectomies. N Engl J Med 1991;324: 1073-78.
20. Morgenstern L, McGrath MF, Carroll BJ, Paz-Partlow M, BerciG.Continuing hazards of the learning curve in laparoscopiccholecystectomy. Am Surg.1995;61: 914-18.
21. Strasberg SM, Hertl M, Soper NJ. An analysis of the problemof biliary injury during laparoscopic cholecystectomy. JACS.1995;180: 101-25.
22. Carroll BJ, Birth M, Phillips EH. Common bile duct injuriesduring laparoscopic cholecystectomy that result in litigation. 1998;12(4): 310-3
23. Hunter JG. Avoidance of bile duct injury during laparoscopiccholecystectomy. Am J Surg.1991;162: 71-76.
24. Russel JC, Walsh SJ, Mattie AS, Lynch JT. Bile duct injuries, 1989-1993: a statewide experience. Arch Surg. 1996; 131: 382-8.
25. Wilson RG, Macintyre I MC, Nixon SJ, Saunders JH. Laparoscopic cholecystectomy as a safe effective treatment for severe acute cholecystitis. BMJ.1992;305: 394-6
26. Calvete J, Sabater L, Camps B, Verdu A, Gomez-ParillaA,Martin J, Torrico MA, Flor B, Cassinello M, Lledo S. Bile ductinjury during laparoscopic cholecystectomy: Myth or reality ofthe learning curve? Surg Endosc. 2000;14: 608-11.
27. Archer SB, Brown DW, Smith CD, Branum GD, Hunter JG.Bile Duct Injury During Laparoscopic Cholecystectomy: Results of a National Survey. Ann Surg. 2001;234(4): 549-59
28. Huang, Q., Liu, C. H., Zhu, C. L., Xie, F. and Hu, S.Y. (2013) The Choice of Surgical Timing for Biliary Duct Reconstruction after Obstructive Bile Duct Injury: An Experimental Study. Hepato-Gastroenterology. 2013;60(128): 1865-1872.
29. Lau, W.Y., Lai, E.C. and Lau, S.H. (2010) Management of Bile Duct Injury after Laparoscopic Cholecystectomy: A Re-view. ANZ Journal of Surgery. 2010;80(1-2): 75-80.
30. Karvonen, J., Gronroos, J.M., Makitalo, L., Koivisto, M. andSalminen, P. Quality of Life after Iatrogenic Bile Duct Injury—A Case Control Study. Minimally Invasive Therapy & Allied Technologies. 2019;22: 177-180.
31. Thompson,C. M., Saad, N.E., Quazi, R. R. , Darcy, M.D., Picus, D.D. andMenias, C. O. Management of Iatrogenic Bile Duct Injuries: Role of the Interventional Radiologist. Radiographics. 2013;33: 117-134.
32. Xu, X.D., Zhang, Y.C. , Gao, P., Bahrani-Mougeot, F., Zhang, L.Y., He, Z.Y. et al.Treatment of Major Laparoscopic Bile Duct Injury: A Long-Term Follow-Up Result. The American Surgeon. 2011;77: 1584-1588.

33. Lovecek, M., Havlik,R. , Klein, J., Maly, T., Kocher, M., Cerna, M., et al. (2010) Iatrogenic Bile Ducts Injuries. Rozhl Chir. 2010;89(3): 183-7

34. Macedo, F.I., Casillas, V.J., Davis, J.S., Levi, J.U. and Sleeman, D.Biliary-Colonic Fistula Caused by Cholecystectomy Bile Duct Injury. Hepatobiliary & Pancreatic Diseases International. 2013;12: 443-445.

35. Lubikowski, J., Post, M., Bialek, A., Kordowski, J., Milkiewicz, P. andWojcicki, M. (2011) Surgical Management and Outcome of Bile Duct Injuries Following Cholecystectomy: A Single-Center Experience. Langenbeck's Archives of Surgery. 2011;396(5): 699-707.

36. Harrison, V.L., Dolan, J.P., Pham, T.H., Diggs, B. S., Greenstein, A.J., Sheppard, B. C. , et al. Bile Duct Injury after Laparoscopic Cholecystectomy in Hospitals with and without Surgical Residency Programs: Is There a Difference? Surgical Endoscopy. 2011;25(6): 1969-1974.

37. Pesce,A., Portale, T.R. , Minutolo, V., Scilletta, R. , Li Destri, G. andPuleo, S. Bile Duct Injury during Laparoscopic Cholecystectomy without Intraoperative Cholangiography: A Retrospective Study on 1,100 Selected Patients. Digestive Surgery. 2012;29(4): 310-314.

Ethical and Social Issues of Using CRISPR/Cas 9

Paroma Arefin[1], Jebunnahar Juthi[2], Sabrina Islam[3], Aishwaryia Arefin[4], Md. Saidul Arefin[5]

Abstract

The utilization and subsequent evolution of CRISPR/Cas 9 in the generation of the defined genetic alteration in the cell to produce the desired traits have tremendous potential applications in the clinical and biomedical researches. This review examines various biomedical, legal, and ethical issues related to CRISPR/Cas9 technology for its widespread utilization. Besides it focuses on the ethical and technical limitation of technology in gene editing, off-target editing, and incomplete editing. Another most important concerns are the germline gene editing, i.e., generating the inheritable changes which may be transmitted to the following generations due to the potential of CRISPR/Cas9 to generate unpredictable mutations.

Keywords: CRISPR/Cas 9, ethical and social issues, germline inheritance,

J Ar M Coll Cu. 2019, July; 2 (2): 49-54
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

The CRISPR (Clustered regularly interspaced short palindromic repeats) system was first recognized in archaea as an adaptive defensive mechanism that gives resistance to foreign genetic elements. Later the CRISPR-Cas system was engineered into a versatile gene-editing tool enabling manipulation of protospacer adjacent motif (PAM) downstream DNA. CRISPR-Cas Systems are recognized acquired immunity systems. [1,2]

CRISPR was discovered in the Escherichia coli genome in 1987 when Japanese scientists discovered a series of repeated fragments of 29 nucleotides (nt) in length interspaced with variable sequence fragments of 32 nt non-repetitive sequences . Research in the CRISPR system and its associated Cas genes evolved similar short-repeat palindromic sequences of 24-40 nt in several groups of bacteria and archaea. The repeat sequences are separated by unique variable sequences of 20-58 nt.

Interspaced bacterial clustered short palindromic repeats (CRISPR)–CRISPR-associated (Cas) systems use dual RNA-guided DNA endonuclease Cas9 to protect against invasive phages and conjugative plasmids by inserting site-specific double-stranded breaks in target DNA. Target recognition requires the presence of a short adjacent protospacer motif (PAM) flanking the target site, and subsequent R-loop formation and strand scission are driven by complementary base pairing between the RNA guide and target DNA, Cas9–DNA interactions, and related conformational changes. [3] The use of CRISPR–Cas9 as an RNA-programmable DNA targeting and editing tool is improved by a synthetic single-guide RNA (sgRNA) imitation of the natural dual CRISPR RNA (tracrRNA)–CRISPR RNA (crRNA) structure. This review is intended to provide an in-depth mechanistic and structural understanding of the targeting and cleavage of Cas9-mediated RNA-guided DNA. [4]

CRISPR Applications [5,6,7]

Due to its robustness and flexibility, CRISPR applications are becoming more and more widespread. CRISPR has been a versatile tool with applications that are transforming not only gene editing studies, but also many other genome and chromatin manipulation efforts. These application areas are largely because of the programmable targeting capacity of catalytically inactive dead Cas9 (dCas9), which cannot cleave DNA but can still be guided to the target sequence. While native Cas9 enables gene editing through its guidable DNA cleavage activity, catalytically impaired Cas9 enzymes have been repurposed to achieve targeted gene regulation, epigenome editing, chromatin imaging, and chromatin topology manipulations. Furthermore, the catalytically impaired nickase Cas9 enzyme has been used as a platform for base editing without double strand breaks (DSBs). Gene editing has already broadened our ability to investigate the

Received January 2020 Accepted March 2020

contribution of specific genes and mutations to disease by facilitating the creation of the accurate cellular and animal models. For the past few years, gene therapy applications have also been demonstrated, e.g. by repairing the cftr gene in cultured cells from human cystic fibrosis patients, by curing dominant cataract disorder and Duchenne muscular dystrophy by altering DNA in mouse germ-line cells, and by curing hereditary tyrosinemia in adult mice. Another important milestone was the first primate with precise genetic modifications, a result of gene editing in embryos. The finding allows for development of disease models in animals very similar to humans. A similar approach could be used to alter DNA in human embryos to prevent non-complex hereditary diseases, but also to attempt alteration of complex traits, which has triggered extensive ethical discussion. CRISPR is becoming an indispensable tool in biological research. The CRISPR-based technologies will undoubtedly continue to transform basic as well as clinical and biotechnological research. However, the road ahead is not free of obstacles. Many more in-depth studies are needed to be done in the future.

Application in human germline[14,15]

Mutation is the backbone of the evolutionary process and the development of a technology that introduces new mutations while repairing others could have a profound effect on the direction of the natural history of man. Gene editing can help or destroy the development of humans. Most of the ethical discussions about human germline editing related to the genome editing center. This is because it will pass on changes made in the germline for future generations. The debate on genome editing is not recent, but after the discovery that CRISPR has the potential to make such editing more accurate and easier Till now, all therapeutic interventions in humans using gene editing have been performed in somatic cells, but the experiment conducted by Chinese researchers Liang and collaborators has created concern about the potential for changes in human germline. Therapeutic genome editing interventions in somatic cells are generally accepted in ethical terms, taking into account the balance between risks and benefits and the use of informed consent. But germline cells are not the same, since the technique of CRISPR-Cas9 can produce mutations and side effects, it is possible to transmit unpredictable changes to future generations. Scientists have accepted that gene editing should be allowed for research purposes in both somatic and embryonic cells, but with ethical concerns and the concerns around safety, gene engineering for therapeutic uses should be restricted to somatic cells.

Advantages of CRISPR-Cas9 system [7,8,9]

The system CRISPR-Cas9 includes the RNA-guided nuclease Cas9, which binds to specific DNA sequences (complementing the RNA-guide sequence) and creates double-stranded breaks (DSB) on the DNA. Use homology-directed repair (HDR) or non homologous end-joining (NHEJ), the ds DNA breaks can be repaired. Based on this principle, the Cas9 and the guide-RNA have been modified in various ways to improve this system's efficiency and specificity, expanding its potential for various applications. This mechanism can be used by insertions, deletions, point mutations, and sequence inversions to change specific genetic loci. The process has recently been changed to serve as a regulator of the genome, by tethering effect or domains to the Cas9 or guide-RNA, and as a visualization tool by fusing with marker molecules. This multiplex capacity of engineering CRISPR-Cas9 enabled scientists to relate this system for genome modifications in a variety of organisms. The CRISPR-Cas9 system comprises a robust technology that has been used in diverse and innovative applications in biology. It has incomparable advantages over other gene editing tools. For example, the CRISPR-Cas9 system has more target sites than ZFNs and TALENs, and Cas9 has many variants that can be used in a variety of studies. Moreover, the system is extremely easy to use and can be executed in almost any laboratory. Cas9-based tools have greatly enhanced our ability to perform systematic analyses of gene function, as well as to reproduce tumor-associated chromosomal translocations precisely. This technology has also paved the way for the dissection of redundant gene functions, epigenetics and possible gene therapy.CRISPR-Cas9 technology is currently the simplest, most accurate and versatile genome editing method in a variety of in vitro and in vivo cells and organisms.

Disadvantages of CRISPR-Cas9 system [8,9,10,11]

The CRISPR-Cas9 system has already shown itself to comprise a robust and flexible tool for genome editing and gene regulation. With further research on CRISPR, however, it became apparent that this technology was not as easy as once assumed. Despite the many advantages of this system, there are some challenges to the current Cas9-based tools. A large number of studies have investigated diverse aspects that affect the efficiency and specificity of CRISPR-Cas9 system, such as Cas9 activity, target site selection and

sgRNA design, delivery methods, off-target effects, and the incidence of homology-directed repair (HDR). Many of the breakthroughs in genome engineering have been seen as enormous scientific triumphs, but the translation of these technologies from bench to bedside is not without vigorous debate on ethical, legal and social issues. One potential drawback of CRISPR-Cas9 technology is that it can produce off-target results. These off-target effects can contribute to the identification and destruction of hypervariable viral nucleic acids or plasmid DNA, which is beneficial for bacteria and archaea. Off-target phenomena, however, generate unwanted mutations at random sites for biological studies and genetic therapies, thus affecting precise gene modification. We need to be careful about the potential effects of off-target effects, lack of targeting specificity, incomplete targeting, and so on, all of which could have devastating effects on patients. Scientists will seek improved nucleases to improve safety and efficacy. The enhanced nucleases minimize off-target effects, which would enhance target gene editing efficacy and mitigate unintended consequences. Improved precision will also improve our ability to identify the system and track effectiveness and security, including over several generations. Another contentious issue is ethical concerns about germline gene editing. There are many questions about heritable modifications if any of the modified embryos are used in reproduction. There are concerns about the risk of mistakes and (unintended) consequences, not just for the resulting child(ren) but also for humanity. There are questions about the likelihood of exacerbating discrimination, sexism, health disparities, and so on in the latter sense as a direct consequence of who will and who will not have access to the technology. A greater barrier to the development of dystopian futures with "designer babies" and style Gattaca: the concepts of evolution. Editing genes could ruin human evolution. While some obstacles remain, the application of this technology to various aspects of sarcoma biology, ranging from basic research to clinical and translational applications, provides many exciting opportunities for better and better care.

CRISPR-Cas9 Ethics [8,9,12]

Scientists have long sought to use cellular repair procedures to intercede and alter life forms DNA by controlled genome editing; to change the genome of the organism by introducing another capability or by correcting a mutation. Due to its high degree of precision, relatively simple design and ease, CRISPR-Cas9 has been selected as the preferred technique for altering the genome in recent years. These qualities make this procedure appealing to scientists to use, but the problem is that, unless regulated, it can be used for any purpose. The utilization of CRISPR-cas9 innovation restores numerous social and moral issues with people, different life forms and the earth, for example, considering the non-maleficence principle in hazard analysis, gene editing in germline, safety issues to stay away from environmental hindrance or the utilization for hereditary improvement. The moral difficulties of CRISPR-Cas9 to a great extent reiterate those of hereditary designing and its clinical applications, and those of quality treatment. Sound science is the primary moral necessity for scientific research. CRISPR-Cas9 has enormous scope of uses and colossal potential outcomes for life transformation, which will take a very long time to consummate. The right utilization of this innovation requires cautious planning and tight control.

Ethical Issues in CRISPR-Cas9 Applications [8,9,10,11,12,13]

Ethical consideration of biotechnological advancements ought to be directed under the presupposition that morals and sciences can and should cooperate to benefit people, for the prosperity of social orders, and for the assurance of all types of life and environments. Morals isn't a boundary to science and ought not restrain logical advancement. Then again, the sciences are not finishes in themselves and are not self-ruling undertakings, standing separated from the consensual destinations of social orders. Despite what might be expected, while the sciences should keep on creating, find and execute the best means for seeking after the objectives of society, morals should work at the cultural level, setting up the best outcomes for a reasonable and equivalent society.

Balance of risks and benefits: In the ethical evaluation of new biotechnologies, the impact on human health is a major concern. A major ethical problem in research at this point is that benefits must be greater than risks. There must be greater attention to risks, as they can endanger living beings or the environment. The implementation of the CRISPR-Cas9 technique entails risks as it may result in off-target mutations that may occur.

Ecological Imbalance: When dealing with biotechnologies that interact with biological entities, the effect on biodiversity and habitats must be addressed. At this point, ethical analysis needs consideration as important in itself for all forms of life. In experiments using RNA-guided gene

drives based on the CRISPR-Cas9 method, it is necessary to testthe specificity considering off target effects. Because gene drive is still operating in created beings, the possibility of off-target mutations continues and each generation may increase. If there is a risk that genes will be transferred to other species, there is a risk that modified sequences will be transferred. Many scientists have cautioned that experimental species engineered using gene drives are at risk of accidental release in the environment. Safety measures are needed to prevent the spread of organisms that can cause ecological damage or affect human health.

Genome editing for enhancement:

Another ethical issue to be addressed is the potential use of genome editing in non-therapeutic interventions. For safety reasons, its use in germ line is prohibited. Nevertheless, the efficacy of the CRISPR-Cas9 technique increases the possibility of interacting with somatic cells to match biology to our interests in life. Apart from the climate, most phenotypical traits have a genetic component that could be interfered with. For example, the technique could be used to improve athletes ' performance or to prevent or diminish addiction to violent behaviour. Generally speaking, gene therapy seeks to improve a patient's health for his own benefit, but in the future it may happen that the criminal justice system is mandated

CRISPR Cas-9 genome editing in religious perspective[14]

Certainly, religion's ' ultimate goal of "protecting human life" by either mitigating hardship or recognizing public interests is to reckon with biomedical innovations that are permissible wherever they cling to ethical, moral and legal principles. If –CRISPRCas-9 genome editing–methods based on the guiding principles of Islamic law and jurisprudence, as "harm must be rectified" can be justified in view of human dignity, honor and prestige. New technologies can therefore be implemented because, with certain exceptions, "necessity makes things forbidden as permissible." Those who see it as bad must think about it, "in the midst of two evils, the one whose damage is grievous “in the presence of two evils, the one whose injury is greater is avoided by the commission of the lesser”. Thus, if the Cas-9-based approach leans to evils, even then it may be appropriate if an atypical germ line sequence will influence the next generation, which is indeed a great evil, and "the lesser evil is favored over the greater evil" makes it reasonable with a view to enhancing human health and living standards. Conversely, curing a minor disease should be prohibited if causing another equal or greater infirmity as "harm can not be removed by harm," then "a greater harm can be removed by a lesser" germ-line editing / alteration will be permitted in severe cases on the basis of necessity.

Social perspective in CRISPR-Cas9 Applications [15,16,17,18]

CRISPR excites scientists and clinicians as it opens up new research and innovation possibilities, but they are also concerned that a public backlash against germline genome editing could threaten both somatic (i.e., non-reproductive) genome editing and embryo research in general. This concern of a public reaction influences the field; even those who champion GGE for human enhancement are required to limit the scope of their research to what is within their so-called social license to operate. We can assume the uneasiness as the inevitable outcome of an approach to the deficit which portrays sound research as battling an ignorant public. One reason this practice continues is that it favors scientific expertise and scientific worldview as the starting point for having any valid say in these discussions. It helps those with technical expertise to stay on familiar, quantifiable ground where research is a value-free account based solely on reason and evidence, and to avoid questions that are not quantifiable and beyond their limited expertise. This dualistic stance actively favours the silo approach, where scientific research is permitted to continue unimpeded with the justification of amassing the data needed to satisfy objective regulatory criteria for safety and efficacy, while non-technical societal concerns are dealt with separately as subjective matters that can not be adjudicated by evidence. Within this context, potential harms can only be considered as issues of safety and efficacy, while contextual factors such as facilitating markets, distribution of benefits and risks, and complexities of global governance are bracketed out. The deficit model prefers expert interpretations of the issue and what is at stake over those of lay publics who have to live with the consequences nonetheless. Separating' ethical' and' technical' aspects prevents meaningful discussion of the social contexts where technology is developed and made available. The interests of states and technology developers therefore take precedence over those of the people and communities affected by the implementation of new technologies in ways that lack democratic legitimacy and can inhibit socially responsible innovation. It isn't appropriate for public approval to be estimated by take-up through the

market. Numerous innovations cause little damage when just a few accept them and have various impacts once they become ubiquitous. It is a moral obligation to edit all of our embryos to make the "most ideal infants. As long as the goal of reaching public consensus remains a priority for many policy makers and scientific authorities, they need to engage robustly with what is meant by ' consensus ' and how we know it has been achieved.

CRISPR-Cas9 Ethical Future Concerns [18]

CRISPR technology appears to have the scope and potential to enhance earth life, but some of the ethical concerns are highly sensitive. When a technology such as genome editing tool is regarded for human genetic variability, it is more restricted to somatic cells and highly denied for its application to make gene alters in a sperm cell or an egg or embryo. Since this can pass the modifications and improvements to the next generation, the surface concerns what this means for the powers and forms of evolutionary life. The use of this technology with germ-line cell and embryo raises various ethical problems including the permissibility to use it to improve normal human characteristics. Looking at these ethical concerns related to the germ line and embryo, in many states the technology has already been governed or shut down.

Authors affiliation

1. *Paroma Arefin , Scientific Officer, Bangladesh Council for Scientific and Industrial Research
2. Dr Jebunnahar Juthi, Lecturer, Department of Biochemistry, Army Medical College , Cumilla
3. Dr Sabrina Islam, Lecturer, Department of Biochemistry, Army Medical College , Cumilla
4. Aishwaryia Arefin, M.Phil, Institute of Nutrition and Food Science , University of Dhaka
5. Md Saidul Arefin, Professor, Institute of Nutrition and Food Science, University of Dhaka

*For correspondence

References:

1. Rodriguez-Rodriguez D, Ramirez-Solis R, Garza-Elizondo M, Garza-Rodriguez M, Barrera- Saldana H. Genome editing: A perspective on the application of CRISPR/Cas9 to study human diseases (Review). International Journal of Molecular Medicine [Internet]. Spandidos Publications; 2019 Feb 26; Available from: http://dx.doi.org/10.3892/ijmm.2019.4112
4. Biagioni A, Chillà A, Andreucci E, Laurenzana A, Margheri F, Peppicelli S, et al. Type II CRISPR/Cas9 approach in the oncological therapy. Journal of Experimental & Clinical Cancer Research [Internet]. Springer Science and Business Media LLC; 2017 Jun 15;36(1). Available from: http://dx.doi.org/10.1186/s13046-017-0550-0
5. Bolotin A, Quinquis B, Sorokin A, Ehrlich SD. Clustered regularly interspaced short palindrome repeats (CRISPRs) have spacers of extrachromosomal origin. Microbiology [Internet]. Microbiology Society; 2005 Aug 1;151(8):2551–61. Available from: http://dx.doi.org/10.1099/mic.0.28048-0
6. Cong L, Ran FA, Cox D, Lin S, Barretto R, Habib N, et al. Multiplex Genome Engineering Using CRISPR/Cas Systems. Science [Internet]. American Association for the Advancement of Science (AAAS); 2013 Jan 3;339(6121):819–23. Available from:http://dx.doi.org/10.1126/science.1231143
7. Laxminarayan R, Sridhar D, Blaser M, Wang M, Woolhouse M. Achieving global targets for antimicrobial resistance. Science [Internet]. American Association for the Advancement of Science (AAAS); 2016 Aug 18;353(6302):874–5. Available from: http://dx.doi.org/10.1126/science.aaf9286
8. https://www.sinobiological.com
9. Mulvihill JJ, Capps B, Joly Y, Lysaght T, Zwart HAE, Chadwick R. Ethical issues of CRISPR technology and gene editing through the lens of solidarity. British Medical Bulletin [Internet]. Oxford University Press (OUP); 2017 Feb 23;122(1):17–29. Available from: http://dx.doi.org/10.1093/bmb/ldx002
10. Mojica FJM, Diez-Villasenor C, Garcia-Martinez J, Soria E. Intervening Sequences of Regularly Spaced Prokaryotic Repeats Derive from Foreign Genetic Elements. Journal of Molecular Evolution [Internet]. Springer Science and Business Media LLC; 2005 Feb;60(2):174–82. Available from: http://dx.doi.org/10.1007/s00239-004-0046-3
11. Patrão Neves M, Druml C. Ethical implications of fighting malaria with CRISPR/Cas9. BMJ Global Health [Internet]. BMJ; 2017 Aug;2(3):e000396. Available from: http://dx.doi.org/10.1136/bmjgh-2017-

12. Pourcel C, Salvignol G, Vergnaud G. CRISPR elements in Yersinia pestis acquire new repeats by preferential uptake of bacteriophage DNA, and provide additional tools for evolutionary studies. Microbiology [Internet]. Microbiology Society; 2005 Mar 1;151(3):653–63. Available from: http://dx.doi.org/10.1099/mic.0.27437-0

13. E R. Ethical Issues in Genome Editing using Crispr/Cas9 System. Journal of Clinical Research & Bioethics [Internet]. OMICS Publishing Group; 2016;07(02). Available from: http://dx.doi.org/10.4172/2155-9627.1000266

14. Nicholson SA, Pepper MS. CRISPR-Cas: Revolutionising genome engineering. South African Medical Journal [Internet]. South African MedicalAssociation NPC; 2016 Aug 1;106(9):870. Available from: http://dx.doi.org/10.7196/SAMJ.2016.v.106i9.11061

15. Dayan F. CRISPR Cas-9 genome editing and Islam: A religious perspective. Bangladesh Journal of Medical Science [Internet]. Bangladesh Journals Online (JOL); 2018 Dec 30;18(1):7–13. Available from: http://dx.doi.org/10.3329/bjms.v18i1.39540

16. Greely HT. CRISPR'd babies: human germline genome editing in the “He Jiankui affair”*. Journal of Law and the Biosciences [Internet]. Oxford University Press (OUP); 2019 Aug 13;6(1):111–83. Available from: http://dx.doi.org/10.1093/jlb/lsz010

17. Savulescu J, Pugh J, Douglas T, Gyngell C. The moral imperative to continue gene editing research on human embryos. Protein & Cell [Internet]. Springer Science and Business Media LLC; 2015 Jun 26;6(7):476–9. Available from: http://dx.doi.org/10.1007/s13238-015-0184-y

18. Iaccarino M. Science and ethics. EMBO reports [Internet]. EMBO; 2001 Sep;2(9):747–50. Available from: http://dx.doi.org/10.1093/embo-reports/kve191

Foreign Body Nose: A Common Problem in Children

Anwar ul Alam[1], Mohammad Shakil[2]

Abstract

We present the case of a 6 year old girl with nasal blockage and recurrent epistaxis. Anterior rhinoscopy showed a polypoidal mass which bled on touching. It was confirmed by non contrast computed tomography (NCCT) and extracted through the nasal route. Later it was found to be a tooth surrounded by a necrotic material.

Keywords: Foreign body, Nose

J Ar M Coll Cu. 2019, July; 2 (2): 55-57
For Authors Affiliation, see end of text.
https://www.amccomilla.edu.bd/jamcu

Introduction

Nasal foreign bodies are frequently encountered, especially in children. The circumstances are usually accidental, with a foreign body trapped or incarcerated in one or both nasal cavities by the anterior (vestibular) or more rarely posterior (choanal) route. Positive diagnosis is often easy, but may be delayed by the context, type of foreign body or nonspecificity of the symptomatology. Early diagnosis can avoid potentially serious complications related to the nature of the foreign body itself or to chronicization of the resultant irritation, with a real risk of superinfection[1]. Nature of the FB varies among different age group, in children common FB include things with which they used to play like bead, toy parts, coin etc, while in adults common FB are food materials like fish bone, meat bone, or artificial denture etc. As majority of the cases have FBs in nose and external ear canal which is quite easily accessible, most of the time it can be removed in emergency department by simple manoeuvre and do not require any assistance from anaesthesia department[2]. Consequences of FB injuries vary from low impact disturbances with or without hospitalization to death. The variability is related to many factors, such as the chemical composition, shape and dimensions of the FBs, and the anatomical site involved[3]. The nose consists of two nasal fossa separated by a vertical septum and subdivided into three passages by the nasal turbinates. Nasal foreign bodies tend to be located on the floor of the nasal passage, just below the inferior turbinate, or in the upper nasal fossa anterior to the middle turbinate. Most nasal foreign bodies can be easily removed in the office or emergency department. Patients often present with unilateral, foul-smelling nasal discharge[4].

Received October 2019 Accepted January 2020

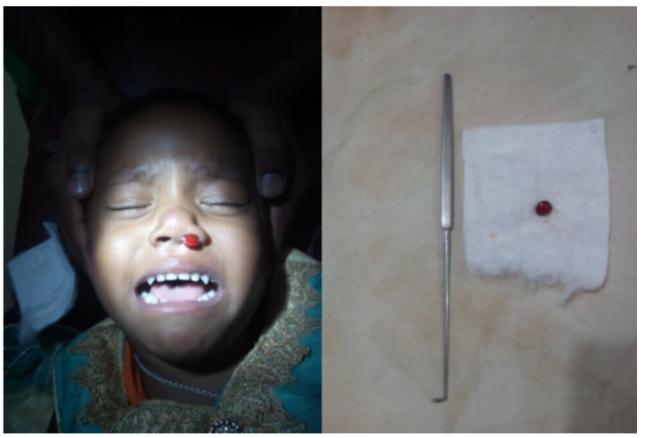


Fig: Image showing foreign body in nasal orifice and after removal

Case description

A 6 years old girl presented to the Otorhinolaryngology outdoor of Eastern Medical College & Hospital, Cumilla, on 11th March 2019, with complain of foul smell from right nasal cavity. There was no active bleeding at presentation. He also complained of right sided nasal obstruction since last 2 months & associated with foul smelling discharge. Clinical examination was done in ENT OPD, Ant. Rhinoscopy showed a radish object in anterior vassal cavity & there was foul discharge. An object was removed using foreign body hook under local anesthesia with 10% cocaine solution. It

hook under local anesthesia with 10% cocaine solution. It was lying along the floor of the nose wedged between the nasal septum & revealed a straight septum & inferior turbinate. Inspection revealed a straight septum with no damage to the inferior turbinate. Minor bleeding was controlled with ant. nasal peaking, which was removed after 24 hours. The patient received a 7 days course of oral penicillin.

Discussion

A review of the literature shows that intra-nasal foreign bodies have been frequently reported especially among children. Among adults, however, they occur very rarely and are caused mostly by injury in an accident, trauma or coexisting mental disorders. In a large study of 420 cases of foreign bodies in the nasal cavity only one adult case, a homeless man with nasal myiasis was described. Unusual foreign bodies including buttons have been described very rarely in adults[5]. The majority of cases of intra-nasal foreign bodies are asymptomatic, except for a history of a foreign body having been inserted in the nose. Common symptoms, if present, include pain or discomfort, nasal discharge, nasal congestion or nasal odor. A unilateral mucopurulent nasal discharge with foul odor is the most consistent finding in patients with a nasal foreign body. Rare symptoms have been reported, including bromidrosis (foul body odor) and infections, such as facial cellulites, epiglottitis, and cephalic tetanus. Differential diagnoses of a unilateral nasal obstruction include nasal polyp, nasal tumor, nasal abscess, septal hematoma, or unilateral choanal atresia[6]. Most nasal foreign bodies can be removed in the clinic. Initially, the patient should be asked to blow their nose; this may need to be demonstrated to young children. It is also possible to generate upper airway positive pressure with the 'mother's kiss' technique. Here, a parent places their lips over that of the child forming an airtight seal and blows hard covering the unobstructed nostril with a finger. In children it can be helpful sit them on a parent's knee swaddled in a blanket or tightly cuddled before attempting manual removal. It may be helpful initially to spray the nose with co-phenylcaine to reduce mucosal oedema. Under direct vision with good illumination most foreign bodies can be removed with a wax hook or Jobson Horne probe. The instrument should be rotated around the foreign body which can be then raked anteriorly. Forceps can be used to grasp items such as paper. In some cases a general anaesthetic will be required to remove the foreign body[7]. After successful removal of an NFB, careful examination of the involved nasal cavity as well as the other body orifices must be undertaken to exclude the presence of other unrecognized foreign bodies. Particular attention must be paid to the examination of the ear and sinuses on the involved side, as acute otitis media or sinusitis are commonly seen if the foreign body has been present for any length of time. Additionally, epistaxis, which frequently accompanies the removal of NFBs, must be appropriately dealt with. Several important complications have been associated with the presence of an NFB. These include formation and development of rhinoliths, erosion into a contiguous structure, and producing infections in surrounding structures. Apart from acute sinusitis or otitis media, other infections reported include periorbital cellulitis, meningitis, acute epiglottitis, diphtheria, and tetanus[8]. The nasal foreign bodies may be classified into organic and inorganic. The plastic and metal are typically encountered as inorganic foreign bodies .The organic foreign bodies usually produces earlier symptoms as they are more irritating to the nasal mucosa . The common examples of plastic and metal foreign bodies include part of toys, paper, button, beads and stones. The examples of organic foreign bodies are food, rubber, wood, sponge and evenmetallic Chinese batteries of toys. The mentally retarded patient accidentally or deliberately introduce foreign bodies in the nose as they may have childish behaviors of often the children less than five[9].It is difficult to diagnose a nasopharyngeal foreign body, more so in children. Technique of foreign body removal has improved enormously. They can be removed with the help of speculum and forceps. Endoscopic removal or removal through oral cavity can also be done. Complications may arise due to the foreign body or with the procedure. It can cause bleeding, pulmonary complications, retropharyngeal abscess and localized infection. Complication rates of 12.6% in adults and 4.6% in children has been reported by Singh B et al., and in their study, pulmonary complications was most common in children and retropharyngeal abscess in adults, which was mostly due to sharp objects[10].

Authors affiliation

1. *Dr. Anwar ul Alam, Assistant Professor, Department of ENT, Eastern Medical College & Hospital, Cumilla
2. Dr. Mohammad Shakil, Associate Professor, Dept of Community Medicine, Army Medical College, Cumilla.

*For Correspondence

References

1. Abou-Elfadl M, Horra A, Abada RL, Mahtar M, Roubal M, Kadiri F. Nasal foreign bodies: Results of a study of 260 cases. European Annals of Otorhinolaryngology. Head and Neck diseases. 2015; 132 (4) 343–346
2. BrianShunyu N, Akhtar H, Karim HR, Lyngdoh NM, Yunus, Jamil. Ear, Nose and Throat Foreign Bodies Removed under General Anaesthesia: A Retrospective Study. Journal of Clinical and Diagnostic Research. 2017:11(2): 1-4
3. Awad AH, Mostafa E, Taher. ENT Foreign Bodies: An Experience. Int Arch Otorhinolaryngol. 2018;22: 146–151.
4. Heim SW, Maughan KL. Foreign Bodies in the Ear, Nose, and Throat. American Family Physician. 2007;76(8): 1185- 1189
5. Ahmed K, Taous A. An Unusual Foreign Body Nose. Bangladesh J Otorhinolaryngol. 2014; 20(2): 102-105
6. Kelesidis T, Osman S, Dinerman H. An unusual foreign body as cause of chronic sinusitis: a case report. Journal of Medical Case Reports. 2010;4: 157
7. Kullar P, Yates PD. Infections and foreign bodies in ENT. Surgery. 2012;30(11): 590–596.
8. Pavan M. Patil, Anand R. Nasal Foreign Bodies: A Review of Management Strategies and a Clinical Scenario Presentation. Cranio- maxillofacial trauma & reconstruction. 2011;4(1): 53-57
9. Shit S, Sarkar A, Sherpa TD, Ray R, Mukherjee M, Dutta M. Unusual Foreign Body in Nasal Cavity: A Case Report. State journal of tolaryngology. https://pdfs.semanticscholar.org/d8ed/3fffe95079fed5d8badefb029d55196722ac.pdf
10. Mudunuri RKR, Gannavarapu DP, Mukkamala ANM, Jameel K M. Unusual Foreign Body in Nose and Nasopharynx - A Rare Case. Journal of Clinical and Diagnostic Research. 2015;9(4): 1-2

INSTRUCTION TO AUTHORS

The Journal of Army Medical College Cumilla (JAMCCu) is a peer reviewed journal will be published biannually in January and July by Army Medical College Cumilla, Cumilla Cantonment. Manuscript should be prepared in accordance with the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals* recommended by the International Committee of Medical Journal Editors (ICMJE).

Conditions for submission of manuscript

- All manuscripts are subject to peer review.
- Manuscripts are received with the explicit understanding that they are not under simultaneous consideration by any other publication.
- Submission of a manuscript for publication implies the transfer of the copyright from the author to the publisher upon acceptance. Accepted manuscripts become the permanent property of the JAMCCu and may not be reproduced by any means in whole or in part without the written consent of the publisher.
- It is the authors responsibility to obtain permission to reproduce illustrations, tables etc. from other publications.
- The journal publishes the identity of authors including email addresses of authors.

Ethical aspects

- Ethical aspect of the study will be very carefully considered at the time of assessment of the manuscript.
- Any manuscript that includes any table, illustration or photographs that have been published earlier should accompany a letter of permission for republication from the author(s) of the publication and editor/publisher of the Journal where it was published earlier.
- Permission of the patients and/or their families to reproduce photographs of the patients where identity is not disguised should be sent with the manuscript. Otherwise the identity will be blackened out.

Preparation of manuscript: Criteria

Information provided in the manuscript are important and likely to be of interest to an international readership.

Preparation

- Manuscript should be written in English and typed on one side of A4 (290 x 210cm) size white bond paper.
- Typing font shall be Arial of 12 size. Double spacing should be used throughout.
- Margin should be 5 cm for the header and 2.5 cm for the remainder
- Style should be that of modified Vancouver
- Each of the following section should begin on separate page:
  a. Title page
  b. Summary/abstract
  c. Text
  d. Acknowledgement
  e. References
  f. Tables and legends

- Pages should be numbered consecutively at the upper right-hand corner of each page beginning with the title page.

Title Page

The title page should contain:

- Title of the article (should be concise, informative and self-explanatory)
- Name of each author with highest academic degree

- Institutional affiliation of each author
- Name of the department and institute where the work was carried out
- Name and address of the author to whom correspondence regarding manuscript to be made and email address

Abstract

- All articles must have a structured abstract.
- It should not exceed 200 words and should state the purpose, basic procedures, main findings and principal conclusions of the study.

Text

The text should be divided into sections with the following headings: Introduction, Materials and Methods, Results, and Discussion.

Introduction: The purpose(s) of the study should be clearly stated. Summarize the rationale for the study or observation. Give strictly pertinent references only, and do not review the subject extensively. Do not include data or conclusions from the work being reported.

Materials and methods:

It should include the place of the study, period, the subjects (number and type), the treatment or intervention and the type of statistical analysis.

Results: Present results of your study in logical sequence in the text, tables, and illustrations. Do not repeat in the text all data in the tables or illustrations, or both: emphasize or summarize only important observations.

Tables

During preparation of tables following principles should be followed:

- Tables should be simple, self-explanatory and should supplement, not duplicate the text.
- Each table should have a title and typed in double space in separate sheet.
- They should be numbered consecutively with roman numerical in order of text. Page number should be in the upper right corner.
- If abbreviations are to be used, they should be explained in footnotes.

The figures and photographs

- Should be used only where data cannot be expressed in any other form
- Should be unmounted, glossy print in sharp focus, 12.7 x 17.3 cms in size.
- Should bear number, title of manuscript, name of corresponding author and arrow indicating the top on a sticky label and affixed on the back of each illustration.

Legend

- Must be typed in a separate sheet of paper.
- Photomicrographs should indicate the magnification, internal scale and the method of staining.

Units

- All scientific units should be expressed in System International (SI) units.
- All drugs should be mentioned in their generic form. The commercial name may however be used within brackets.

Discussion: Emphasize the new and important aspects of the study and conclusions that follow from them. Highlight the important/major findings first, then highlight the less-important findings. Do not repeat in detail data or other material given in the Introduction section or the Results section. Relate the observations to other relevant studies. Link the conclusions with the

priority and alluding to work that has not been completed. State new hypotheses when warranted, but clearly label them as such. Recommendations, when appropriate, may be included.

References

The Vancouver system of reference should be used. In the text, reference should be cited using superscripted and numerical. The references should be numbered and listed in order of appearance in the text. Reference to unpublished data and personal communication should not appear in the list but should be cited in the text only (e.g Smith A, 2000, unpublished data). Use 'et al' after three authors where number of authors is more than six.

Acknowledgements

Individuals, organizations or bodies may be acknowledged in the article and may include:

- Name (or a list) of funding bodies.
- Name of the organization(s) and individual(s) with their consent.

Manuscript submission

Manuscript should be submitted to the Executive Editor and must be accompanied by a covering letter and following inclusions:

- A statement regarding the type of article being submitted.
- A statement that the work has not been published or submitted for publication elsewhere.
- A statement of financial or other relationships that might lead to a conflict of interests.
- A statement that the manuscript has been read approved and signed by all authors.
- A statement of financial or other relationships that might lead to a conflict of interests.
- A letter from the head of the institution where the work has been carried out stating that the work has been carried out in that institute and there is no objection to its publication in this journal
- If the article is a whole or part of the dissertation or thesis submitted for diploma/degree, it should be mentioned in detail and in this case the name of the investigator and guide must be specifically mentioned.
- The authors have followed the official secret act.Submissions must be in triplicates with three sets of illustrations. Text must be additionally submitted in a CD.

Online submission

Online submission shall only be accepted for author submitting paper from outside of Bangladesh. Papers should be prepared following instructions mentioned and shall be submitted to address of the journal as Microsoft word attached file. The email shall include letter mentioning that the work has been carried out in an institute that has no objection to its publication in this journal and that the work has not been published or submitted for publication elsewhere.

Editing and peer review

All submitted manuscripts are subjected to scrutiny by the Editor in Chief/Executive Editor and any other member of the Editorial Board. Manuscripts containing materials without sufficient scientific value and/or a priority issue, or not fulfilling the requirement for publication may be rejected or it may be sent back to the author(s) for resubmission with necessary modifications to suit one of the submission categories. Manuscripts fulfilling the requirements and found suitable for consideration are sent for peer review by the subject editors. Submissions found suitable for publication by the reviewer, may need revision/ modifications before being finally accepted.Editorial Board finally seats together and decides upon the publishability of the reviewed and revised/modified submission. Proof of accepted manuscript may be sent to the authors and should be corrected and returned to the editorial office within one week. No addition to the manuscript at this stage will be accepted. All accepted manuscripts are edited according to the Journal's style.

Reprints for the author(s)

Three copies of each published article will be provided to the corresponding author free of cost. Additional reprints may be obtained by prior request and only on necessary payment.

Online Communication

The journal is available on line at https://www.amccomilla.edu.bd/jamcu Interested authors can contact and foreign authors can submit articles by email.

Official email address: Email: amccomilla2015@gmail.com

Example of Title Page

The title of the article :

A. Author's names and institutional affiliations:

B. The name of the department(s) and institution(s) to which the work should be attributed:

C. Disclaimers any:

D. Corresponding author:
The name:
Mailing address:
Telephone:
E-mail address:

E. The name and address of the author to whom requests for reprints should be addressed:

F. Source(s) of support in the form of grants, equipment, drugs, or all of these-
G. A running head:
H. Word counts of abstract:
I. The number of tables:
J. The number of figures:

Disclosure of Contribution of Authors

Corresponding author

As principal investigator Dr

had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design .....

Acquisition of data .....

Analysis and interpretation of data .....

Drafting of the manuscript.....

Critical revision of the manuscript for important intellectual content .....

Statistical analysis .....

Administrative, technical, or material support .....

Supervision.....

.

Covering Letter for Article Submission

Date .....

To
The Editor
Journal of Army Medical College Cumilla (JAMCCu)

Sub: **Submission of manuscript**

Dear Sir,

We are submitting our manuscript titled .....

by.....1.....

2.....3.....4 etc.
for publication in your esteemed journal. This article has not been published or submitted for publication elesewhere.

We believe that this article may be of value to health professional engaged physiology/biochemistry/ pharmacology/— We are submitting 2 copies of manuscript along with an electronic CD.

We therefore hope that you would be kind enough to consider our manuscript for publication to your journal as original/review article/ letter to editor/short communication

Thanks and best regards

1.x 2.x 3.x

Calboral-D™ Tablet

Calcium 500 mg (Coral source) & Vitamin D_3 200 IU

Coral Calcium with diverse benefits

Calboral-DX™ Tablet

Calcium 600 mg (Coral Source) & Vitamin D_3 400 IU

Who needs extra care

Rapid **absorption** within **15 minutes**

Vitamin D benefits **immune function**

Calboral-D™ & Calboral-DX™

Contains **74 Trace minerals**

Less chance of **constipation** & **IBS**

Since 1958

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH

www.squarepharma.com.bd

SQUARE

This is circulated with the prior approval of Licensing Authority (Drugs). For Medical Professionals only. TM - Trade Mark.

For type 2 diabetic patients at **High CV Risk**
including CAD, PAD, or History of MI or Stroke

Rx

Jardian®

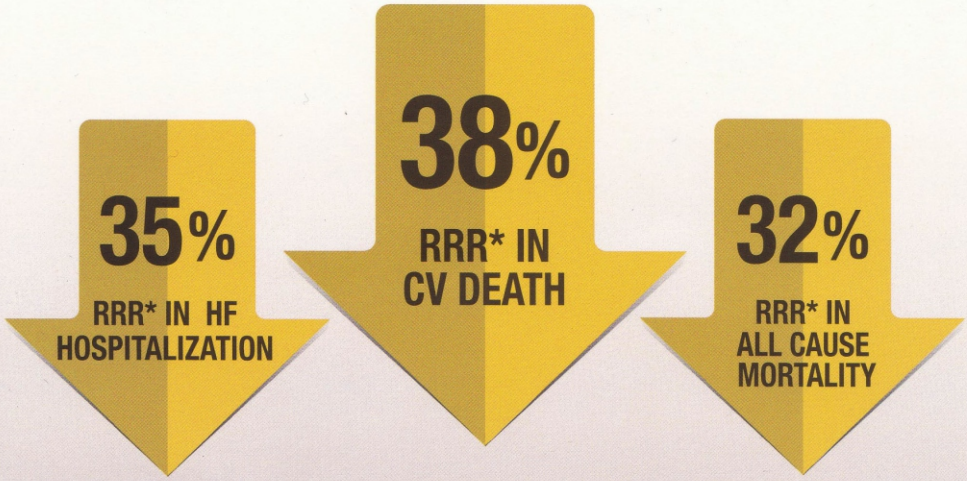
Empagliflozin 10 & 25 mg Tablets

The ONLY OAD approved by the FDA & EMA to reduce the risk of CV death in T2DM

Getting to the HEART of type 2 diabetes management

Empagliflozin (Jardian®) offers[1]

Breakthrough Cardiovascular Benefits



Breakthrough CV benefits ensure early and sustained reductions in CV death

*RRR= Relative Risk Reduction
**Prescribing information will be available upon request.

Reference:
1. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015;373(22):2117-28.

BEXIMCO PHARMA here's to Life

BEXIMCO PHARMACEUTICALS LTD.
Dhaka, Bangladesh

Approved by the U.S. FDA
also Certified by

Therapeutic Goods Administration · AGES Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH · Health Canada

For more information visit: www.beximcopharma.com

9010008391/08-20/15000 HPL

Printed at: ZAM Printing & Publications, 374/3 Haji Mainur Rahman Road, Jhawtala, Cumilla
Cell: 01711123602, E-mail: zamprinting99@gmail.com