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Address for Correspondence: Prof. Sharmeen Yasmeen, Professor & Head, Dept. of Community Medicine
Bangladesh Medical College, House # 34, Road # 14A, Dhanmondi R/A, Dhaka-1209
Phone: (88-02) 44812101-6, Fax: (88-02) 9125655
E-mail: sharmeenbmc@yahoo.com, Web: www.bmcjournal.org

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Editorial

COVID-19 & mental health- The dark shadow

Haq AI[a], Yasmeen S[a]

SARS-CoV-2, a single stranded corona virus is the pathogen responsible for the ongoing COVID-19 pandemic. Corona viruses have been responsible for several outbreaks in recent times including severe acute respiratory syndrome(SARS) and Middle East respiratory syndrome(MERS) outbreaks. The negative impact of these outbreaks on mental health have already been documented in the literature.[1-3]

The COVID-19 pandemic, due to its threatening nature and significant impact on daily life, is no exception. With effective intervention of the health care systems worldwide, well co-ordinated vaccination schedules and increased public awareness, the physical morbidity associated with COVID-19 is declining. However, experts fear that psychological morbidity associated with the pandemic may last longer compared to physical morbidity.[4]

Impact on mental health:

The effect of COVID-19 pandemic on our psyche can be described in two ways-i) Direct impact on COVID-19 patients and survivors and ii) impact effect on general population.

Neuropsychiatric complications in COVID-19 patients and survivors

Several studies have found increased prevalence of dementia, delirium, depressive and anxiety symptoms, post-traumatic stress and chronic fatigue symptoms even in mild or asymptomatic COVID-19 infection.[5,6] A retrospective cohort study on more than sixty-two thousand COVID-19 patients found that new onset dementia was 2-3 times more common in hospitalized COVID-19 patients compared to hospitalization due to other causes.[7] In older COVID-19 patients, delirium is one of the commonest and often the only primary symptom. Several studies have identified delirium in more than 30% of hospitalized patients.[8,9] Several cross sectional studies have found 31%-38% depressive symptoms, 22%-42% anxiety symptoms and 20% obsessive-compulsive symptoms in patients one month after COVID-19 infection. Mood symptoms were more common in female and were associated with severe infection and raised inflammatory markers.[10-12]

The prevalence of post-traumatic stress disorder (PTSD) among COVID-19 survivors ranged from 20%-30%. Most common risk factors associated with PTSD were young age, female sex and need for intensive care treatment.[13-16]

The neuropsychiatric symptoms in COVID-19 are thought to arise from interaction between several biological and environmental factors. Postulated biological theories include-a) Hypoxemia, b) immune response to SARS-CoV-2 may result in autoimmune reaction which may damage the blood brain barrier in the CNS, c) Hypercoagulable state in COVID-19 infection may result in organ damage, such as stroke, d) direct viral infiltration of the CNS. Psycho-social stressors like fear about the fate of the disease, stigma may also play an important role.[17-20]

Impact on general population

The staggering effect of COVID-19 pandemic on mental health of people around the world is being observed.[21] The global burden disease study 2020 estimated an increase of 27.6% in major depressive disorder (MDD) cases and 25.6% increase in anxiety disorder cases worldwide due to the pandemic. The pandemic has caused 137.1 additional disability adjusted life years per 100000 populations for MDD.[22] It has been observed that the pandemic has caused an increase in acts of self-harm and suicide especially in young people.[23] A systematic review on cross sectional studies in Bangladesh found an increase in the prevalence of suicidal thoughts during the pandemic.[24] Although many people have adjusted to life in the pandemic, others are suffering from psychological disorders due to COVID-19. Vulnerable groups include females, young people and individuals with pre-existing health conditions.[22]

The increased prevalence of psychological morbidity due to the COVID-19 pandemic may be explained by a variety of factors. Fear of the illness, the impact of helpless watching of the sufferings and deaths of family members and friends, public health and social measures (PHSM) including social isolation and restricted movement are contributing to feelings of loneliness, economic hardship due to loss of jobs are few of the reasons. Maladaptive behaviors like lack of physical exercise, unusually prolonged on screen time, abnormal sleep habits, substance abuse are contributing to our mental health burden.[22] Women are more exposed to domestic violence due to quarantine and this also results in mood and anxiety disorders.[25]Absence of structured educational environment and social interaction with peers and friends may have a long term consequence on children and adolescents. Several studies have reported increased prevalence of emotional disturbances and behavioral problems in children.[26]

Impact on mental health care system

The pandemic has had a devastating impact on mental health care system. Closure of outpatient departments, high rate of infections among health care professionals and reluctance of both patients and clinicians for face to face interview are some of the effects. The pre-pandemic underinvestment in mental health care system with less than of 2% health budget allocated to mental health in high income countries & less than 0.5% in low & middle income countries (LMIC) is contributing to the pandemic's effect.[21]

Measures for mitigation:

Mitigation is possible by- adhering to a structured daily routine, regular physical exercise, maintaining a strict sleep schedule, taking healthy diet, reducing screen time, avoiding distressing news on social media, regular contact with friends & family members- both online and physical, spending quality time with friends & family specially children, ventilating one's emotions & worries, avoiding use of illicit drugs, educating young people about mental health with special attention on resilience & healthy coping strategies.

Conclusion:

To function as an effective unit of society a person must be of sound mental health. Mental health problems can be severely debilitating & put an enormous pressure on society & state. A huge gap already existed between mental health needs of the people & available mental health care. The COVID-19 pandemic has widened this gap. To fight this coming catastrophe there must be increased investment in mental health & co-operation between individual, state & international organizations.

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a) Dr. Arman Ibne Haq; FCPS (Psy), MBBS
Assistant Professor (Dept. In-charge), Department of Psychiatry, Bangladesh Medical College
Email: arman0913@gmail.com

b) Prof. Dr. Sharmeen Yasmeen; M. Phil, MPH, MBBS
Professor and Head, Department of Community Medicine
Bangladesh Medical College, Dhaka, Bangladesh

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Antibiogram of Extended-spectrum Beta-lactamases producing organisms isolated in a tertiary care hospital in Dhaka, Bangladesh

Nahar A[a], Sharmin S[b], Hasnat S[c], Akhter H[d], Moony FA[e]

Abstract

Background: The emergence and spread of Extended-spectrum beta-lactamases (ESBLs) producing bacteria have been threatening the ability to treat an infection. Careful detection of these ESBL producing bacteria in laboratory will reduce infection prevention efforts in healthcare facilities.

Objectives: This study was conducted to detect ESBL by double disk synergy test (DDST) among laboratory isolates from different clinical specimens and to find out their antibiotic susceptibility pattern.

Methods: A laboratory based cross sectional study was conducted from January to December, 2020 at Microbiology department, Bangladesh Medical College, Dhanmondi, Dhaka. A total 1058 non repetitive isolates from different clinical specimens (like urine, sputum, wound swab/pus, blood, tracheal aspirate, high vaginal swab & catheter tips) were included to detect ESBL producing organisms phenotypically. Screening for potential ESBL-producing isolate was done and were selected for phenotypic confirmation for ESBLs production using double disc synergy test (DDST) as recommended by CLSI guideline. Antimicrobial susceptibility testing was done by using Kirby- Bauer disc diffusion technique on Mueller-Hinton agar according to the CLSI guidelines.

Results: A total 1058 organisms are detected from sputum, wound swab/pus, catheter tips, tracheal aspirates, high vaginal swab, urine & blood. Among them 233(22.012%) isolates are ESBL producers. Highest detection of ESBL producing organisms were in urine sample. The most frequent isolate is *E.coli* 168(35.52%) followed by *Klebsiella* 29(24.78%) and *Enterobacter* spp. 36(22.78%). Higher sensitivity shows in imipenem 223 (95.71%), meropenem 200 (85.84%), amikacin 203 (87.12%), netilmicin 180 (77.25%) & gentamicin 179 (76.82%). Lower sensitivity shows in nitrofurantoin 126 (54.07%), micellinum 97 (41.63%), ciprofloxacin 73 (31.3%) & co-trimoxazole 73 (31.33%). Nalidixic acid showed 100% resistance.

Conclusion: Highest detection of ESBL producing organisms was in urine sample and the most frequent isolate was *E. coli.* Higher sensitivity shows in imipenem, meropenem, amikacin, netilmicin & gentamicin. It is necessary to strengthen clinical bacteriology research and diagnostic capacity of laboratory professionals for the detection and surveillance of antibiotic resistance. In every hospital there must be antibiotic guideline policy and infection prevention & control program which will reduce spread and mortality associated with ESBL infections.

Keywords: ESBL, *E. coli*, Double disc synergy test, Antibiogram.

a. Dr. Azizun Nahar; M.Phil, MBBS
Associate Professor, Department of Microbiology
Bangladesh Medical College, Dhaka

b. Dr. Sohely Sharmin; M.Phil, MBBS
Professor (CC), Department of Microbiology
Bangladesh Medical College, Dhaka

c. Dr. Shahed Hasnat; M.Sc (U.K), MBBS
Assistant Professor, Department of Microbiology
Bangladesh Medical College, Dhaka

d. Dr. Hasina Akhter; M. Phil, MBBS
Associate Professor, Department of Microbiology
Bangladesh Dental College, Dhaka

e. Prof. Dr. Farhana Alamgir Moony; M.Phil, MBBS
Professor & Head, Department of Microbiology
Bangladesh Medical College, Dhaka

Correspondence to:
Dr. Azizun Nahar; M.Phil (BSMMU), MBBS
Associate Professor, Department of Microbiology
Bangladesh Medical College, Dhaka
Email: azizunnahar26@gmail.com

Introduction:

The emergence and spread of Extended-spectrum beta-lactamases (ESBLs) producing bacteria are serious and expanding public health problems globally.[1] There is also a growing concern regarding the lack of new antibiotics especially for multidrug-resistant Gram-negative bacteria which produce extended spectrum β-lactamases (ESBLs).[2] β-lactamases are hydrolytic enzymes which cleave the β-lactam ring and are responsible for bacterial resistance to β-lactam antibiotics, such as penicillins and cephalosporins.[3]

The prevalence of bacteria producing ESBLs varies worldwide, with reports from North America, South America, Europe, Africa, and Asia.[4] The rate of ESBL production was highest among the *K. pneumoniae* isolates collected in Latin America, followed by Asia/Pacific Rim, Europe, and North America (44.0%, 22.4%, 13.3%, and 7.5%, resp.).[5,6]

ESBLs are produced by the *Enterobacteriaceae* family of Gram-negative organisms, particularly in Klebsiella

pneumoniae and *Escherichia coli*.[7] They are also produced by non-fermentative Gram-negative organisms, such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.[8] Furthermore, it has been reported that *Enterobacter* spp., *Proteus* spp., *Citrobacter* spp., *Morganella* spp., *Providencia* spp., *Salmonella* spp. and *Serratia* spp. also produces ESBL.[9,10,11]

Being plasmid mediated, many ESBL-producing *Enterobacteriaceae* are also resistant to other commonly used antibiotics, namely, aminoglycosides, sulphonamides, and the fluoroquinolones.[12,13] Consequently, many patients impelled to take the 'last resort' antibiotics treatment such as carbapenems drugs.[14,15] However, the use of carbapenems has led to the rapid selection of carbapenem-resistant *Enterobacteriaceae*.[16] Only a few antibiotic such as carbapenems, colistin, tigecycline are available to treat infection caused by ESBL producing bacteria but there *in vivo* efficacy and/or toxicity is not well known.[17,18]

ESBLs detection remains a challenge for microbiologists. The importance of detection of ESBL is not fully alert by many clinical laboratories because of lack of understanding or resources.[19,20] Careful detections of these ESBL producing bacteria facilitates infection prevention efforts in healthcare facilities. The aim of this study was to detect ESBL by Double disk synergy test (DDST) among laboratory isolates from different clinical specimens and to find out their antibiotic susceptibility pattern.

Materials & Methods:

A laboratory based cross sectional study was conducted from January to December, 2020 at Microbiology department, Bangladesh Medical College, Dhanmondi, Dhaka. A total 1058 non repetitive isolates from different clinical specimens (like urine, sputum, wound swab/pus, blood, tracheal aspirate, high vaginal swab & catheter tips) were included to detect ESBL producing organisms phenotypically.

Screening for potential ESBL-producing isolate

The isolates that showed an inhibition zone size of ≤22mm with ceftazidime (30 µg) and/or ≤25mm ceftriaxone (30 µg) were considered as potential ESBL-producer (screening ESBL positive) and were selected for phenotypic confirmation for ESBLs production using double disc synergy test (DDST) as recommended by CLSI guideline.[21]

Phenotypic confirmation of ESBL producers

Confirmation of suspected ESBLs producers was done by using the double-disk synergy (DDS) method on Mueller–Hinton agar, as recommended by CLSI guidelines. A disc of amoxicillin + clavulanic acid (20/10 μg) was placed in the center of the Mueller–Hinton Agar plate, and then ceftazidime (30 μg) and ceftriaxone (30 μg) were placed at a distance of 20mm (center to center) from the amoxicillin+ clavulanic acid disc on the same plate was incubated at 37^{0}C for 24 hours. Then, the diameter of inhibition zone was measured. According to CLSI guidelines, an increase of ≥5 mm in the zone diameter around the clavulanic acid combination disks versus the same disks alone confirmed the presence of ESBL producer strains.[22]

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was done by using Kirby–Bauer disc diffusion technique on Mueller–Hinton agar according to the CLSI guidelines [15] for the following antimicrobial discs: amoxicillin/clavulanic acid (20/10 μg), cefotaxime (30 μg), ceftriaxone (30 μg), ceftazidime (30 μ g), ampicillin (10 μg), cephalothin (30 μg), ciprofloxacin (5 μg), nalidixic acid (30 μg), norfloxacin (10 μg), gentamycin (10 μg), amikacin (30 μg), tetracycline (30 μg), trimethoprim sulfamethoxazole (1.25/23.75 μg), imipenem (30 μg), and chloramphenicol (30 μg) (Oxoid; UK). Selections of antimicrobial agents depend on the availability and recommendations from CLSI [15]. After overnight incubation of the Mueller-Hinton agar plate with antimicrobial discs at 37°C, the zone of inhibition was measured by using a ruler and interpreted by comparing the Kirby-Bauer chart.[22] Nitrofurantoin was used only in urine sample.

Results:

Table 1: Rate of isolation of ESBL from different clinical specimens

Specimens	No. of isolates	ESBL producing prganisms (%)
Urine	552	163 (29.53%)
Sputum	163	28 (17.18%)
Wound swab/Pus	109	14 (12.84%)
Blood	177	11 (6.21%)
Tracheal aspirates	36	9 (25%)
High vaginal swab	16	5 (31.25%)
Catheter tips	32	3 (9.38%)
Total	**1058**	**233 (22.02%)**

A total 1058 organisms are detected from sputum, wound swab/pus, catheter tips, tracheal aspirates, high vaginal swab, urine & blood. Among them 233(22.012%) isolates are ESBL producers. Highest detection of ESBL producing organisms 163(29.53%) were from urine isolates followed by 28(17.18%) from sputum isolates, 14(12.84%) from wound swab/pus, 11(6.21%) from blood isolates, 9(25%) from tracheal isolates, 5(31.25%) from high vaginal swab isolates & 3(9.38%) from catheter tips isolates.

Table 2: Rate of isolation of ESBL producing Gram negative organisms

Organisms	No. of isolates	ESBL producers (%)
E. coli	473	168(35.52%)
Klebsiella spp.	117	29(24.78%)
Enterobacter spp.	158	36(22.78%)
Total	**748**	**233 (31.15%)**

The most frequent isolate is *E. coli* 168(35.52%) followed by *Klebsiella* spp. 29(24.78%) and *Enterobacter* spp. 36(22.78%).

Table 3: Antibiotic sensitivity pattern of ESBL producing Gram negative isolates

Drugs (S)	*E. coli* N= 168	*Klebsiella* spp. N= 29	*Enterobacter* spp. N= 36	Total 233 (%)
Amikacin	151 (89.88%)	23 (79.31%)	29 (80.55%)	203 (87.12%)
Ciprofloxacin	47 (27.97%)	9 (31.03%)	17 (47.22%)	73 (31.3%)
Co-trimoxazole	63 (37.5%)	2 (6.89%)	8 (22.22%)	73 (31.33%)
Micellinum	80 (47.61%)	4 (13.79%)	13 (36.11%)	97 (41.63%)
Nalidixic acid	0 (%)	0 (0%)	0 (0%)	0 (0%)
Gentamycin	138 (82.14%)	18 (62.06%)	23 (63.88%)	179 (76.82%)
Imipenem	162 (96.42%)	25 (89.20%)	36 (100%)	223 (95.71%)
Meropenem	140 (83.33%)	26 (89.65%)	34 (94.44%)	200 (85.84%)
Netilmicin	136 (80.95%)	22 (75.86%)	22 (61.11%)	180 (77.25%)
Nitrofurantoin	118 (70.23%)	3 (10.34%)	5 (13.88%)	126 (54.07%)

Higher sensitivity shows in imipenem 223 (95.71%), meropenem 200 (85.84%), amikacin 203 (87.12%), netilmicin 180 (77.25%) & gentamicin 179 (76.82%). Lower sensitivity shows in nitrofurantoin 126 (54.07%), micellinum 97 (41.63%), ciprofloxacin 73 (31.3%) & co-trimoxazole 73 (31.33%). Nalidixic acid showed 100% resistance.

Discussion:

ESBL-producing bacteria have become a serious problem worldwide. These problems cause rapid dissemination of ESBL producing organisms, ultimately treatment failure and are expensive to control the spread of resistance.[23,24]The occurrence of ESBL among clinical isolates vary greatly worldwide and geographically and are rapidly changing over a period of time.[25] In Bangladesh, rate of ESBL producing bacteria isolated were 23% in 2008, 24.85% in 2012 and 16.07% in 2014.[26, 27, 28] Selective pressure caused by the use of 3rd generation cephalosporin is one of the most important factors in the emergence of ESBLs production.[29] Misuse of antibiotics, lack of antibiotic surveillance and weak infection control measures may also contribute to the high magnitude of ESBL.

In this current study, a total 1058 isolates isolated from urine, sputum, wound swab/pus, blood, tracheal aspirates, high vaginal swab & catheter tips and 233(22.02%) isolates were detected as ESBL producing organisms. Highest ESBL producing organisms were detected in urine 163(29.53%) sample followed by sputum 28(17.18%), wound swab/pus 14(12.84%), blood 11(6.21%), tracheal aspirates 9(25%), high vaginal swab 5(31.25%) and catheter tips 3(9.38%). This finding is not in agreement with the previous report done in Bangladesh, where urine (70.4%) was the main source of ESBL producing isolates from all patients, followed by blood (16.5%), tracheal aspirates/sputum (8.7%), swabs (3.5%) and fluids (0.9%).[30] Another study found 54.75% ESBL from wound swab followed by pus (24.02%), tracheal aspirate (5.03%), urine (3.91%), blood (3.35%), sputum (2.79%), and others (6.15%).[28]

During the past decade, ESBL producing Gram-negative bacilli especially *Escherichia coli and Klebsiella pneumoniae* have emerged as serious pathogens in hospital acquired infections worldwide.[31] In our study among 233(22.02%) ESBL producers *E. coli* was 168(35.52%) followed by *Klebsiella* spp. 29(24.78%) & *Enterobacter* spp. 36(22.78%). In a study, *E. coli* was found *(*32%) & *Klebsiella* species (24%) which is similar with our study.[32] In another study *E. coli* was the most common isolated bacteria 34(42.5%) followed by *Proteus* species 17(21.2%), *Pseudomonas* species 9(11.3%), *Staph. aureus* 9(11.3%), *Klebsiella* species 7(8.7%) and *Acinetobacter* species 3(3.7%) which is dissimilar with our study.[33]

Carbapenems were the most efficacious drugs; imipenem and meropenem showed 95.71% & 85.84% sensitivity in this study which is in accordance with findings of recent study.[34] It is a great concern for the clinician because of increasing resistance of these reserve drugs. The majority of the ESBL producers in our study showed a good sensitivity to amikacin 87.12%, gentamycin 76.82%, netilmicin 77.25%. The reason behind such higher sensitivity might be the less use of antibiotics in this hospital. So, these drugs may be considered as an alternative drug in infections caused by ESBL producers. All ESBL producers showed very low sensitivity to ciprofloxacin (31.33%) in this current study. This finding is consistent with other studies where they reported very low sensitivity to ciprofloxacin.[34,35] Ciprofloxacin is used widely in our country for many infections such as enteric fever which is endemic in Bangladesh. Low sensitivity to this commonly used drug is becoming alarming. In this study, ESBL producers were completely resistant to nalidixic acid. Lower sensitivity was observed to nitrofurantoin (54.07%), micellinum (41.63%) & co–trimoxazole (31.33%). The results of our study are in line with the findings of study where nalidixic acid showed 17.4% sensitivity which does not match with our study.[30]

Co-trimoxazole and nitrofurantoin showed 13% & 57.4% sensitivity in a study, co-trimoxazole was also showed 23% sensitivity in another study.[30,36] With above findings in our study there are very limited treatment options available for these pathogens. Early detection and appropriate antibiotic application will control the development and spread of ESBL producing organisms. So, rational use of antibiotics in health care settings should be a concern for health policymaker.

Conclusion:

In our findings, highest detection of ESBL producing organisms was in urine sample and the most frequent isolate was *E. coli.* Imipenem, meropenem, amikacin, netilmicin & gentamicin were the best options for antibiotic therapy. ESBL-producing infections are of grave concern to the medical world because of increased morbidity and mortality. It is necessary to strengthen clinical bacteriology research and diagnostic capacity of laboratory professionals for the detection and surveillance of antibiotic resistance. In every hospital there must be antibiotic guideline and infection prevention & control program which will reduce spread and mortality associated with ESBL producing bacterial infections.

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Original Article

Attenuation of cardiovascular responses to laryngoscopy and intubation by intravenous metoprolol

Khan MRH[a], Ullah A[b] , Deepa TC[c], Taskin R[d], Ibrahim K[e]

Abstract

Background: Cardiovascular response to laryngoscopy and intubation is a reflex stimuli affecting the hemodynamic stability. This may prove detrimental in high risk patients with compromised cardiovascular system, such as hypertension, ischemic heart diseases or cerebrovascular diseases. Attenuation of this response is extremely important and various techniques have been studied to attenuate this stress response. Some of the beta blockers including metoprolol showed effective results in some studies to attenuate cardiovascular responses.

Objective: To assess the effect of cardiovascular responses to laryngoscopy and intubation by intravenous metoprolol 4mg given 3 minutes before induction of anesthesia.

Methods: This was a cross-sectional comparative study. The study consists of 92 adult patients both male and female, ASA I and II, aged 18-60 years, scheduled for elective surgeries requiring general anaesthesia, randomly divided into two equal Groups- Group A (control group) & Group B (study group). Group A received Inj. 0.9% normal saline and group B was received Metoprolol 4mg IV 3 min prior to induction. Haemodynamic variables (heart rate, systolic and diastolic blood pressure), ECG changes and SpO2 were recorded before induction (Basal), just before intubation (post induction), immediately after laryngoscopy and endotracheal intubation and 1, 3, 5, 10 minutes after intubation then after every 10 minutes' interval till the end of surgery.

Results: Our study showed that, with Metoprolol (4mg) group, there were significant reduction in heart rate immediately after induction, 1 minute, 3 minutes & 5 minutes after endotracheal intubation (p value <0.01), significant reduction in Systolic Blood Pressure, Diastolic Blood Pressure and Mean Blood Pressure after 1 minute, 3 minutes & 5 minutes of endotracheal intubation (p value <0.01) and reduction in Rate Pressure Product immediately after induction and 1 minute, 3 minutes & 5 minutes after endotracheal intubation (p value <0.01).

Conclusion: Metoprolol (4mg) effectively attenuates the cardiovascular stress response during laryngoscopy and endotracheal intubation.

Keywords: Cardiovascular responses, Laryngoscopy, Tracheal intubation, Metoprolol.

Introduction:

The cardiovascular responses to laryngoscopy and intubation may become hazardous in patients with compromised cardiovascular system, such as hypertension, ischemic heart diseases or cerebrovascular diseases. Attenuation of this response is extremely important.[1] Induction of anesthesia is a hazardous phase in the management of patients during surgery. The cardiovascular responses to laryngoscopy and intubation may be less harmful in an otherwise normal individual.[2] But in a patient with compromised cardiovascular system such as hypertension,[3] ischemic heart disease or cerebrovascular disease, these pressor responses may be of disastrous consequences.[4] Attenuation of this response, at least in such patients is extremely important. Many studies have been conducted to attenuate the cardiovascular responses to laryngoscopy and intubation using, deeper plane of Anesthesia, β-blockers,[5,6] agonist clonidine, opioids like fentanyl, alfentanil,[7] buprenorphine, calcium channel blockers (sublingual nifedipine),[8] vasodilators[9] (nitroglycerine), topical anesthesia with lignocaine and intravenous lignocaine[10] etc. Administration of intravenous metoprolol (selective β-blocker) as a method to attenuate the cardiovascular responses has been studied by many researchers and is found to be useful in this regard.[5] Laryngoscopy results in stimulation of larynx, pharynx, and trachea which are extensively innervated by the

a. Dr. Md. Rafiqul Hasan Khan; FCPS, MCPS, MBBS
Associate Professor, Department of Anesthesiology
Bangladesh Medical College Hospital, Dhaka

b. Dr. Ahamad Ullah; DA, MBBS
Junior Consultant, Department of Cardiac Anaesthesia
National Heart Foundation Hospital & Research Institute, Dhaka

c. Dr. Taslema Chowdhury Deepa; DA, MBBS
Junior Consultant, Department of Anaesthesia
Bangladesh Medical College Hospital

d. Dr. Roksana Taskin; MBBS
Medical Officer, Department of Gynae & Obs
Monowara General Hospital, Dhaka

e. Prof. Kamal Ibrahim; FCPS, FICS, MBBS
Professor and Head, Department of Anaesthesiology
Bangladesh Medical College and Hospital

Correspondence to:
Dr. Rafiqul Hasan Khan; MCPS, FCPS, MBBS
Associate Professor, Department of Anesthesiology
Bangladesh Medical College and Hospital
Email: azad300769@gmail.com

autonomic nervous system. Stimulation of these areas leads to sympathetic system activation leading to various cardiovascular changes like increase in heart rate, blood pressure, intracranial pressure, intraocular pressure, dysrhythmias, cardiac asystole and even sudden death.[11,12] The reflex cardiovascular responses to laryngoscopy and tracheal intubation were known to anaesthesiologists since long.[13] Anaesthesiologists aim at suppressing the sympathetic responses at the time of laryngoscopy and tracheal intubation, and quickly get back the protective sympathetic reflexes thereafter. Failure to blunt the responses to intubation may have disastrous consequences like cardiac failure, myocardial infarction, cerebrovascular accidents and precipitates the condition in patients with coronary artery disease, systemic arterial hypertension and aneurysmal vascular disease. Effect of drugs on the haemodynamic responses can be known by monitoring the heart rate (HR), respiratory rate (RR), blood pressure, mean arterial pressure (MAP), electrocardiography (ECG) and by calculating the Rate Pressure Product (RPP= HR x Systolic Blood Pressure).[14] ß adrenergic blocking drugs[15] and calcium channel blocking drugs[16] have been in use for blunting the hemodynamic responses during intubation procedures. As this study was done to find the better and safe drug in suppressing the hemodynamic responses we decided to study effect of intravenous use of metoprolol on induction of anesthesia and effect on cardiovascular responses during laryngoscopy and endotracheal intubation.

Materials & Methods:

This prospective cross-sectional comparative study was done to assess the attenuation of cardiovascular responses to laryngoscopy and intubation by intravenous metoprolol among adult patients undergoing general anaesthesia for elective surgery conducted in the indoor patients of department of Surgery in Bangladesh Medical College Hospital.

Ethical clearance was taken from the IRB of BMCH. A total of 92 patients were included in this study between 18-60 years who required tracheal intubation with IPPV for surgery patients in both genders, ASA I or II (no or minimal co-morbid disease) and patients scheduled for elective surgeries. Ninety-two patients undergoing surgery under general anesthesia were divided into two groups, Group-A and Group-B. All patients received premedication (Tab. Diazepam 0.2mg/ kg oral, maximum dose 15mg.) 2 hours before admission into the operation room. After reaching to the operation room, an 18G IV catheter was inserted in a peripheral vein and was infused with Ringer's lactate solution. Patient's baseline vital data were recorded using pulse oximeter for O_2 saturations, ECG and non-invasive blood pressure (NIBP). Both groups received inj. Fentanyl (1micg/kg) I/V. Group-A received Inj. 0.9% normal saline and group-B was received Metoprolol 4mg I/V 3 min prior to induction. During induction Inj. Fentanyl (during which the patient will be pre-oxygenated with 100% oxygen) & Propofol 2.5 mg/kg will be administered by a colleague anaesthetist in both groups. The induction agent will be injected at a constant rate over 30 seconds. Adequacy of anaesthesia were assessed (loss of verbal contact). Then Inj. Succinylcholine 1.5 mg/kg I/V was given. Lungs were ventilated with 100% oxygen using intermittent positive pressure ventilation. When it was found adequate relaxation, Laryngoscopy was performed with a macintosh laryngoscope blade and trachea will be intubated with an appropriate sized cuffed endotracheal tube by investigator and confirmation of correct placement was done. Anaesthesia was maintained with 60% nitrous oxide in oxygen along with halothane. Inj. Vecuronium 0.1 mg/kg bolus then 0.01mg/kg dose every 15 to 20 minutes was used for per-operative muscle relaxation. Heart rate, Blood pressure, SpO_2 and ECG changes was recorded, just before induction basal, just after Laryngoscopy and intubation and then 1, 3, and 5 minutes after tracheal intubation. During this 10 minutes all surgical stimulation was avoided. At the end of surgery, the effect of muscle relaxant was reversed with 0.04 mg/kg of Neostigmine, 0.01 mg/kg of Glycopyrrolate. Before extubation adequacy of ventilation and protective response was confirmed. All the observations and particulars of the patient were recorded.

Statistical analysis

Statistical analysis was carried out by using the Statistical Package for Social Sciences version 19.0 for Windows. The mean values were calculated for continuous variables. Comparison of numerical variables between the studies was done using Students t-test. For comparing categorical data, Chi square (X^2) test with Yates correction was performed. p values less than 0.05 was considered statistically significant.

Results:

Table: Demographic characteristics of the study population

Demographic characteristics	Study group		Total No. (%)
	Control n=46	Metoprolol n=46	
Age in years (Mean ±SD)	41.97 (±12.89)	41.45 (±9.44)	45 (48.91%)
Sex			
Male	28 (60.87%)	17 (36.96%)	45(48.91%)
Female	18 (39.13%)	29 (63.04%)	47 (51.09%)
ASA I	46 (100)	46 (100)	92 (100%)
ASA II	00	00	00

Table 1 shows mean age was 41.97(±12.89) years in control group and 41.45 (±9.44) years in Metoprolol, males were 45(48.91%) and 47(51.09%) were female. All (100%) had ASA I in both group.

Table 2: Comparison of heart rate between the two groups

	Study group		
Heart rate	Control n=46	Metoprolol n=46	**p value**
Before Induction	88.65 (±6.54)	88.78(±8.77)	0.93
Post Induction	104.08 (±8.51)	89.84 (±8.76)	<0.001
1 min after intubation	113.41 (±7.67)	87.39 (±8.53)	<0.001
3 min after intubation	104.15 (±5.54)	85.15 (±7.38)	<0.001
5 min after intubation	96.97(±3.80)	83.34 (±7.63)	<0.001

Values are in mean± SD, number and percent Inter group comparison of heart rate is shown in Table- 2. The difference in heart rate between the two groups before induction was insignificant. But there was significant reduction in between the two groups' immediately after induction and after 1 minute, 3 minutes & 5 minutes of endotracheal intubation (p<0.001).

Table 3: Comparison of Systolic Blood Pressure (SBP) between the two groups

	Study group		
Systolic Blood Pressure (SBP)	Control n=46	Metoprolol n=46	**p value**
Before Induction	135.04 (±6.97)	133.95 (±12.73)	0.61
Post Induction	125.34 (±14.94)	120.28 (±12.39)	0.08
1 min after intubation	150.04 (±11.27)	127.17 (±21.33)	<0.001
3 min after intubation	138.65 (±8.40)	119.52 (±16.73)	<0.001
5 min after intubation	131.84 (±6.10)	113.47 (±7.87)	<0.001

Inter group comparison of Systolic Blood Pressure (SBP) is shown in Table-3. The difference in Systolic Blood Pressure between the two groups before induction and immediately after induction was insignificant. But there was significant reduction in Systolic Blood Pressure between the two groups' and after 1 minute, 3 minutes & 5 minutes of endotracheal intubation.

Table 4: Comparison of Diastolic Blood Pressure (DBP) between the two groups

	Study group		
Diastolic Blood Pressure (DBP)	Control n=46	Metoprolol n=46	**p value**
Before Induction	79.17 (±10.12)	81.93 (±14.35)	0.29
Post Induction	69.36 (±9.77)	75.43 (±13.05)	0.01
1 min after intubation	98.65 (±9.77)	74.50 (±8.60)	<0.001
3 min after intubation	90.65 (±11.08)	72.02 (±10.29)	<0.001
5 min after intubation	83.63 (±8.97)	69.34 (±8.92)	<0.001

Inter group comparison of Diastolic Blood Pressure (DBP) is shown in Table- 4. The difference in Diastolic Blood Pressure between the two groups before induction was insignificant. But there was significant reduction in Diastolic Blood Pressure between the two groups' immediately after induction and after 1 minute, 3 minutes & 5 minutes of endotracheal intubation.

Table 5: Comparison of Mean Blood Pressure (MBP) between the two groups

	Study group		
Mean Blood Pressure (MBP)	Control n=46	Metoprolol n=46	**p value**
Before Induction	97.30 (±8.42)	95.03±5.66	0.38
Post Induction	84.30 (±11.21)	90.45 (±11.64)	0.01
1 min after intubation	114.08 (±13.13)	92.00 (±11.30)	<0.001
3 min after intubation	107.80 (±16.77)	87.80 (±10.28)	<0.001
5 min after intubation	98.13 (±8.80)	84.08 (±6.00)	<0.001

Inter group comparison of Mean Blood Pressure (MBP) is shown in Table-5. The difference in Mean Blood Pressure between the two groups before induction was insignificant. But there was significant reduction in Mean Blood Pressure between the two groups immediately after induction and after 1 minute, 3 minutes & 5 minutes of endotracheal intubation.

Table 6: Comparison of Rate Pressure Product (RPP) between the two groups

	Study group		
Rate Pressure Product	Control n=46	Metoprolol n=46	**p value**
Before Induction	11974.86 (±1111.89)	95.03±5.66	0.38
Post Induction	11952.36 (±1380.51)	90.45 (±11.64)	0.01
1 min after intubation	17027.93 (±1840.62)	92.00 (±11.30)	<0.001
3 min after intubation	14468.86 (±1463.58)	87.80 (±10.28)	<0.001
5 min after intubation	12786.36 (±801.02)	84.08 (±6.00)	<0.001

Inter group comparison of Rate Pressure Product (RPP) is shown in Table-6. The difference in Rate Pressure Product between the two groups was found significant immediate after induction. Similar reduction was found in Rate Pressure Product between the two groups after 1 minute, 3 minutes & 5 minutes of endotracheal intubation.

Discussion:

Direct laryngoscopy and tracheal intubation cause increase in blood pressure and heart rate.[17] Mechanism of cardiovascular response to intubation assumed to be a reflex sympathetic reaction to the mechanical stimulation of larynx and trachea. Reflex changes in the cardiovascular

system after laryngoscopy and intubation lead to an average increase in blood pressure by 40-50% and 20% increase in heart rate.[18] Significant elevations in serum levels of norepinephrine and epinephrine following laryngoscopy, with and without tracheal intubation, have been demonstrate.[19,20]

In this study mean age was 41.97(±12.89) years in control group and 41.45 (±9.44) years in Metoprolol, males were 45(48.91%) and 47(51.09%) were female. All (100%) had ASA I in both group (Table-1). In Sharma and Singh[21] study most of the patients belonged to age group 30-40 years followed by those in 40-50 years. Raju et al.[22] showed mean age 32±7.33 in Metoprolol group and 33.16±9.04 years in control group. Age may be an important factor influencing cardiovascular response to tracheal intubation. lsmail observed exaggerated increase in Systolic blood pressure following laryngoscopy and intubation in elderly and middle aged patients as compared to young. This may be due to variation in balance between Sympathetic and parasympathetic outflow or receptor hypersensitivity.[23]

In this study the difference in heart rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Blood Pressure (MBP) and Rate Pressure Product (RPP) between the two groups before induction was insignificant. (Table-2,3,4,5,6). But there was significant reduction in Systolic Blood Pressure between the two groups immediately after induction and after 1 minute, 3 minutes & 5 minutes of endotracheal intubation ($p<0.001$).Heart Rate**:** In Gurudatta and Kumara study[24] we observed a similar trend with mean HR reduced in metoprolol group by 8.86% following induction and increased by 5.08% (4.24 bpm) following intubation at 1 minute which was significant reduction in intubation response in comparison to our control group which had a rise of 45.46% (37.96 bpm) at the same time. Singh et al,[25] observed an increase in HR by 17% from the pre-induction value in the metoprolol group (82.9±14 to 97.8±11.5 bpm) at one minute after intubation, while corresponding increase in the control group was 24.85% (87.3±114.3 to 109±110.8 bpm). Similarly, in study by Kumar and Tikle,[26] they found that the mean HR decreased by 6.7 bpm following intravenous metoprolol and later increased by 10.26 bpm following intubation from basal value, which was significantly less as compared to the control group with maximum rise in HR after intubation of 27.53 bpm. Magnusson et al, [27] have reported an incidence of bradycardia in one patient which was effectively reversed with I.V. atropine. Kumar and Tikle also have reported one such incidence. But in our study, we didn`t have such incidence of bradycardia in any of patients in both the groups. Systolic Blood Pressure**:** In our study, mean SBP decreased by 9.23% (11.36 mmHg) following induction and then increased by 10.63% (13.08 mmHg) at l min. after intubation from the basal value in the study group, whereas the corresponding changes in the control group were -1.99% (2.4mmHg.) and +38.14% (46mmHg) following induction and intubation respectively. SBP changes in this study are thus in comparison with the changes observed by Kumar and Tikle[26], as they observed reduction of mean SBP by 11.14mmHg at induction and then increased by 13.8 mmHg soon after intubation in the study group. Coleman and Jordan[5] noted the mean increase of 9.8mm Hg which occurred at intubation in control group where as in metoprolol groups (2mg and 4mg) there were significant mean reduction in blood pressure by 7.1 mmHg and 8.1 mmHg following metoprolol I.V. respectively, this persisted following induction and thereafter, there was a small increase in systolic arterial pressure with intubation. They observed mean increase in systolic arterial pressure with intubation in metoprolol 4mg group was still below the basal level compared to slight increase in SBP in metoprolol 2 mg group.

Singh et al[25] reported 5.5% reduction in mean MAP following induction (95.5±8.3 to 90.1±12.6 mm Hg) and they noticed 18% increases in MAP (113±12 mm Hg) following intubation in metoprolol group compared to increase in mean MAP by 34.8% following intubation (from 95.2±10.1 to 128.4±17.3 mm Hg in their study. Similarly, in Gurudatta and Kumara[24] study in the metoprolol group mean MAP decreased by 8% following induction (94.34 ±7.40 to 86.79±6.28 mm Hg), and mean MAP increased by 11.6% from the basal value at l min after intubation (105.44±15.02 mm Hg). Thereafter it returned to basal level by next 5 minutes which was in comparison with study by Singh et al.[25]

Rate Pressure Product**:** According to Marey's law heart rate rises with fall in blood pressure and vice-versa and this keeps rate pressure product fairly constant. Any condition which increases heart rate and systolic blood pressure multiplies the rate pressure product, which may cross critical limits of ischemia. Roy et al,[28] found that RPP of above 22000 was associated with ischemic changes in ECG in healthy volunteers. In Gurudatta and Kumara study, [24] the mean RPP rose from the basal value of 9972.12±1228.28 to a value of 10565.6±1256.10 following induction (5.34%) and reached a peak of 20279.2±2121.5 (103.35%) at T4 i.e. one minute after intubation in the control group, whereas in metoprolol group the mean RPP decreased from basal value of 10287.01±1046.35 to 7596.44±956.74 (26%) following induction and then reached a peak of 11938.16±1386.28 (16%) following intubation (T4). At the end of 5mins it was 9840.64±1271.4 (4.3%).

Study by Singh et al[25] found that their study group had 25% increase in mean RPP (10448±591 to 13072±734) at 1 minute after intubation, while there was 57% increase in mean RPP in the control group (10866±716 to 15839±832). Similarly, Kumar and Tikle[26] (1995), found in the study group 13% increase in mean RPP (10311.4 to 11734.9) following intubation, while it was 56% in the control group (9988.1 to 15603.3).

Attempts were made to differentiate between effects of laryngoscopy and those of tracheal intubation and their

individual contribution to haemodynamic changes. Prys Roberts et al (1971) observed that a majority of patients produced reflex tachycardia and hypertension well before the act of intubation and was often enhanced by intubation, so it is laryngoscopy rather than endotracheal intubation which generates the stimulus.[3,29] These changes are probably of little consequence in healthy individuals but of great consideration and potentially dangerous in patients with hypertension, ischemic heart disease, and other states of cardiovascular compromise. Anaesthetists want to suppress sympathetic responses at one time (e.g., before tracheal intubation) but observed enhanced responses very soon after intubation. Strategies to blunt these responses include minimizing duration of laryngoscopy to less than 15 seconds, the administration of IV lidocaine/ vasodilators/narcotics/beta blockers. In this aspect selective beta adrenergic blocking agents are paid more attention to prevent the reflex sympathetic discharge mediated tachycardia and hypertension during procedures of laryngoscopy and endotracheal intubation. Metoprolol[30,31]are cardioselective ß1-blockers commonly used by the anaesthesiologists. Raju et al[22] study findings that Esmolol attenuates the hemodynamic responses were comparable to the findings of other studies done by Menkhaus G.et al[32].

Sharma and Singh[21] study also demonstrates that metoprolol was more effective in normalizing the HR and decreasing the chances of arrhythmia. This could be due to the release of renin from juxtaglomerular apparatus stimulated by the sympathetic system is blocked by metoprolol.[33] Metoprolol also improves the relationship between cardiac oxygen supply and demand.[24]

We concluded from this study that intravenous metoprolol 4 mg given 3 minutes before induction of anesthesia significantly attenuates the cardiovascular responses to laryngoscopy and intubation.

Conclusion:

This study done to evaluate the effects of intravenous metoprolol in attenuating the cardiovascular stress response to laryngoscopy and endotracheal intubation. There was no difference in the baseline demography of the patients in respect to mean age, weight, sex and the hemodynamic variables. Our study showed that, with Metoprolol (4mg) group, there were significant reduction in heart rate immediately after induction, 1 minute, 3 minutes -& 5 minutes after endotracheal intubation (p value <0.01), significant reduction in Systolic Blood Pressure, Diastolic Blood Pressure and Mean Blood Pressure after 1 minute, 3 minutes & 5 minutes of endotracheal intubation (p value <0.01) and reduction in Rate Pressure Product immediately after induction and 1 minute, 3 minutes & 5 minutes after endotracheal intubation (p value <0.01) . So, it can be concluded that, Metoprolol (4mg) effectively attenuates the cardiovascular stress response during laryngoscopy and endotracheal intubation.

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Isolation of uropathogenic *E. coli* and their antimicrobial sensitivity pattern from patients with urinary tract infections in a tertiary care hospital in Dhaka city

Begum T[a], Emotuddowllah[b], Lucky JS[c], Kabir S[d]

Abstract

Background: *E. coli* is one of the most common causative agent of urinary tract infection (UTI).

Objective: This study was conducted to isolate the uropathogenic E. coli and their antimicrobial sensitivity pattern from patients with urinary tract infections in a tertiary care hospital in Dhaka city

Methods: This study was done in the department of Microbiology, Holy Family Red Crescent Medical College Hospital, Dhaka from January 2020 to December 2020. A total 4030 urine samples were collected. Of them 562 (13.95%) samples showed culture positive. Midstream clean catch urine was collected by standard procedure. Semi quantitative culture was done on Blood agar and Mac Conkey agar media. Typical colonies were selected and examined microscopically and relevant biochemical test were done according to standard laboratory methods. Sensitivity pattern of isolated organisms were determined by modified Kirby- Bauer technique using Mueller- Hinton agar.

Results: Among 562 culture positive isolates majority of the isolates were from female 379(67.44%) & remaining 183(32.56%) from male. Highest culture positive was found in 21-30 years' age group (16.19%). Among the isolates, *E. coli* was the most predominant urinary pathogens (43.2%). High level of sensitivity was found to tetracycline (95.47%), imipenem (93.0%), meropenem (92.59%), nitrofurantoin (91.35%).

Conclusion: The study illustrates that *E. coli* is an important cause of urinary tract infections (UTI). Appropriate antibiotic should be used for the treatment of UTI after urine culture and sensitivity to minimize drug resistance.

Keywords: UTI, Uropathogenic *E. coli*, Ntimicrobial sensitivity, Nitrofurantoin.

Introduction:

Urinary tract infection (UTI) is a collective term that describes any infection involving any part of the urinary tract, namely the kidneys, ureters, bladder and urethra. Both Gram-negative and Gram-positive bacteria and certain fungi are responsible for urinary tract infections (UTIs). The most common causative agent is uropathogenic *E. coli* (UPEC).[1,2,3,4]

a. Dr. Taslima Begum; M. Phil, MBBS
Associate Professor, Department of Microbiology
Holy Family Red Crescent Medical College, Dhaka

b. Dr. Emotuddowllah; MBBS
Assistant Registrar, Department of Cardiology
Bangladesh Medical College, Dhaka

c. Dr. Jasmin Sultana Lucky; BDS, MPH
Assistant Professor, Dental Public Health, OSD, DGHS, Dhaka

d. Dr. Silvia Kabir; BDS, MPH
Lecturer, Dental Juries, Law and Ethics, Dental Unit
Shaheed Suhrawardy Medical College, Dhaka

Correspondence to:
Dr. Taslima Begum; M. Phil, MBBS
Associate Professor, Department of Microbiology
Holy Family Red Crescent Medical College Hospital, Dhaka
E mail: pannataslima@gmail.com

E. coli are responsible for both communities as well as in hospital acquired UTIs.[5] Worldwide about 150 million people are diagnosed with UTI each year costing the global economy in excess of 6 billion US dollars. [6] All over the world *E. coli* accounts for 75% to 90% UTI isolates.[7] *E. coli* is one of the leading causes of neonatal meningitis and neonatal sepsis which often serious complications to death and also shows features of extra intestinal infection such as osteomyelitis, cellulitis and wound infection.[8,9] Uropathogenic *E. coli* are the primary cause of community acquired UTI with an estimated 20% women over the age 18 years suffering from at least one UTI in their life time.[10] Appropriate and rational use of antibiotics should consider by the physician to treat UTI. The aim of the present study was to find out the rate of isolation of *E. coli* causing UTI and their antimicrobial sensitivity pattern among patients with UTIs in Dhaka city, Bangladesh.

Materials and Methods:

This retrospective study was carried out in the laboratory of the department of Microbiology, Holy Family Red Crescent Medical College Hospital (HFRCMCH), Dhaka, Bangladesh. The duration of the study was one year (January 2020 to December 2020). From both inpatient & outpatient of HFRCMCH, 4030 urine samples were

collected. Of them 562 (13.95%) samples showed culture positive. Midstream clean catch urine was collected by standard procedure. Semi quantitative culture was done on Blood agar and MacConkey agar media. Typical colonies were selected and examined microscopically and relevant biochemical test were done according to standard laboratory methods.[11] Sensitivity pattern of isolated organisms were determined by modified Kirby- Bauer technique using Mueller- Hinton agar.[12] The antibiotic discs used in antibiogram for *E. coli* were amoxicillin/ clavulanic acid (30µg), ciprofloxacin (5µg), cefuroxime (30µg), mecillinam (25µg), gentamycin (10µg), trimethoprime/ sulphamethoxazole (25µg), amikacin (30µg), ceftriaxone (30µg), nitrofurantoin (300µg), imipenem (10 µg), meropenem (10µg) and tetracycline (10µg).

Results:

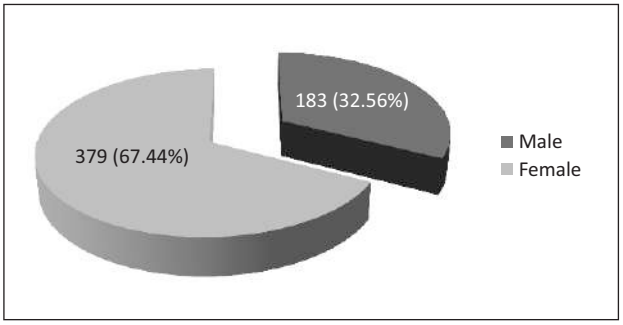

Figure1: Sex distribution of patients with UTI (n=562)

Figure 1 shows the sex distribution of patients with UTI. Among 562 culture positive isolates majority of the isolates were from female 379 (67.44%) while the remaining were from male 183 (32.56%).

Table 1: Distribution of the respondents by age group (n=562)

Age group (years)	No. of patients	Percentage
1-10	47	8.36
11-20	54	9.61
21-30	91	16.19
31-40	87	15.48
41-50	62	11.03
51-60	57	10.14
61-70	88	15.66
>71	76	13.53
Total	**562**	**100.00**

In table 1 highest culture positive was found in 21-30 years' age group (16.19%), followed by 61-70 years' age group (15.66%), 31-40 years (15.48%), >71 years (13.53%), 41-50 years (11.03%), 51-60 years (10.14%), 11-20 years (9.61%) and 1-10 years (8.36%).

Table 2: Pattern of bacteria isolated from urine culture (n=562)

Isolated organisms	No. of patients	Percentage
E. coli	243	43.24
Klebsiella spp.	189	33.63
Staph. aureus	44	7.83
Pseudomonas spp.	51	9.07
Acinetobacter spp.	26	4.63
Proteus spp.	9	1.6
Total	**562**	**100.00**

Table 2 shows the pattern of bacteria isolated from urine culture among 562 isolates 243 (43.24%) were *E. coli* followed by *Klebsiella* spp 189(33.63%), *Pseudomonas* spp 51(9.07%), *Staph. aureus* 44(7.83%), *Acinetobacter* spp. 2694.63%) & *Proteus* spp. 9(1.6%).

Table 3: Antimicrobial sensitivity pattern of *E. coli* (n=243)

Antibiotics	Sensitive (%)
Amoxycillin/clavulanic acid	98 (40.32)
Ciprofloxacin	98 (40.32)
Cefuroxime	37 (15.22)
Micellinum	123 (50.61)
Gentamicin	184 (75.72)
Trimethoprim/Sulfamethoxazole	127 (52.26)
Amikacin	177 (72.83)
Ceftriaxone	66 (27.16)
Nitrofurantoin	222 (91.35)
Imipenem	226 ((93.0)
Meropenem	225 (92.59)
Tetracycline	232 (95.47)

Table 3 showed the antimicrobial sensitivity pattern of *E. coli*. Among 243 isolates 232 (95.47%) were sensitive to tetracycline followed by imipenem 226 (93.0%), meropenem 225 (92.59%) and lowest sensitive to cefuroxime 37 (15.22%).

Discussion:

Urinary tract infections are amongst the most common infections encountered in clinical practice and are a common clinical condition worldwide. But the pattern of antimicrobial sensitivity varies in different regions. The present study emphasizes the rate of isolation of *E. coli* as a cause of UTI among different age and sex and their antibiotic sensitivity pattern against commonly used antibiotics.

In this study, a total 562 (13.95%) uropathogens were isolated from 4030 urine samples. Among them 379(67.44%) were female and male 183(32.56%) (figure 1).

The sex distribution of patients in our study is analogous with those of other reported studies in our country showing a predominance of females (64.5%) with UTI.[13,14] The reason behind this high prevalence of infection among females is related to the differences between male and female genitourinary systems in anatomy and host factors such as changes in normal vaginal flora.[15] In our findings maximum organisms were isolated from the age group 21-30 years (16.19%) followed by 61-70 years (15.66%) then 31-40 years (15.48%) and lowest age group was 1-10 years (8.36%) (Table 1). Urinary infections frequently occur in both genders and across all age groups but women, particularly those aged 16-64 years, are significantly more likely to experience UTIs than men.[16,17] Pregnant women, the elderly or patients with spinal cord injuries, catheters, or diabetes are also at increased risk of UTI.[18,19]

This study showed that the predominant organism was *E. coli* 243(43.24%) among the total 562 culture positive cases followed by *Klebsiella* spp. 189(33.63%), *Pseudomonas* spp. 55(9.07%), *Staph. aureus* 44(7.83%), *Acinetobacter* spp. 26(4.63) and *Proteus* spp. 9(1.6%) (Table 2). The findings are similar to studies done by others.[20] It supports the previous finding indicating that *E. coli* is the principal etiological agent of UTI, accounting for 60.02% of the cases.[21] In another study, it was reported that predominant uropathogens are *E. coli* followed by *Klebsiella* species which also support our study.[22] The similarities and differences in the type and distribution of uropathogens may results from different environmental conditions and host factors and also from some practices such as health care and education programmers' socioeconomic standards and hygiene practices in each country.[23]

Antibiotics resistance among uropathogens has become a public health concern in Bangladesh.[24] Antibiotic resistance in *E. coli* has increased worldwide and its susceptibility patterns show substantial geographic variation as well as differences in population and environment.[25] In this novel study, majority isolates were sensitive to tetracycline 232(95.47%), imipenem 226(93.0%), meropenem 225 (92.59%), nitrofurantoin 222(91.35%) gentamycin 184 (75.72%), amikacin 177(72.83%) and lowest sensitive ceftriaxone 66(27.16%) respectively. Ciprofloxacin sensitivity was also lower 98 (40.20%) shown in table 3. We found tetracycline sensitive for *E. coli* about (95.47%) because now a day tetracycline is being used less due to its some toxicity like suppression of normal flora of intestinal tract, rise in pH, teratogenic effects etc.[26]

It has been reported that amikacin and imipenem are the most effective antibiotic against uropathogens.[27] Our results were further supported by another study where the susceptibility rate of uropathogen to amikacin and imipenem remained 93-100%.[28]Nitrofurantoin would bean excellent choice for UTI empiric therapy according to culture & sensitivity as it showed higher sensitivity in this current study.[29] Ciprofloxacin was considered as drug of choice for UTI bit due to lack of rational use, it lost its efficacy not only in UTI but to other common infection too.[30] So, misuse or overuse of fluroquinolones should be restricted.

Conclusions:

UTI is the leading public-health problem mainly in women in our country. Typically, urine samples are sent for microbiological testing only after treatment failure, recurrent or relapsing infection. In our study, the predominant isolated organism responsible for UTI was E. coli. Appropriate antibiotic should be used for the treatment of UTI after urine culture and sensitivity. According to local antimicrobial susceptibility trends empiric antibiotic therapy guidelines can be framed. This approach may improve the quality and cost of patient care in the developing world thus minimize misuse of antibiotic & prevent resistance.

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Original Article

Post-tonsillectomy taste distortion: An observational study of 600 cases

Chowdhury NH[a], Islam MA[b], Mohammad T[c], Khan SR[d]

Abstract

Background: Tonsillectomy is a safe procedure in expert hand, but associated with certain complications. One unusual and rare complication is temporary loss of taste sensation. To the best of the author's knowledge, only 29 cases of altered taste associated with tonsillectomy have been previously reported in the literature since 1966.

Objective: To assess frequency of post-tonsillectomy taste distortion in different surgical techniques of tonsillectomy.

Method: This observational study carried out in Bangladesh Medical College Hospital over a period of 10 years from 2011 to 2020. Operation, follow up and assessment of patient done in dept. of ENT Bangladesh Medical College hospital. Study population were young adult. Evaluation period was 1 month to 6 months after operation. Sampling type: Purposive type of non-probability sampling was done to select the patients. Patient who were complaining for taste disturbance after 1 month of tonsillectomy were evaluated.

Results: Total 600 operated patients were assessed under this study. Among them 345 (57.5%) were male and 255 (42.5%) were female. Rate of post-operative transient taste distortion slightly higher in female 65.88% than male patients 58.84% & temporary loss of taste perception in female was 2.35% and male was 0.86%. Taste distortion is higher in cold steel dissection method (1. 18%).Taste distortion rate is higher when operation time exceed than 45-60 minutes and incidence rate is less when operating time became less than 30-45 minutes & there is no loss of taste distortion when operation time less than 20-30 minutes.

Conclusion: Minimizing operation time less than 30 minutes, intermittent release of pressure on tongue by mouth gag and avoiding overenthusiastic dissection beyond lower pole of tonsil can reduce the incidence of post operative taste distortion.

Keywords: Post-tonsillectomy, Taste distortion, Methods of operation, Duration of operation, Heat injury.

Introduction:

Tonsillectomy is one of the most commonly performed procedures in ENT. As with any surgery, head and neck surgeons must be aware of possible complications and their potential effects even though rare. [1] At our center, we have been received several patients in 6-months period with the complaint of taste distortion after tonsillectomy. As many of the surgeons are unaware about such type of complication, there are very few reports in the literature. But long clinical and surgical experience of authors evaluate the exact cause of taste disturbance at per-operative period as- a) Direct injury to lingual branch of the glossopharyngeal nerve branch (LBGN) due to over enthusiastic dissection beyond the lower pole of tonsils and b) microcirculatory compromise to taste receptors as cyanosis occurs due to prolong compression of tongue tissue.[2-3]

We report taste disturbance following tonsillectomy that was performed for chronic tonsillar hypertrophy. During surgery, hypertrophic tonsils were found to be sited deeply into the tonsillar bed, especially at the lower pole of the tonsil. Pathologic examination following tonsillectomy revealed chronic infection at the tonsil, and lymphoid hyperplasia at the lower pole. Depending on the literature data and long surgical experience of authors, possible indirect damage to the LBGN was suspected as the cause of the taste disturbance.[4] This symptom may be reversible within two years after tonsillectomy, but it can also be irreversible. Therefore, tonsillectomy should be performed with minimal trauma to the tonsillar bed, especially when there is pathology extends beyond the lower pole. Such a patient should be informed about the risk of post-operative taste disturbance after tonsillectomy as being one of the

a. Dr. Nazmul Hossain Chowdhury; FCPS
Assistant Professor, Department of Otolaryngology-Head & Neck Surgery, Bangladesh Medical College, Dhaka

b. Dr. Md. Ashraful Islam; FCPS, FRCS
Professor and Head, Department of Otolaryngology-Head & Neck Surgery, Bangladesh Medical College, Dhaka

c. Dr. Tareq Mohammad; FCPS
Assistant Registrar, Dept. of Otolaryngology-Head & Neck Surgery, Popular Medical College, Dhaka

d. Dr. Saif Rahman Khan; FCPS
Assistant Registrar, Department of Otolaryngology-Head & Neck Surgery, National Institute of ENT, Dhaka

Correspondence to:
Dr. Nazmul Hossain Chowdhury; FCPS (Otolaryngology), MBBS
Assistant Professor, Dept. of Otolaryngology-Head & Neck surgery
Bangladesh Medical College
Email: caesar23rd@gmail.com

rare &unusual complication of tonsillectomy.[5] Dysgeusia is impairment or dysfunction of taste sensation is the result of damage to the gustatory pathway. Impaired perception of all tastes is called total dysgeusia and of some selected tastes – partial dysgeusia. Transient post-tonsillectomy dysgeusia (PTD) is a common complaint.[6] Long-lasting PTD is less frequent but has significant consequences on patients' quality of life. The most common cause of reduced sense of taste is rhinitis and other diseases with nasal blockage or coexisting smell disorders.[7,8] Transient taste perception changes seem to be relatively frequent after tonsillectomy. They are mostly manifested by a metallic or bitter taste and generally maintain from 4 days to 2 weeks after the procedure. Persistent dysgeusia may last for 2 years or longer and retreat spontaneously.[9] We report in this article the surgical causes to avoid such a unusual complication that seriously hamper the quality of life of the patient. Our center is a large tertiary level hospital in Bangladesh. We are capable of handling large number of patient volume yearly in ENT & HNS department, operating near about 100 tonsillectomy patients. A study of last 10 years since 2011 to 2020, 600 adult patients underwent tonsillectomy; Among them 9 patient complaints for taste disturbance after 30 days of operation. These patient kept under regular surveillance and monitoring for a period of 6 months. Taste distortion after tonsillectomy documenting by clinical and subjective evaluation.

Materials and Methods:

The clinical course of a patient with taste distortion after tonsillectomy, the gustatory function was investigated by spatial taste testing. Threshold measurements were determined at three left- and three right-side tongue regions: 1) the tongue tip region (innervated by the chorda tympani branch of the facial nerve); 2) the lateral margin of the tongue (anterior to the foliate papillae); 3) the posterior tongue region (innervated by the lingual branch of the glossopharyngeal nerve).

This prospective study carried out in Bangladesh Medical College hospital over a period of 10 years from 2011 to 2020. Operation, follow up and assessment of patient done in dept. of ENT, Bangladesh Medical College hospital. Total 600 operated patients were assessed under this study. Study population were young adults. Patients complaining of post-operative taste distortion after 1 month of operation were included in this study. Patients below 16 years and patients having history of chronic rhinitis, habitual drug intake and diabetes mellitus were excluded from the study. Evaluation period was 1 month to 6 months after operation. Purposive type of non-probability sampling was done to select the patients. Patient who were complaining for taste disturbance after tonsillectomy were evaluated in following manner:

Taste distortion persisted upto 1 month post operatively- Transient taste distortion.

Taste sensation regained within 6 months - Temporary taste distortion.

Taste distortion persisted after 6 months – Permanent taste distortion.

Results:

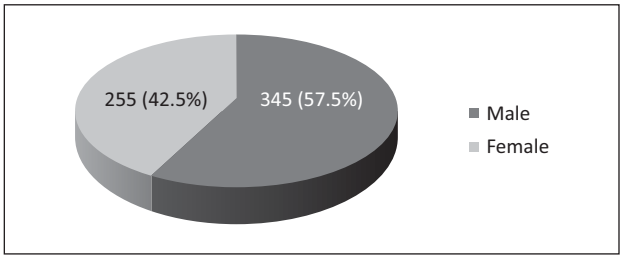

Figure 1: Gender distribution among 600 tonsillectomy patients.

A total 600 tonsillectomy patients were included in this study. Among them 345 (57.5%) were male and 255 (42.5%) were female (Figure 1).

Table 1: Rate of post-operative taste distortion (both transient & temporary)

Sex	No. of patient operated	No. of patient complaint of transient taste distortion	No. of patient with temporary loss of taste perception
Male	345	203 (58.84%)	3(0.86%)
Female	255	168(65.88%)	6(2.35%)
Total	600	371(61.83)	9(1.50)

Rate of post-operative transient taste distortion slightly higher in female 65.88% than male patients 58.84% & temporary loss of taste perception in female was 2.35% and male was 0.86% (Table 1).

Table 2: Methods of operations applied

Methods	No. of patients operated	No. of patients with taste distortion	Percentage
Cold steel dissection	338	4	1.18
Coagulation Diathermy (Bipolar)	196	2	1.02
Snare Dissection	60	0	0
Coblation surgery	6	0	0

Taste distortion is higher in cold steel dissection method (1.18%)as shown in Table 2.

Table 3: Time range of operation required

Operation time	No. of patient with taste distortion
20-30 minutes	0
30-45 minutes	1
45-60 minutes	2

Table 3 shows higher taste distortion in 45-60 minutes' operation time, less in 30-45 minutes & there is no loss of taste distortion in 20-30 minutes' operation time.

Discussion:

Regardless of the etiology, most cases of post-tonsillectomy dysgeusia spontaneously resolves within a few months without any specific intervention. Post-tonsillectomy taste dysgeusia may result from surgical injury, tongue compression, inflammatory processes.[10] In this article authors emphasis the taste distortion as a complication after tonsillectomy to make head and neck surgeons aware of this serious complication and to rule out the surgical causes of taste distortion. As one of the most important special senses, correct perception of taste determines proper physical and mental function.[11] Taste distortion after tonsillectomy is rarely reported as a complication but has a significant impact on quality of life of patients such as depression. Stathas et al and Scinska et al claim that both taste and smell are responsible to a large extent, for the food selection, affect human nutritional status, and their dysfunction can lead to diseases such as depression.[12,13] Among the 371 outpatients complaining of taste disturbance whom we have treated at our center in the last 10 years, 9 (1.5%) were found to be suffering from temporary taste distortion triggered by tonsillectomy. Among these 9 cases, the taste disturbance in 6 cases caused by direct or indirect damage to the lingual branch of the glossopharyngeal nerve, whereas in another 3 cases taste disturbance initiated by tonsillectomy but actually caused due to prolong compression of tongue by boyle's Davis mouth gag (Table 2 & 3). It is therefore important that patients must be informed regarding the risk of post-operative taste disorder following tonsillectomy, at the time of informed consent for tonsillectomy is obtained. It is equally important to ask the patients what drugs, if any, they take habitually.[12] In this study we found the incidence of taste distortion is slightly higher in female (Table 1). The exact cause cannot be evaluated and needs further more study. We also found use of unipolar diathermy at lower pole of tonsils during haemostasis is directly related to transient taste distortion. It is due to heat eviction and electro caution to lingual br. Of glossopharyngeal nerve (Table 2). This observational study was undertaken to evaluate the incidence of post tonsillectomy dysgeusia and its relationship to extension of surgical wound, surgical technique and operating time. Clinical examination include - evaluation of the patient's history and psychophysical testing with cottons soaked in bitter, sweet, sour and salt after 30 days of operation to 6 months following tonsillectomy at a tertiary care research based hospital. Subjective taste dysfunction was registered in 9 patients after 30 days of surgery. In all patients this dysgeusia regressed within 6 months. Routine postoperative follow up at 7th and 14th POD revealed transient taste changes developed in more than 58-65 % of patient but > 95% recovered within 30th POD (Table 1) probably due to complete wound healing and resolution of surgical edema. Investigated factor such as operating time, or hemostatic technique with unipolar diathermy, time for wound healing were also associated with the occurrence of transient taste disturbance. Transient taste perception changes seem to be relatively frequent after tonsillectomy. Actual measurement of the distance between the lingual branch of the glossopharyngeal nerve, which controls taste in the posterior portion of the tongue, and the lower pole of the palatine tonsil, using a cadaver, showed the distance to be only 2-4 mm, thereby suggesting the danger of direct or indirect disturbance of this nerve by tonsillectomy.[13] According to world literatures this complaint occurs anywhere from 0.3% to as high as 9% of tonsillectomy cases that supports the incidence occurs in our study. According to Donna Petrozzello et all and literature published on Acta Otolaryngology dysgeusia after tonsillectomy is felt to be due to a number of different surgical causes-a) massive tongue compression>30 minutes. b) Injury to lingual branch of glossopharyngeal nerve. These findings also support evaluated findings in our study. Some researchers like Leong SC et al[14] and Hanna Temporale et al[9] suggested that meticulous cold steel dissection of tonsils and limited use of electro cautery to the lower pole of tonsils, limit damage to the throat muscles and consequently reduce the risk of destruction to branches of the nerves responsible for the reception of taste sensations. These two researcher also recommend careful fixation and release of tongue retractor intermittently that reduce circulatory jeopardy to sensory nerve ending of taste buds. Prolonged tongue depression from a mouth gag that's inserted during tonsillectomy could bring greater potential especially in adults.[14] Tonsillectomies in adults often take longer duration, because the tonsil tissue tends to be more scarred down, and the operation tends to be bloodier that makes the lingual br. of glossopharyngeal nerve more vulnerable to injury.[14] Gustatory symptoms can occur even after uneventful tonsillectomy. We tried not to press the tongue for too long, If the surgery is taking a little longer duration, we took the patient out of the mouth gag and let their tongue rest a little bit, get the blood flow going and then re-suspend them.

Conclusion:

Authors observation is not to dissect hypertrophied tissues beyond the lower pole of tonsils to avoid injury to lingual branch of glossopharyngeal nerve as it lies within very close perimeter to lower pole tonsils (2-3mm). Tonsillar tissue remain in lower pole after cold steel dissection of tonsils should be cauterized superficially with bipolar diathermy. This procedure reduces the incidence of post tonsillectomy taste distortion. Our long surgical experience

and observation also observed reduced operation time less than 30 minutes and release the pressure of mouth gag over tongue intermittently, prevent circulatory jeopardy to sensory nerve ending of taste buds. In our center we are following such technique and rate of incidence significantly reduced for the last few years.

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Evaluation of clinical profiles and radiologicalimaging of Tuberculous Meningitis patients in a tertiary care hospital in Dhaka city

Saber S[a], Alam RF[b], Hossain MM[c], Islam MR[d], Alam MT[d]

Abstract

Background: Tuberculous meningitis (TBM) is associated with significant mortality and morbidity if it is not promptly identified and treated. One of every 300 untreated pulmonary tuberculosis cases is complicated with TBM. In developing and poor resourceful countries like Bangladesh TBM diagnosis is still challenging and difficult.

Objective: To evaluate the clinical profiles and radiological imaging of TBM patients attending in a tertiary care hospital in Dhaka city.

Methods: This hospital based cross sectional study was done at indoor and outdoor departments of Medicine in Bangladesh Medical College Hospital, Dhanmondi, Dhaka, Bangladesh. A total of 116 diagnosed patients of TBM were included in this study from January 2018 to December 2022. A pretested questionnaire was used for data collection. Demographic profiles, clinical features, laboratory findings, radiological features were collected from the patient's records. Data analysis was done in SPSS version 16.0.

Results: We found that tuberculous meningitis was predominant in males (58%) with predominant age group of 18-25 years (40.52%). Among various clinical manifestations the predominant features were fever (100%) followed by headache (92.24%). Duration of TBM presentation was 10-15 days (59.48%) but presentation after 30 days usually less (16.38%) but these patients presented with more complications. Majority (66.38%) our patients presented to us at the stage 2 according to the BMRC criteria. Most common CT scan findings among our TBM patients were basal enhancement (50.86%), hydrocephalus (19.83%) followed by tuberculoma (7.76%). Although among 9.48% patients had normal CT Scan findings. Among the 63 TBM patients with abnormal chest x -ray findings, the majority showed parenchymal infiltration (77.78%), cavitary lesions (6.35%), pleural effusion (14.29%) and miliary pattern (1.59%). There were no mortality records during our study period

Conclusion: TBM is a complicated form of extrapulmonary TB which needs to be identified promptly correctly otherwise it accounts for significant morbidity and mortality. In our study we tried to evaluate the clinical profiles and radiological imaging so that it can guide us further to diagnose and treat the TBM cases accurately.

Keywords: Tuberculous meningitis, Clinical profile, Radiological imaging, CSF

a. Dr. Sadia Saber; MBBS, FCPS, MRCP (UK), MRCP (Ireland), MRCP (Glasgow)
Assistant Professor, Department of Medicine
Bangladesh Medical College, Dhaka.

b. Dr. Rafa Faaria Alam; MBBS
Registrar, Department of Medicine
Bangladesh Medical College.Dhaka.

c. Dr. Mohammad Monower Hossain; MBBS
Medical Officer, Department of Medicine
Bangladesh Medical College Hospital, Dhaka.

d. Dr. MD. Rafayel Islam; MBBS
Assistant Registrar, Department of Medicine
Bangladesh Medical College Hospital, Dhaka.

e. Prof. Dr. Mohammad Tarek Alam; MD (USA), MBBS
Professor & Head, Department of Medicine
Bangladesh Medical College, Dhaka.

Correspondence to:
Dr. Sadia Saber; MBBS, FCPS, MRCP (UK), MRCP (Ireland), MRCP (Glasgow)
Assistant Professor, Department of Medicine
Bangladesh Medical College
Email: sadiasaber201477@gmail.com

Introduction:

Tuberculosis is remaining as one of the top 10 causes of death worldwide. Till now 2 billion people were infected with TB among which 1.3 billion people belonged from developing countries. According to that majority of TB patients belonged from Southeast Asia (44%), Africa (24%) and Western Pacific region (18%). Two-thirds of the total global cases of TB were accounted in 8 countries, that is, India (27%), China (9%), Indonesia (8%), Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%), and South Africa (3%).[1] Among various forms of extrapulmonary TB, TBM always considered as complicated ones as without prompt diagnosis and treatment patient may result in significant mortality and morbidity. TBM accounts for 5-15% of extrapulmonary TB and has become the commonest type comprising 70% cases of TB affecting neurological system.[2]

Among various type of central nervous TB, TBM has been always considered as the most prevalent one with increased number of neurological events as well as high mortality if

not promptly diagnosed and treated. Moreover, the duration of treatment is also prolonged that's why many patients became reluctant and the dropped the medications in the middle of the course which creates another problem with development of other serious complications like multidrug resistant TB specially in the developing countries.[3-7]

In a high TB burden country like Bangladesh TBM should be ruled out in all the patients presenting with fever, headache and altered sensorium otherwise it will be difficult for us to correctly identify and treating the cases of TBM in a short period of time. In this study we tried to focus more on the clinical profiles and radiological findings of our patients presented to us with the features of TBM after fulfilling the inclusions and exclusions criteria.

Materials and Methods:

This is cross sectional study was carried out on 116 confirmed cases of TBM from both inpatient and outpatient dept. of Medicine and allied departments of Bangladesh Medical College (BMCH), Dhanmondi, Dhaka, Bangladesh. The study was carried out for 5 years from January 2018 to December 2022. The study was carried out after obtaining approval from the Institutional Ethical Committee. A total number of 116 patients were included in the study within this 5 years' study period. Cases were selected fulfilling the inclusion and exclusion criteria.

Clinical diagnostic criteria of TBM includes- i) Symptoms duration more than 7 days; ii) Systemic features suggestive of TB; iii) Close contact in patients with TB; iv) Presence of focal neurological deficit; v) Cranial nerve palsy and vi) Altered level of consciousness

Diagnostic Criteria for TBM includes-i) Presence of *Mycobacterium tuberculosis* within cerebrospinal fluid (CSF); ii) Detection of acid-fast bacilli (AFB) on microscopy, iii) Molecular techniques such as nucleic acid amplification test (NAAT).

CSF findings suggestive of TBM includes- i) Appearance of CSF is turbid; ii) Protein level more than 1g/L; iii) CSF to plasma glucose ratio of less than 50% or an absolute CSF glucose concentration is less than 2mmol/L; iv) Cell count analysis revealed Lymphocytic predominance; v) CSF Adenosine deaminase (ADA) level 10 or more than 10IU/L.

Cerebral imaging criteria suggestive of TBM includes- i) Hydrocephalus; ii) Basal meningeal enhancement; iii) Tuberculoma; iv) Precontrast basal hyper density and v) Infarct.

Evidences of tuberculosis elsewhere during the presentation of TBM are- Chest X-ray suggestive of active pulmonary TB and radiological evidence of milliary TB.

Exclusion Criteria included- i) Patients presented with features of meningitis other than TBM like subarachnoid hemorrhage, viral encephalitis, brain abscess and intracerebral bleeding**;** ii) Patients not willing to participate in the study.

Data Collection Procedure

Demographic profiles, clinical features, laboratory findings, radiological features were collected from the patient's records. Diagnostic timing categorized as the admission to the hospital due to suggestive clinical symptoms and the starting of anti-tubercular therapy. Clinical severity during admission was assessed by the British Medical Research Council (BMRC) staging system for TBM as mentioned below;[8]

Grade I: Corresponds to alert and oriented patient without any focal neurological deficit

Grade II: Glasgow coma scale 11 to 14 or 15 with focal neurological deficit

Grade III: Glasgow coma scale 10 or less with or without focal neurological deficit.

Radiological imaging included chest X- ray and cerebral imaging when available were collected from the data records.

Statistical Analysis

Data were recorded into semi-structured pre-tested questionnaire. It was entered into Microsoft Excel and analyzed using SPSS v 16.0. Summarization of data was done according to data types and appropriate statistical tests were done. The various modes of clinical presentation were expressed as the total number of patients presenting with a particular presenting feature and then calculated as a percentage of the total number of patients. Statistical analysis was done by using appropriate statistical tool like 'chi-square' test, student 't' test, where applicable. A p-value of <0.05 was statistically significant and p-value of > 0.05 was considered not significant statistically.

Results:

Table 1: Age group distribution of the study population (n=116)

Age group (years)	No. of patients (n=116)	Percentage (%)
18-25	47	40.52
26-40	35	30.17
41- 60	23	19.8
>60	11	38.73
Total	**116**	**100**

Table 1 shows majority (40.52%) of our study population belonged from the age group 18-25 years and 30.17% were in 26-40 years' age-group.

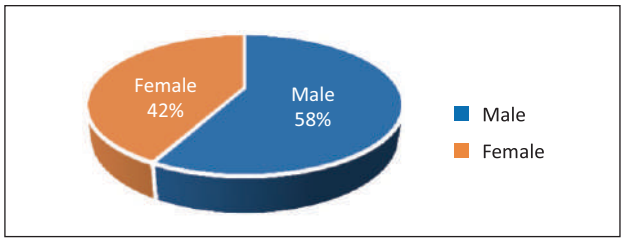

Figure 1: Gender wise distribution of the study group

Figure 1 shows predominance of male (58%) patients than females (42%).

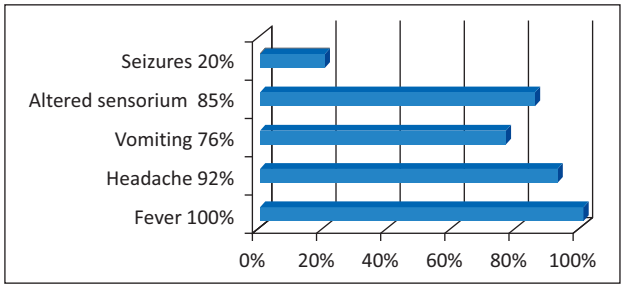

Figure 2: Clinical presentations of TBM patients

Figure 2 shows that 100% of our study population had fever followed by headache (92.24%). Only 19.83% patients presented with seizure as well along with other symptoms.

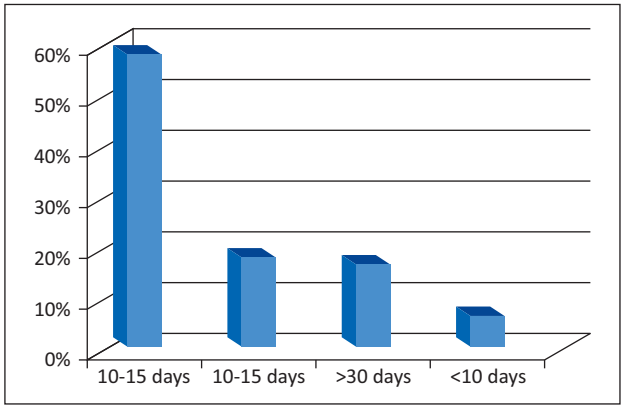

Figure 3: Duration of symptoms of TBM cases

Figure 3 shows most of the patients 69(59.48%) presented to us within 10-15 days of symptoms onset. Presentation after 30 days usually less (16.38%) but these patients presented with more complications.

Table 2: BMRC criteria for staging in our TBM patients (n = 116)

Stage	No of patients	Percentage (%)
Stage I	30	25.86
Stage II	77	66.38
Stage III	9	7.76
Total	**116**	**100**

Table 2 shows majority 77(66.38%) our patients presented to us at the stage-II according to the BMRC criteria.

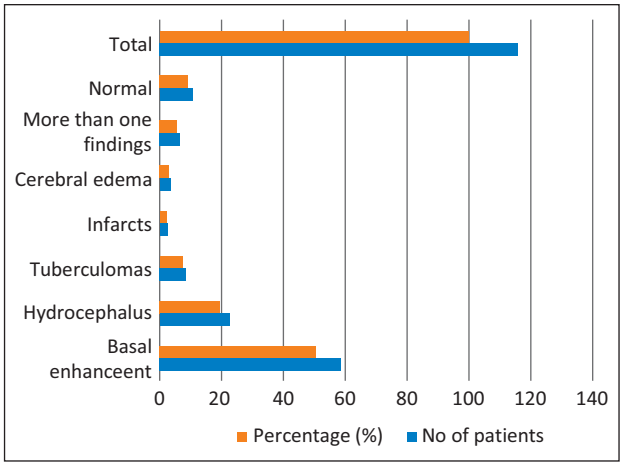

Figure 4: CT Scan findings among TBM patients

Figure 4 shows most common CT scan findings among our TBM patients were basal enhancement (50.86%), hydrocephalus (19.83%) followed by tuberculoma (7.76%). Although among 9.48% patients had normal CT Scan findings.

Table 3: Chest X-ray Findings among TBM patients (n= 63)

Features of abnormal Chest X-ray	No. of patients	Percentage (%)
Parenchymal infiltration	49	77.78
Pleura l effusion	9	14.28
Cavitary lesions	4	6.35
Military pattern	1	1.59
Total	**63**	**100**

Most of our patients had chest X- ray as a routine investigation. Among 63 TBM patients (54%) had findings on their routine Chest-X ray. The findings which were predominant among our TBM patients: parenchymal infiltration (77.78%), pleural effusion (14.29%), cavitary lesions (6.35%) and miliary pattern (1.59%) as shown on Table 3.

Discussion:

TBM always consider as an extremely serious disease. Majority (66.38%) our patients presented to us at the stage 2 according to the BMRC criteria (Table-2). There are several researches which have got the similar findings.[9,10] Most of the patients (59.48%) presented to us within 10-15 days of symptoms onset (Fig-3). Presentation after 30 days usually less (16.38%) but complications were more predominant among these group. Some previous studies reported about duration of symptoms more than one week which was consistent with subacute meningitis.[11-13]

The most common clinical presentation in our study were fever, headache, vomiting and altered sensorium. Other studies also got the similar presentations among their TBM patients[15]. About 7.76% patients presented with alarming features in stage III as per BMRC criteria (Table-2). These alarming features are usually attention seeking in contrast to stage I illness with nonspecific presentation which are usually overlooked both by the patients and the caregivers. Apart from various clinical presentation and complications, in developing countries the lack of adequate health care coverage and the weakness of the healthcare system led patients to delay their approach to the hospitals due to the financial burden among the patients. This can be used to explain the delay in admission of TBM patients.

The diagnosis of TBM often create difficulty and dilemma among the health professionals as this dreaded infection can mimic a good number of other CNS diseases.[14] Goodhart and Still mentioned that experience makes it even more clear how tremendous the disease is and how impossible it is not to err in some cases.[15]

Among 63 TBM patients (54%) had findings on their routine chest X-ray (Table-3). Predominant findings among our TBM patients: parenchymal infiltration (77.78%), cavitary lesions (6.35%), pleural effusion (14.29%) and miliary pattern (1.59%). Although Chest X- ray suggestive of active pulmonary TB or radiological evidence of miliary TB patients may present with aseptic meningitis but its absence does not rule it out completely. In a developing country like Bangladesh CSF analysis always plays the pivotal role in the diagnosis of TBM but PCR of the CSF fluid is a difficult test to perform in all cases and only available in tertiary health care centers.[16] Here, we tried to detect high ADA level in the CSF[17] fluid to diagnose it as TBM as well as low CSF glucose and elevated protein were the characteristic abnormalities found in TBM. CSF may be normal in rare cases in where the disease has been definitively diagnosed.[18] Low CSF glucose level were found among 89% of patients in another study.[19]

In this study most common CT scan findings were basal enhancement (50.86%), hydrocephalus (19.83%) followed by tuberculoma (7.76%). Although among 9.48% patients had normal CT Scan findings. Most of the intracranial abnormalities can be visible to the naked eyes through computed axial tomographic scanning with contrast and magnetic resonance imaging. Kingsley DP et al found marked ventricular enlargement associated with extensive basal enhancement. Sometimes radiological abnormalities develop during treatment and does not resolve completely.[20]

Conclusion:

From this study, we concluded that the complications of TBM could be overcome by the early clinical suspicion in a suitable clinical setting followed by CSF analysis. CT scan of brain can be used as the best available diagnostic tool to strengthen the clinical suspicion specially if there is some evidence for extracranial TB. Most importantly, health awareness among general population, proper education, funding and campaigning need to be implemented and redirected to halt the predisposition and propagation of this dreaded disease in developing countries like ours.

Limitations:

As PCR test on CSF is a costly procedure so we couldn't be able to do this in all patients. Moreover, CSF culture and sensitivity is a time-consuming procedure as majority patients in our country presented in later stages where we can't wait for it. As high TB burden country the clinical findings and CSF analysis still play a pivotal role in our management strategy. As our current research has done on a tertiary care teaching hospital in the urban location so it doesn't reflect the exact picture of the entire nation. Moreover, we have not done CSF PCR in all the patients which need to be done soon. More ongoing research need to be accomplished to bring a definitive conclusion in this communicable disease.

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Review Article

Dengue fever in Bangladesh: An updated review

Arefin KE[a], Nahar A[b], Bhuiyan ME[c], Lucky MA[d], Shourov MMH[e], Ali L[f], Haq AI[g]

Abstract

Dengue fever is increasing in Bangladesh, one city after other getting affected, it is very essential to know more about this disease and prevalence, any change in the viral strain, severity of the disease pattern, early detection of the virus and early management of the disease resulting in good recovery. In most of the cases with dengue virus infection remain asymptomatic; however, it can cause a wide spectrum of clinical manifestations from mild febrile illness with spontaneous recovery to hemorrhagic dengue fever (DF) and/or dengue shock syndrome (DSS).International travelling and trading, unplanned urbanization, abundance of vector breeding place, suitable climatic condition for vector breeding and virus transmission as well as inefficient vector control strategies are considered as determinants of current dengue situation in Bangladesh.Measures should be taken to control the aforementioned causes to prevent disease spread and reduce epidemic flare up.

Keywords: Dengue, Flaviviridae, NS1 Protein, DHF, DSS.

Introduction:

Dengue is one of the highest and rapidly spreading vector-borne viral diseases with high mortality rates. Dengue disease is a mosquito-borne viral infection caused by the dengue virus (DENV). It is hyperendemic in tropical and subtropical climates worldwide, with increasing incidence over recent years placing nearly half of the world's population at risk.[1]

Dengue causes a wide spectrum of disease and clinical manifestations ranging from asymptomatic to dengue fever (DF) or severe dengue (SD), including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[2,3] It was estimated that there were 390 million dengue infections per year, of which 96 million manifested symptomatically; additionally, it was estimated that there were 565,900 disabilities and 9110 deaths in 2013.[4,5] According to World Health Organization (WHO), approximately 2.5 billion people living in dengue-endemic countries.[6] Severe & fatal cases were reported in Southeast Asia, the Western Pacific, and the Americas.[7,8,9] Some Asian & Latin American countries reported that mortality rate of DSS is 50 times higher than that of DF, and SD has been a leading cause of serious illness and death among children.[6,10] People develop severe dengue, which can be any number of complications associated with severe bleeding, organ impairment and/or plasma leakage. Severe dengue has a higher risk of death when not managed appropriately. In 1950s during dengue epidemic, severe dengue was first recognized in the Philippines and Thailand. Today, severe dengue affects most Asian and Latin American countries and has become a leading cause of hospitalization and death among children and adults in these regions.[11] SD mortality would reduce from 20% to less than 1% if SD were identified and properly treated timely.[3] Early foresee and recognition of severe cases are critical for dengue disease management.

Global Burden

The number of dengue cases reported to WHO increased over 8-fold over the last two decades, from 505,430 cases in 2000, to over 2.4 million in 2010, and 5.2 million in 2019. Reported deaths between the year 2000 and 2015 increased from 960 to 4032, affecting mostly younger age group. Number of total cases decreased during years 2020 and 2021, as well as for reported deaths. COVID-19 pandemic might have hampered case reporting in several countries.[11]

a. Dr. Khondoker Ehsanul Arefin; MBBS, MPH, MD
Associate Professor, Department of Paediatrics
Bangladesh Medical College, Dhaka.

b. Dr Azizun Nahar; M.Phil, MBBS
Associate Professor, Department of Microbiology
Bangladesh Medical College

c. Dr. Md Elias Bhuiyan; MBBS, MRCP, FCPS
Assistant Professor, Department of Medicine
Bangladesh Medical College, Dhaka.

d. Dr. Mohsina Akter Lucky; MBBS, MPH, MD
Associate Consultant, Department of Paediatrics
MEDIX (United Health Care), Dhanmondi, Dhaka.

e. Maj Md Mehedhi Hasan Shourov; MBBS, DCP, MCPS (Clinical Pathology)
Graded Specialist in Pathology, Armed Forces institute of Pathology, Dhaka Cantonment

f. Dr. Liaquat Ali; MBBS, MD
Associate Professor, Department of Paediatrics
North Bengal Medical College, Sirajganj.

g. Dr. Arman Ibne Haq; MBBS, FCPS (PSY)
Assistant Professor, Department of Psychiatry
Bangladesh Medical College

Correspondence to:
Dr. Khondoker Ehsanul Arefin; MBBS, MPH, MD
Associate Professor, Department of Paediatrics
Bangladesh Medical College, Dhaka.
Email: drarefin@yahoo.com

Bangladesh Situation

Between 1 January and 20 November 2022, a total of 52 807 dengue cases including 230 related deaths (case fatality rate = 0.44%) were reported. The cases were confirmed either by non-structural protein (NS1) diagnostic kits or by Immunoglobulin M (IgM) tests. According to information available for 40% of reported cases (n=20 982) the median age is 25 years (range: 0-89) with males accounting for 60% of the cases. This is the second highest annual number of cases since 2000, the highest having occurred in 2019, when 101,354 cases including 164 deaths were reported. The most affected division is Dhaka, accounting for 70.6% of cases and 60.4% of deaths.[12]

A study done on dengue situation in Bangladesh were analyzed from 2000 to 2017. In total, 40,476 confirmed dengue cases were reported. Two peaks were demonstrated in 2002 and 2016. Maximum number of deaths occurred in 2000, when the dengue cases first emerged in an epidemic form in Bangladesh. Most dengue cases occurred in the monsoon and post-monsoon season. Of all the deaths reported within 2013-2017, more than 70% occurred within 24 hours 24 hours of admission to the hospital & 65% of the deaths were due to complications, such as DSS or DHF It is alarming in terms of case management of dengue-related complications, such as DHF or DSS. In most dengue cases, body temperature usually subsides within 3-5 days and patients are released from hospitals, if admitted. [13] ere reported. Two peaks were demonstrated in 2002 and 2016. Maximum number of deaths occurred in 2000, when the dengue cases first emerged in an epidemic form in Bangladesh. Most dengue cases occurred in the monsoon and post-monsoon season. Of all the deaths reported within 2013-2017, more than 70% occurred within 24 hours 24 hours of admission to the hospital & 65% of the deaths were due to complications, such as DSS or DHF It is alarming in terms of case management of dengue-related complications, such as DHF or DSS. In most dengue cases, body temperature usually subsides within 3-5 days and patients are released from hospitals, if admitted.[13]

Virological features:

Dengue virus (DENV) is a small, spherical, single-stranded RNA virus, belongs to the genus Flavivirus in the family Flaviviridae. Zika virus, West Nile virus and tick-borne encephalitis virus are also included in Flaviviridae family. Three structural and seven non-structural proteins are present in DENV.[14,15]

According to WHO, Dengue has distinct epidemiological patterns, associated with all four serotypes of the virus. These can co-circulate within a region, and indeed many countries are hyper-endemic for all four serotypes. DENV is frequently transported from one place to another by infected travelers; when susceptible vectors are present in these new areas, there is the potential for local transmission to be established.[11] The viruses are maintained in nature in two cycles, a jungle cycle in which several syllabic mosquito species mediate viruses to several species of sub-human primates, and an urban cycle in which the virus is transmitted predominantly by Aedes aegypti to human beings. The dengue viruses are unique in that a single dengue infection may 'sensitize' individuals to severe and fatal disease accompanying infection with a second serotype.[16] Four serotypes of dengue virus- DEN1 to DEN4 depending on differences in the viral structural and non-structural proteins. Due to mutations of the virus, the severity of the infection varies from time to time. Infection with each serotype confers lifelong immunity for the causative serotype, but not for the other serotypes. On the contrary, reinfection with a different serotype causes severe disease. Development of complete herd immunity for all four serotypes in the community is not achievable because periodic outbreaks occur due to different serotypes over decades and the disease may remain without natural elimination.[15-17]

A two years (2015-2017) study reported DEN-1 & DEN-2 serotype were prevalent in Bangladesh.[18] Another study conducted in Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment reflects that, 2021 Dengue epidemic in Bangladesh was caused predominantly by DEN-3 serotype.[19]

Continuous monitoring of dengue virus serotype is important for prevention and control of sudden epidemic by other serotypes.

Vector Ecology:

Dengue is transmitted from person to person via the bite of an infected mosquito. The primary vector Aedes aegypti, a day time feeder; its peak biting periods are early in the morning and in the evening before sunset, breeding in water containers in peri-domestic areas. It could breed in natural containers such as tree holes and bromeliads, but nowadays it breeds in man-made containers including buckets, mud pots, discarded containers and used tyres, storm water drains etc.[20] Eggs could survive without desiccation in dried condition for months and, with the first opportunity of contact with water, the life cycle begins. The second dengue vector is Aedes albopictus which is called “tiger mosquito” due to its characteristic morphology.[21]

Immunopathogenesis:

After a bite from an infected mosquito, initial viral replication occurs in subdermal Langerhans dendritic cells, then the virus migrates to regional lymph nodes. Viraemia occurs through circulating monocytes and macrophages and infects the solid organs and bone marrow.[22] Dengue is a self-limiting infection and majority of patients recover without any complication- designated as dengue fever (DF). Conversely, dengue haemorrhagic fever (DHF) is the severe form, characterized by increased vascular permeability leading to plasma leak and haemorrhagic

tendency. Plasma leaking into peritoneal spaces, the pleural cavity and tissue plains called third spaces due to increased vascular permeability. May be due to the occurrence of an abnormal immune response with cytokine production, also named a cytokine storm which leads to increased microvascular permeability without inflammation or vasculitis and altered thromboregulatory mechanisms.[23]

Antibody-dependent immune enhancement is an increased risk of DHF in the presence of pre-existing DENV antibodies for a different serotype, which are non-neutralizing antibodies. The formed immune complexes are composed of non-neutralizing DENV antibodies for a different serotype attached to current DENV that would have the ability to fix complement and bind to cell surface Fc receptors, facilitating viral entry into macrophages. Exponential viral replication takes place inside the phagocytic cell and development of viraemia. In cases of severe viraemia, the chance of severe DHF is high, even leading to shock- dengue shock syndrome (DSS).[23]

Disease characteristics (signs and symptoms:

While majority of dengue cases are asymptomatic or show mild symptoms, it can manifest as a severe, flu-like illness that affects infants, young children and adults, but seldom causes death. Symptoms usually last for 2-7 days, after an incubation period of 4-10 days after the bite from an infected mosquito.[4] The World Health Organization classifies dengue into 2 major categories: dengue (with/without warning signs) and severe dengue. The sub-classification of dengue with or without warning signs is designed to help health practitioners triage patients for hospital admission, ensuring close observation, and to minimize the risk of developing the more severe dengue. Dengue should be suspected when a high fever (40°C/104°F) is accompanied by 2 of the following symptoms during the febrile phase (2-7 days) which are severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands, rash. In severe Dengue, a patient enters what is called the critical phase normally about 3-7 days after illness onset. During the 24-48 hours of critical phase, a small portion of patients may manifest sudden deterioration of symptoms. It is at this time, when the fever is dropping (below 38°C/100°F) in the patient, that warning signs associated with severe dengue can manifest. Severe dengue is a potentially fatal complication, due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment. Warning signs that doctors should look for includes severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums or nose, fatigue, restlessness, liver enlargement, blood in vomit or stool. If patients manifest these symptoms during the critical phase, close observation for the next 24-48 hours is essential so that proper medical care can be provided, to avoid complications and risk of death. Close monitoring should also continue during the convalescent phase.[4]

Expanded dengue syndrome/Isolated organopathy (unusual manifestations):

Patients with dengue illness can sometimes develop unusual manifestations such as involvement of liver, kidneys, brain or heart with or without evidence of fluid leakage and therefore do not necessarily fall into the category of DHF. These conditions are very rare and management is symptomatic. Such unusual manifestations may be associated with coinfections and comorbidities. However, these manifestations if seen in DHF patients are mostly a result of prolonged shock leading to organ failure.[24]

Stepwise approaches of management of Dengue:

History taking and overall assessment followed by clinical examination and diagnosis of dengue phase and severity, management decision, disease notification, hospital admission and urgent referral are the steps of management of dengue fever.

Laboratory Investigations

Dengue virus infection needs early laboratory confirmation of clinical diagnosis because some patients progress within short period from mild to severe form and sometimes death may occur. Laboratory methods for diagnosis of dengue virus infection includes viral antigen (NS1), antibodies (IgM & IgG), viral nucleic acid and detection of dengue virus, But these biomarkers appear in different time period of the disease for instance NS1 antigen could be detected with good sensitivity (71-100%) till day 3 of fever, NS1 remains positive up to 4 days of onset of fever. Beyond day 4, IgM antibody detection was superior to NS1. In that case only reliable test is viral nucleic acid detection by real time PCR which is costly and accessible in limited health care facilities. Antibody IgG is generally detectable at low titer at the end of first week and remains at detectable level for months or even lifelong.[25] But in case of secondary dengue infection IgG is detectable at acute stage of infection and the titer is higher than IgM thus laboratory confirm dengue infection is the tip of iceberg. Considering the reality more emphasis should be given on clinical assessment and relevant laboratory investigations.[25]

Other tests

Dengue virus Isolation from serum, plasma and leucocytes is the most definitive test for dengue virus infection.[25]

Disease Monitoring Tests

CBC should be done on first consultation of the patient to have the baseline information. Leucopenia is common in both adults and children with DF and has an important diagnostic implication in early period. The change in total white cell count (≤5000 cells/mm3) and ratio of neutrophils to lymphocyte (neutrophils <lymphocytes) is useful to predict the critical period of plasma leakage. This

finding precedes thrombocytopenia or rising haematocrit. These changes seen in DF and DHF both.[26] Thrombocytopenia is observed in some patients with DF. Mild thrombocytopenia of 100000 to 150000 cells/mm3 is common and about half of all DF patients have platelet count below 100000 cells/mm3.A sudden drop in platelet count to below 100000 occurs before the onset of shock or subsidence of fever. The level of platelet count is correlated with severity of DHF.[26]

Haematocrit

Slight increase may be due to high fever, anorexia and vomiting which occur in 10% of cases. A sudden rise in haematocrit is observed simultaneously or shortly after the drop in platelet count. Haemoconcentration or rising haematocrit by 20% from the baseline, e.g. from haematocrit of 35% to >42% is objective evidence of leakage of plasma. It should be noted that the level of haematocrit may be affected by early volume replacement and by bleeding.[25]

Biochemical Tests

Serum AST (SGOT) and ALT (SGPT) levels are frequently elevated with DF and DHF. AST and ALT levels are significantly higher at 5 to 15 times in patients with DHF. Commonly AST is increased more than ALT in these cases. In Special Cases, Hyponatremia is frequently observed in DHF and is more severe in shock. Hypocalcemia has been observed in DHF. Metabolic acidosis is frequently found in cases of prolonged shock. Blood urea nitrogen is also elevated in prolonged shock.[25]

Coagulation Profile

Coagulation failure may occur in DSS. Activated Partial Thromboplastin Time (APTT) and Prothrombin time are prolonged in about half and one third of DHF respectively. Thrombin time is also prolonged in severe cases.[25]

Treatment of Dengue:

Virus specific treatment is not yet available, so early recognition of warning signs of DHF or DSS and immediate intervention with supportive treatment with close monitoring are of utmost importance to reduce case fatality rate. The management Dengue fever is based on severity of presentation. According to the existing WHO classification. Group A includes dengue patients without warning sign. These Patients will be advised to adequate bed rest adequate fluid intake (>6 glasses for an average-sized adult, or accordingly in children)- e.g. milk, fruit juice (caution with diabetes patient), oral rehydration solution (ORS) or barley/rice water/coconut water. Take paracetamol and tepid sponging. Acetyl salicylic acid (aspirin), mefenamic acid, ibuprofen or other NSAIDs, steroids and antibiotics should be avoided.[24] Group B includes patients with warning signs. These are patients who should be admitted for in-hospital management for close observation as they approach the critical phase. Obtain a reference haematocrit before intravenous fluid therapy begins. General principles of fluid therapy in DHF includes both crystalloids and colloids. Crystalloids are 0.9% NaCl (Preferable), 0.45% half strength normal saline solution (For children <6 months), 5% dextrose in lactated Ringer's solution, hartman solution (Preferable). Colloidal solution includes plasmasol, dextran 40, human albumin, Plasma, blood & blood Components. Platelet transfusion is not recommended for thrombocytopenia (no prophylaxis platelet transfusion). The indications are very severe thrombocytopenia who need urgent surgery and clinical judgement of the treating physician. If platelet concentrate is not available fresh whole blood may be transfused. [24] Group C includes severe dengue who require emergency treatment and urgent referral because they are in the critical phase of the disease and have severe plasma leakage leading to dengue shock and/or fluid accumulation with respiratory distress, severe organ impairment (hepatic damage, renal impairment), myocarditis, cardiomyopathy, encephalopathy or encephalitis, severe metabolic abnormalities (metabolic acidosis, severe hypocalcaemia etc).The goals of fluid resuscitation includes improving central and peripheral circulation and urine output ≥0.5 ml/kg/hour or decreasing metabolic acidosis.[24]

Some Important Notes

Treatment of hemorrhagic complications- Source of bleeding should be stopped if identified e.g. severe epistaxis may be controlled by nasal adrenaline packing. Give aliquots of 5-10 ml/kg of fresh- packed red cells or 10-20 ml/kg. of fresh whole blood.[24]

There is no evidence that supports the practices of transfusing platelet concentrates and/or fresh-frozen plasma for severe bleeding in dengue. Transfusions of platelet concentrates and fresh frozen plasma in dengue were not able to sustain the platelet counts and coagulation profile. Instead, in the case of massive bleeding, they often exacerbate the fluid overload. In gastrointestinal bleeding, H-2 antagonist and proton pump inhibitors have been used. It is essential to remember that blood transfusion is only indicated in dengue patients with severe bleeding.[24]

Role of steroid- Basis of DHF pathogenesis is hypothesized to be immunologic that is tempting for immunomodulatory drugs for therapy most common of which is steroid. the evidence for using corticosteroids in dengue is inconclusive and the quality of evidence is low. Beneficial therapeutic effects were seen in some studies, which used high doses or multiple doses of steroids.[27]

Fluid Overload- During the recovery phase the extracellular fluid which was lost due to capillary leakage returns to the circulatory system and signs and symptoms improve. This phase usually after 6-7 days of fever and last for 2-3 days. Excessive fluid replacement and continuation for a longer period after cessation of leakage will cause respiratory distress from massive pleural effusion, ascites, and pulmonary congestion or edema due to fluid overload. This may be dangerous.[24]

In order to ensure adequate fluid replacement and avoid fluid over infusion, the rate of intravenous fluid should be adjusted throughout the 24 to 48 hour period of plasma leakage by periodic HcT determinations and frequent assessment of vital signs. HcT measurement every hour is more important than platelet count during management. If fluid over load occurs in early convalescence phase, Dextran & Furosemide are given. If it happens in reabsorption phase (>36 hours after shock) only Furosemide is given.[24]

Discharge Criteria

No fever for at least 24 hours without the usage of antipyretic drugs, at least two days have lapsed after recovery from shock, good general condition with improving appetite, normal HcT at baseline value or around 38-40% when baseline value is not known, no distress from pleural effusions, no ascites, platelet count has risen above 50,000/mm3 with no other complications.[24]

Prevention of Dengue

Everybody should remember "4S" in the fight against dengue. "4S" stands for "Search and destroy" mosquito breeding sites, cleaning and covering water storage, keeping surroundings clean; "Secure self-protection measures" like wearing long pants and long-sleeved shirts, and daily use of mosquito repellent, hospitalized patients should be kept under mosquito net during febrile phase even during day time; "Seek early consultation"; and "Support fogging/spraying.

Care provider's role in educating the patients and attendants during clinical management has an important value for increasing awareness for Dengue/DHF control. Community awareness should be done through mass media campaign. The recombinant live-attenuated first licensed dengue vaccine (Dengvaxia) recently became clinically available. But high risk of adverse outcomes was found among vaccinated individuals who had not been previously exposed to dengue.[28,29]

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Case Report

Tubercular Appendicitis: A rare cause of a common disease

Rahman SA[a], Chowdhury RA[b], Hasan SK[c], Ahmed N[d]

Abstract

Tuberculosis of the vermiform appendix is extremely rare even in tuberculosis endemic areas. It can occur as a primary or secondary infection. Commonly it is associated with ileo-caecal or peritoneal disease. The disease can be acute, chronic or latent type. Laboratory findings of tuberculous appendicitis are non-specific. Since there are no clinical and radiological features that are pathognomonic of tubercular appendicitis. Suspicion is usually per-operatively and diagnosis confirmed by histopathological examination. Surgery followed by standard anti-tubercular therapy is the treatment.

Here we present two cases of tubercular appendicitis. The first case presented with features of recurrent appendicitis and the second patient presented with post-appendicectomy chronic discharging sinus.

Introduction:

Tuberculosis (TB) of the vermiform appendix is extremely rare even in TB endemic areas.[1] William J Mayo had observed in 1914: "It was curious that the appendix, which contained abundant lymphoid tissue analogous to that of the tonsils and Peyer's patches of ileum, was seldom the primary seat of tuberculosis".[2] Appendicular TB can occur as a primary or secondary infection. Primary lesion is by infection of the intestinal mucosa by M. bovis; secondary infection is usually a consequence and complication of primary pulmonary TB by M. tuberculosis. Prevalence of primary tubercular appendicitis varies from 0.1% to 3.0% of all appendectomy specimens and secondary tubercular involvement in the case of diagnosed TB is 1.5–30% in previous literatures.[3] Most commonly TB of appendix is associated with ileo-caecal or peritoneal disease.

Case Presentation:

Case 01

A 14-year-old female patient was admitted with moderate right lower abdominal pain, nausea and vomiting for 10 days. She had occasional cramping abdominal pain associated with low grade fever for 2 months. She did not have any cough, night sweats or weight loss. Her bowel habit was normal.

a. Dr. Saber Aminur Rahman; FCPS, MBBS
Assistant Professor, Department of Surgery
Bangladesh Medical College Hospital.

b. Prof. Riaz Ahmed Chowdhury; FCPS, MBBS
Professor and Head, Department of Surgery
Bangladesh Medical College Hospital.

c. Dr. Syed Khalid Hasan; FCPS, MRCS, MBBS
Associate Professor, Department of Surgery
Bangladesh Medical College Hospital.

d. Dr. Nabila Ahmed; MBBS
Registrar, Department of Surgery
Bangladesh Medical College Hospital.

Correspondence to:
Dr. Saber Aminur Rahman; FCPS, MBBS
Assistant Professor, Department of Surgery
Bangladesh Medical College Hospital.
Email: saber.rah@gmail.com

On admission she was mildly febrile with mild tachycardia and normal blood pressure. Per-abdominal examination revealed moderate tenderness in right lower abdominal with maximum tenderness in Mcburney's point and positive rebound tenderness. She had clear bilateral lung fields and other systemic examinations also revealed normal findings. She was clinically diagnosed as a case of Recurrent Appendicitis.

Haematological investigations reveled total count of white cells 10,000 /cumm of blood, with 68% neutrophils, 22% lymphocytes and an ESR of 70 mm in 1st hr. Her routine urine examination showed no abnormalities. Ultrasound showed an ill-defined complex area measuring 28x24 mm with surrounding mild collection in the RIF and inflamed surrounding bowel loops with the impression of a developing appendicular lump.

Since clinically no palpable lump was present per-abdominally Appendicectomy was planned. On opening the abdomen with Lanz incision there were numerous whitish seedlings over the parietal peritoneum, omentum and small intestines with enlarged mesenteric lymph nodes. Mild adhesion was present between the terminal part of ileum and caecum with surrounding omentum. Appendix was moderately inflamed and oedematous. After adequate adhesiolysis appendicectomy was done and biopsy taken from whitish seedlings and a mesenteric lymph node.

Histopathological examination of resected appendix, mesenteric lymph node and omental tissue showed epithelioid cell granulomas with caseous necrosis, consistent with tuberculous granulomatous inflammation. Standard four drug anti-tubercular therapy was started and given for six months. Her recovery was uneventful. Stitches were removed on tenth post-operative day. One month and six months' follow-up were unremarkable.

Case 02

A 40 years old female was admitted with a discharging sinus from her operative scar following open appendicectomy outside Dhaka 3 months back. Histopathological examination of her appendix and omental tissue showed

multiple caseating and non-caseating granulomas composed of epithelioid cells, consistent with tuberculosis. Post-operatively there was wound dehiscence with foul smelling yellowish discharge from the wound. She was re-admitted locally and following wound debridement, she was hospitalized for almost one month for regular dressing. The wound dehiscence healed partially and she was discharged with a non-healing wound with mild sero-purulent discharge with which she was admitted to Bangladesh Medical College Hospital for further management. She did not have any cough, fever or history of weight loss.

Haematological investigation on admission revealed total count of white blood cells was 5,520 /cumm of blood with 48% neutrophils, 45% lymphocytes; haemoglobin was 11.50 g/dl and ESR 55 mm in 1st hr. Wound discharge for culture and sensitivity showed E. coli growth but negative for acid fast bacilli. Her chest X-ray was normal and sputum was also negative for acid fast bacilli.

She received standard four drug anti-tubercular therapy. Regular dressing of her wound continued till discharge became scanty and eventually ceased with subsequent healing of the wound by secondary intention. On six months' follow-up her recovery was satisfactory.

Discussion:

TB is a major global health concern. Abdominal TB is the infection of the peritoneum, hollow or solid abdominal organs, and abdominal lymphatics with Mycobacterium organisms. The estimated incidence of abdominal TB is 1-5% of all cases of TB worldwide.[4] Appendicular TB can occur as a primary or secondary infection. Primary lesion is by infection of the intestinal mucosa by Mycobacterium bovis; secondary infection is usually a consequence and complication of primary pulmonary TB by Mycobacterium tuberculosis. Incidence of primary TB of appendix is very rare, ranging from 0.1% to 3% of all appendectomies.[5] Secondary tubercular appendicitis is reported in 1.5-3% of cases.[5]

It was first recognized by Corbin in 1873.[6] Rarity of appendicular involvement is likely due to minimal contact of appendicular mucosa with the intestinal contents. Pathology of tubercular appendicitis has been explained in different literatures by hematogenous spread, extension from adjacent ileocecal TB, spread by infected intestinal contents, lymphatic spread from distant gastro-intestinal lesions, peritoneal spread, and rarely genito-urinary tract.[7] Tubercular appendicitis is a disease of young adults and females have been found to be more commonly affected than males.[8] Tubercular appendicitis may present in three clinical forms: acute, chronic, or latent. The acute form may be indistinguishable from acute suppurative appendicitis and occurs due to pyogenic infection superimposed on the tubercular appendicitis. This type of presentation is seen during the quiescent phase of pulmonary tuberculosis, if present. The chronic form is more common, and usually present with the recurrent attack of abdominal colic, diarrhoea, and vomiting. The latent type is discovered on histopathology of an incidental appendicectomy.[9]

There are no clinical, radiological or sonological features that are pathognomonic of tubercular appendicitis. So diagnosis is usually made after histopathological examination of the appendicectomy specimen. Histological examination with routine hematoxylin-eosin stain reveals a typical granulomatous inflammation with caseation necrosis. Based on histopathological structure tubercular appendicitis has historically been described as ulcerative (commonest form), hyperplastic and ulcero-hyperplastic form.[10] Other causes of granulomatous inflammation of the appendix, termed by some authors as granulomatous appendicitis, include Yersinia pseudotuberculosis, Crohn's disease, Sarcoidosis and foreign body-induced granuloma.[11]

Mycobacterial culture is the gold standard test for diagnosing tuberculosis but is time-consuming. Standard cultures can take 2 to 6 weeks for Mycobacterium tuberculosis complex to grow. Ziehl-Neelsen (ZN) stain is a further test to confirm the acid-fast bacilli but ZN stain is less sensitive and could give a false negative result. Polymerase chain reaction (PCR) of tissue specimen for identification of the Mycobacterium can be helpful in confirming a diagnosis of tuberculosis when ZN staining is negative.[12] An enzyme-linked immunospot assay (ELISPOT) and PCR assay (GeneXpert MTB/RIF) are novel, rapid, noninvasive test for Mycobacterium detection.[13,14]

Surgery followed by anti-tubercular therapy is the treatment of choice. Corticosteroid may be required if associated with peritoneal TB. Standard anti-TB treatment with four anti-tuberculous drugs: Isoniazid 5 mg/kg/day, Rifampicin 10 mg/kg/day, Pyrazinamide 30 mg/kg/day, and Ethambutal 20 mg/kg/day for two months followed by Isoniazid and Rifampicin for 4 months.

Conclusion:

Tubercular appendicitis is a rare cause of a common disease. In tuberculosis endemic areas, there should be a high index of suspicion if per-operative findings are evocative and should be confirmed or excluded by histopathological examination of the resected specimen of the appendix as well as any lymph node, omental or peritoneal tissue.

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Crusted Scabies: A case report

Khanam R[a], Jahan F[b]

Abstract

Crusted Scabies is a skin condition caused by a tiny burrowing mite called Sarcoptes scabiei, also known as Norwegian scabies. Crusted scabies mostly differs from normal scabies by the exuberance of its lesions, body distribution and high contagiousness, requires different and more prolonged treatment. We are presenting a rare case of 15-year-old girl with an almost 6-year history of pruritic, thickened patches, papule and plaque which was diagnosed as crusted scabies. Treatment can be challenging and effective management of the condition requires a karyolitic agent in conjunction with a scabicidal agent.

Keyword: Crusted scabies, Parasitic disease, Itch mite infestation.

Introduction:

Crusted scabies, also called Norwagian scabies as it was first described in Norway by Danielssen and Boek in the mid-19th century as a different type of scabies infestation caused by millions of mites in patients with leprosy.[1] Scabies has spread globally, mainly in tropical populations and impoverished regions, as well as in areas with limited healthcare resources. The World Health Organization (WHO) estimates there are 200 million scabies cases at any time globally and Indonesia has the greatest scabies burden among 195 countries.[2]

A more severe of scabies is called crusted scabies. Crusted scabies is most frequently reported in immuno-compromised, malnourished, and disabled individuals, as well as in patients with systemic or potent topical glucocorticoids, organ transplant recipients, human immunodeficiency virus (HIV)- infected or human T-lymphocytic virus-1 (HTLV-1)-positive individuals, and patients with hematologic malignancies.[3,4] Complications like secondary impetigo, cellulitis, and sepsis with a high mortality rate occur due to delayed diagnosis and treatment.[2]

Crusted scabies mostly differ from classic scabies by the exuberation of the lesion and characterized by large thick crusted lesions, generalized grey scales, thick hyperkeratinized compared to typical inflammatory papule and vesicle of classic scabies.[4]

a. Dr. Rehana Khanam; M. Phil (Path), MBBS
Associate Professor, Department of Pathology
Bangladesh Medical College, Dhaka

b. Dr. Fauzia Jahan; M. Phil (Path); MBBS
Professor (CC), Department of Pathology
Bangladesh Medical College, Dhaka

Correspondence to:
Dr. Rehana Khanam; M. Phil (Path), MBBS
Associate Professor
Department of Pathology
Bangladesh Medical College, Dhaka
Email: rehana-khanam@hotmail.com

Early and accurate diagnosis, effective medical management of patients and healthcare settings, and specific principles and strategies for disease management are required to prevent the spread of the disease in communities.

We are presenting a rare case of 15-year-old girl with an almost 6-year history of pruritic, thickened patches, papule and plaque which was diagnosed as crusted scabies.

Case Presentation:

A 15-year-old girl from Barura, Comilla was referred to our Dermatology Clinic and Pathology Lab for confirmation of clinical diagnosis of psoriasis. The patient received multiple topical treatment, different drugs as well as homeopathic for 6 years by general practitioner, pharmacy attendants, homeopathic doctors and the disease was gradually increasing and became generalized. Her menarche started at 12 years of age with regular cycle. There is no family history of such a disease.

On dermatological examination, she had foul smelling scaly, thickened, patch, papules and plaque with overlying scaling distributed over the scalp, middle of the posterior trunk, both upper and lower extremities (Fig: Ia & Ib). Lesions were bilaterally symmetrical and more pronounced over flexures especially finger webs, wrist, cubital fossa, axilla. Scales could not be easily removed and after removal base of the lesion were slightly erythematous. The lesion was pruritic. Clinically the case resembles psoriasis. She had sparse scalp hair. Her blood pressure was 110/70 mm of Hg. and pulse 78/min. following that day patient improved dramatically.

Fig. 1: Patient of crusted scabies

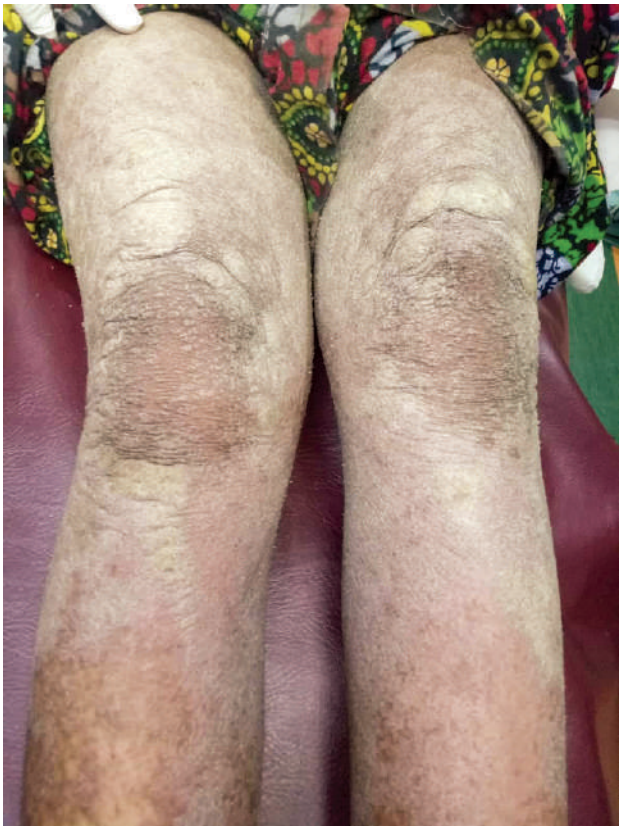

Fig. 1b: Patient of crusted scabies

On investigation, laboratory diagnosis revealed haemoglobin 11.4%, ESR 42 mm (1st hour), total count of WBC-11,800/cmm. Differential count of WBC showed neutrophils 78%, lymphocytes 15%, monocytes 01%, eosinophils 06%, basophils 00%, circulating eosinophils 708/mm. Biochemical report showed S. Bilirubin-10.3mg/dl, HBA1c - 3.80%, SGPT(ALT)-12.0 U/L, SGOT(AST)-18.0/L, S. Alkaline Phosphatase- 107.0U/L. Skin biopsy was taken from the thick, scaly, crusted white plaques. The epidermis showed massive hyperkeratosis (Fig 2). The sub-corneal layer contained numerous eggs, scyballa and mites of sarcopte scabies var hominis (Fig 3 & 4). The dermis showed dense chronic inflammatory infiltrate including few eosinophils. The patient subsequently was diagnosed as crusted scabies.

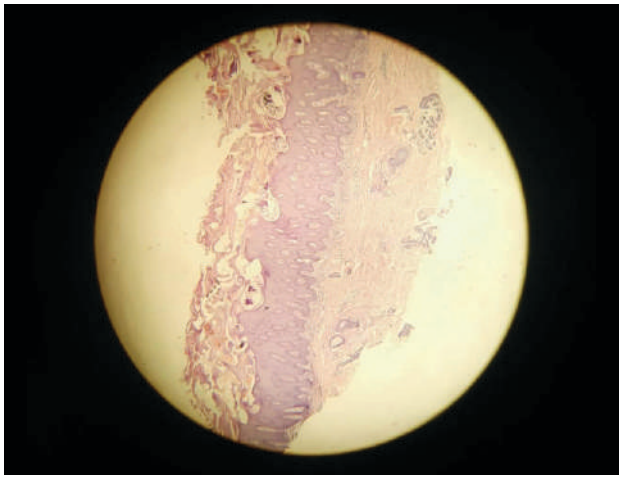

Fig 2: Skin biopsy showing in the epidermis

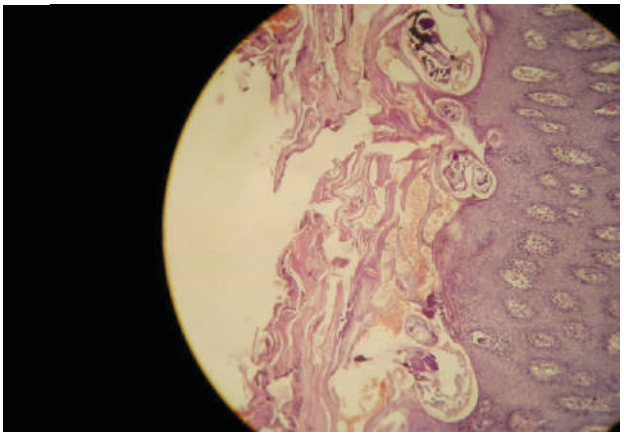

Fig 3: Skin (H & E stain) with multiple scabies mites in the epidermis

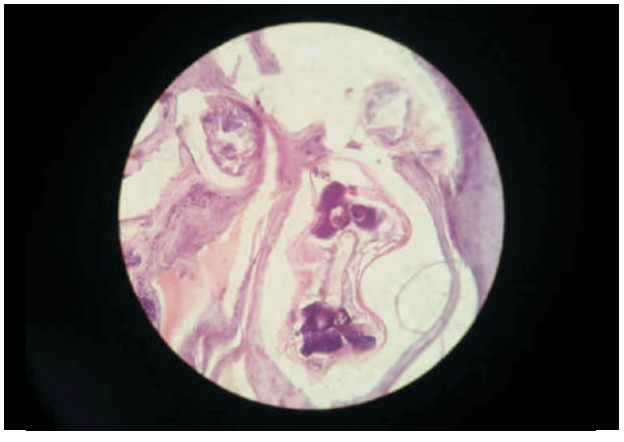

Fig 4: Close view of the scabies mite in skin epidermis

The patient was successfully treated with ketoconazole 2% shampoo, 2-3 days wkly 5 min before taking shower; Permethrin cream 5% (all the members of the family) from head to toe and shower after 24 hr, after 7 days' repeat, after one-day Salicylic acid 5% at bed time and mild to moderate steroid at day time for 21 days. Tab Azithromycin 250mg one tab daily for five days; Tab Loratadin 10mg, one tab at night for one month, Tab Scabo (Ivermactin) 6mg-three tab before meal single dose. Within two weeks, the scaly plaques had disappeared and the erythematous plague had faded. The pruritus had resolved. No new plaques had emerged.

Discussion:

Crusted scabies was described by Boek and Danielssen in 1848 in Norway among lapers and was named as "Scabies Norvegi Boeki" in 1862.This variant of scabies occurs as widespread hyperkeratotic crusted lesion and hence the name "crusted scabies".[1]

Crusted scabies is a severe, rare variant of highly contagious scabies, caused by the mite, Sarcoptes scabiei.[1] It is characterized by uncontrolled proliferation of mites in the skin, extensive hyperkeratotic scaling, crusted lesions and variable pruritus.[2] The uncontrolled proliferation of mites in the skin typically develops in patients with a defective T-cell response or decreased cutaneous sensation and reduced ability to mechanically debride the mites.[3] The stratum corneum thickens and forms warty crusts as a reaction of the high mite burden. [4] Patient should be investigated for a predisposition to crusted scabies due to an underlying condition. Crusted scabies also has been shown to develop in Australian natives with normal immunity, though the etiology of the increased susceptibility in this patient population remains unclear. Certain studies have shown an association with HLA-A11.[5,6]

Crusted scabies usually do not present as an acute eruption as in classical scabies. The eruption is slow in onset and insidious in progression as in our patient. Patients develop severe erythroderma in over 90% of their body surface, followed by intense erythema and desquamation. The differential diagnosis of crusted scabies includes psoriasis, eczema, seborrheic dermatitis, darier disease, contact dermatitis.[7]

It is well documented that immunocompromised patients are at increased risk of developing crusted scabies infestation. Several pediatric reports of crusted scabies in patients with Down syndrome have been published.[8,9] However, our patient had no evidence of immuno-suppression.

The diagnosis of crusted scabies is based on clinical findings and confirmed by examination of scrapings and biopsies, as in classic scabies.[10]

Conclusion:

Diagnosis of Norwagian scabies is rare finding in our country. This diagnosis gives us a new dimension of thinking that sometimes the physician may be confused with very simple clinical sign and symptoms. If the diagnosis is made properly the patient can be cured by proper medicine. Physicians should be very cautious to handle this type of patients initially. Sometimes they think in a complicated way clinically without proper investigation. In case of skin diseases, the histopathological diagnosis can give the real solution to treat the patient.

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Sister Mary Joseph′s Nodule: A classical presentation of parietal wall metastasis of advanced Carcinoma Cervix

Habib A[a], Imam NA[b]

Abstract

A peri-umbilical mass in patient with a recent history of carcinoma cervix evokes much clinical interest in the surgeon's mind. The historical association of Sister Mary Joseph's nodule with intra-abdominal malignancy instigated investigations which lead to the confirmation of the diagnosis in this particular case; that is the metastatic presence of moderately differentiated neoplastic cell of squamous cell variety in the mass. The patient had underwent radical hysterectomy followed by one cycle of chemoradiation for carcinoma cervix stage IIa. Comprehensive evaluation also demonstrated the presence of pelvic recurrence with fixity to the vault and bladder base.

Keywords: Umbilical nodule, Intra-abdominal malignancy, Advanced carcinoma cervix, Pelvic recurrence

Introduction:

Sister Mary Joseph Dempsey (1856-1939) was the surgical assistant of William J. Mayo, one of the seven founders of the Mayo Clinic. She had initially described the link between intra- abdominal malignancy and umbilical nodules which was later discussed by Mayo in an article in 1928. In 1949 Sir Hamilton Bailey utilized the eponym of Sister Mary Joseph's Nodule, in his book "Physical Signs in Clinical Surgery" to describe umbilical metastases, in honor of Sister Mary.[1] Here we report a case of umbilical metastasis in a case of Carcinoma cervix (Squamous cell carcinoma Grade II) Stage IIA (post Hysterectomy and Chemoradiation status) presenting with synchronous pelvic recurrence. The parietal mass was removed completely with negative margins and the abdominal wall closure was achieved by subfascial vicryl mesh buttress. The patient was referred to Oncology for management of pelvic recurrence.

Case Presentation:

A 50-year-old post-menopausal Muslim widow para:5 presented to the department of Surgery in Uttara Adhunik Medical College Hospital with a lump at peri-umbilical region for 8 months associated with pain at lump-site for 6 months. She also experienced a sensation of incomplete urination for 3 months. According to the statement of the patient, she had a history of radical hysterectomy 1 year ago due to Carcinoma Cervix Stage IIa. She received one cycle of cisplatin-based chemotherapy along with 7 sessions of fractionated external beam radiotherapy of a total scheduled 45-50 Gy dose. The patient deliberately refused further chemoradiation. She felt a lump at peri-umbilical area 4 months after surgery which was initially small in size. She noticed rapid growth of the mass with heaviness in the lower abdomen. The lump was associated with intermittent dull aching pain which radiated to back, relieved to some extent after taking NSAIDs.There were no aggravating factors. She had further complaints of sensation of incomplete voiding of urine for 3 months. The patient had no increase in frequency, urgency during micturition or passage of blood-stained urine. She was hypertensive for 15 years. There was no history of carcinoma in her family. There was no history of vaccination against HPV or Hepatitis B.

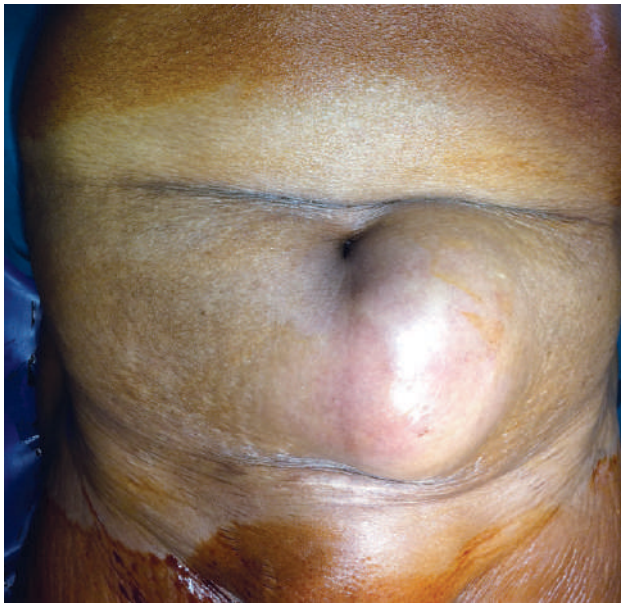

Fig 1: Anterior view of the lower abdominal wall showing the parietal mass.

a. Dr. Asma Habib; FCPS
Associate Professor, Department of Obstetrics & Gynaecology, Bangladesh Medical College and Hospital

b. Prof. Dr. Nayeem-Al-Imam; FCPS
Professor & Head, Department of Surgery
Uttara Adhunik Medical College and Hospital

Correspondence to:
Dr. Asma Habib; FCPS
Associate Professor
Department of Obstetrics & Gynaecology
Bangladesh Medical College and Hospital
E-mail: asma.imam2003@yahoo.com

On general examination, the patient was ill-looking and anxious with average body built. She was mildly anemic and had no jaundice, leukonychia, koilonychia, cyanosis, edema, clubbing were absent. Lymph nodes & thyroid gland: Not enlarged. BP: 100/60 mm of Hg, pulse: 96 beats/min, Temperature: 100°F, Respiratory Rate: 25 breaths/min. On abdominal examination, abdomen is soft, tender lump at peri-umbilical region. No organomegaly and ascites. Umbilicus is centrally placed, flank is not full. There was a lower transverse incision of radical hysterectomy. On local examination: lump was at peri-umbilical area, more prominent on the left side of the umbilicus, hard in consistency, 9x5 cm in size, globular in shape, local temperature was normal, mildly tender to touch, overlying skin was fixed and apparent fixation of the mass with underlying structures. Slipping sign, fluctuation and trans-illumination test were negative. There was slight hyperemia of the overlying skin but no ulceration or discharge. No engorged vein and or visible pulsation over the swelling (Figure: 1). Other systemic examination revealed normal findings. Trans-vaginal ultrasonography revealed an ill-defined mass measuring about 50.7x 43.0mm in the vaginal vault fixed with the base of the bladder.

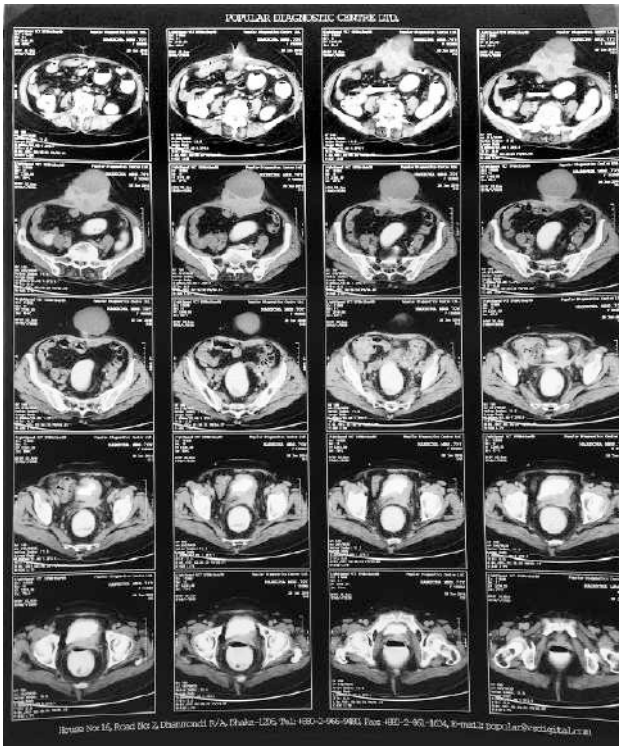

Fig 2: Coronal section image of CT scan of the abdomen showing parietal mass with pelvic vault recurrence.

CT scan of the abdomen (Figure: 2) confirmed recurrence of carcinoma cervix delineated as a fairly large mixed density mass (50x 50x75 mm) in the anterior abdominal wall with intra-peritoneal component with invasion to the base and left lateral wall of the urinary bladder and middle third of the vagina suggesting Stage IV disease (bladder mucosal involvement with pelvic recurrence). There was no significant lymphadenopathy or ascites. Fine needle aspiration cytology FNAC of the parietal solid mass lesion revealed squamous cell carcinoma confirming Sister Mary Joseph's Nodule.

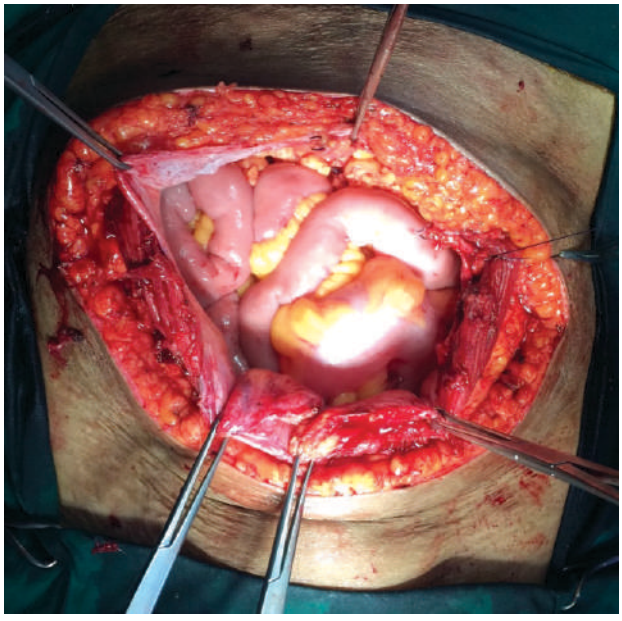

Fig 3 (a): Per-operative view showing intra-peritoneal condition.

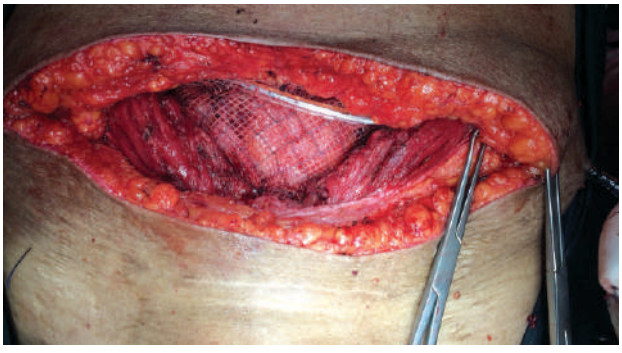

Fig 3 (b): Per-operative view after placement of the vicryl mesh.

The plan of management was Metastasectomy and abdominal wall closure with vicryl mesh (Fig- 3a & 3b). The pelvic recurrence was planned to the managed with palliative chemoradiation as per oncologist's opinion. After attaining operative fitness, the patient underwent the surgical procedure which involved enmass removal of the parietal mass including the umbilicus (Fig- 4). The peritoneal cavity was explored, which revealed no evidence of peritoneal or bowel involvement by malignancy and an irregular, indurated mass in the region of the vault fixed to the bladder.

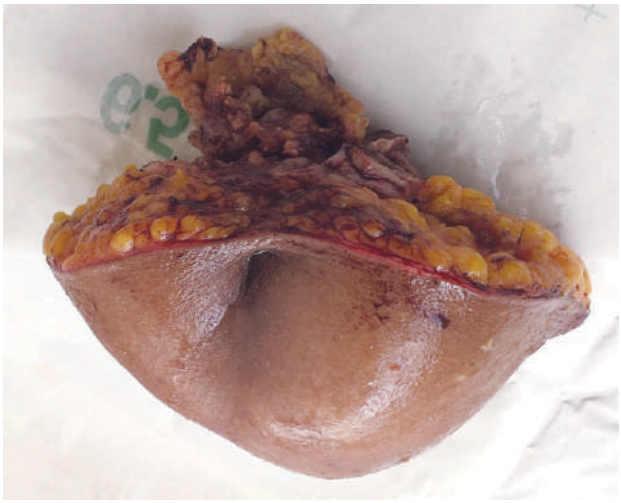

Fig 4: Resected parietal wall mass

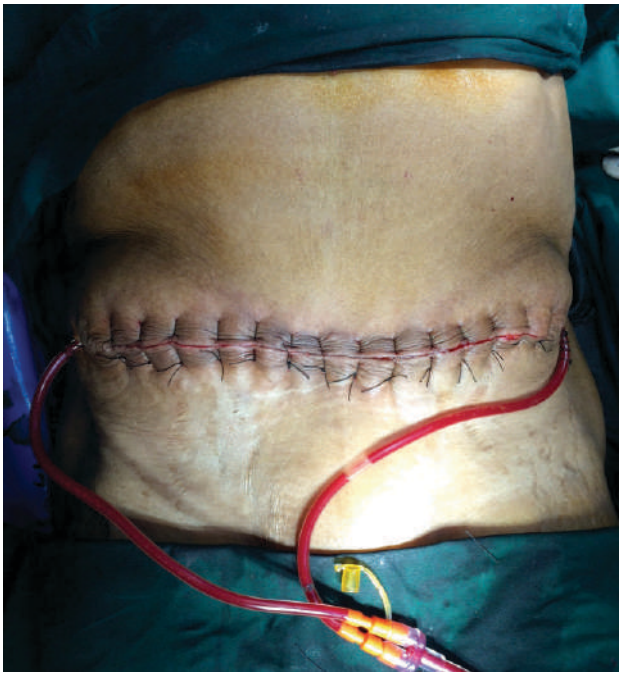

Fig 5: Post-operative view showing closure of the abdominal wall after reconstruction.

The abdominal wall was reconstructed with vicryl mesh and the abdominoplasty procedure was completed (Fig- 5). The patient had an uneventful recovery. Histopathology of the mass reconfirmed the diagnosis with negative margins. The patient was referred to National Institute of Cancer Research and Hospital for further management.

Discussion:

The occurrence of Sister Joseph's nodule remains low with incidence rates of 1-3% in patients with intra-abdominal malignancy. The proposed mechanism of umbilical metastasis include direct transperitoneal spread, via the lymphatics which run alongside the obliterated umbilical vein, hematogenous spread, or via remnant structures such as the falciform ligament, median umbilical ligament, or a remnant of the vitelline duct.[1] Sister Mary Joseph nodule is associated with multiple peritoneal metastases and a poor prognosis.[2] However the differential diagnosis that should not be forgotten in the evaluation of umbilical lump include benign lesions such as fibroma, urachal duct cyst, abscess, umbilical hernia, cutaneous endometriosis, pyogenic granuloma, melanocytic nevus, keloid, melanoma, and basal cell carcinoma .[2,3,4]

The gastro-intestinal tract (stomach) remains the most common location (35-65%) of the primary neoplasm in case of initial presentation of Sister Joseph's nodule. In female patients, ovarian cancer should be screened out as for the primary origin. Other less frequent sites include the cervix, peritoneum, gallbladder and urinary bladder.[1] Adenocarcinoma is the most common histological finding in literature, more rarely have squamous cell carcinoma as in our case, undifferentiated carcinoid tumour have also been reported.[2] A recent retrospective study of 34 cases in Tanzania demonstrated that nearly a third of have an unknown primary and majority of patients presented with advanced intra-abdominal malignancy.[3]

The recognition of Sister Mary Joseph's Nodule is important because it may be the first presenting sign of occult malignant disease in a patient, although it represents the involvement of the umbilicus and adjacent parietal wall by metastasis. Most recurrences of carcinoma cervix are diagnosed within the first 2 years of detection, 50% in the first year, 75% in the second year; 95% of recurrence in the first 5 years.[5] Our case presented within one year of surgery and incomplete chemoradiation. Clinically the triad of symptoms which indicate that the pelvic recurrence has reach the lateral pelvic wall (e.g. sciatica, lower extremity oedema and costovertebral angle tenderness) were absent in our case. The 5-year overall survival for Stage IV (Squamous cell carcinoma) disease is less than 15%. For unresectable recurrent disease, External beam radiation (EBRT) followed by interstitial iridium-loaded stainless-steel or plastic needle implants placed via laparotomy guidance have been reported to yield a 71% rate of local control with 36% of patients having no evidence of disease at follow-up.[6] With the increasing use of pelvic irradiation, less classical patterns of recurrence such as peritoneal carcinomatosis and umbilical metastatic nodules can occur.[7]

Conclusion:

Evaluation of any umbilical or peri-umbilical mass should be done carefully correlating with the clinical context. Comprehensive directive investigations may rule out occult malignancies or reveal an entirely benign etiology.

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College News

College Events:

- International Mother Language Day was observed in Bangladesh Medical College and Hospital on 21st February 2022 at the local premises.

- Bangladesh Medical College and Hospital celebrated birth anniversary of Father of the Nation, Bangabandhu Sheikh Mujibur Rahman on 17th March, 2022. In this event special prayers, national flag hoisting and remembrance speech, wreath laying in the mural of Bangabandhu were conducted in local premises.

- National Independence Day was observed on 26th March, 2022 in Bangladesh Medical College and Hospital at the local premises.

Seminar/Workshops:

- Seminar on "Cardiovascular impact & changing paradigm in the treatment of Type- 2 Diabetes" was held on 13-1-2022. The speakers were Dr. Md. Akhtaruzzaman, Associate Professor, Dept. of Cardiology, BMC and Dr. Yasmin Aktar, Assistant Professor, Dept. of Endocrinology, BMC.

- Seminar on "Psoriasis: A common skin disease with variable presentation" was held on 10-3-2022. The speaker was Prof. Dr. Md. Jamal Uddin, Professor and Head, Dept. of Dermatology, BMC.

- Seminar on "Colorectal Cancer: Prevention and Awareness" was held on 24-3-2022. The speaker was Dr. Syed Khalid Hasan, Associate Professor, Dept. of Surgery, BMC.

- Seminar on "Orientation on COVID-19 risk communication for private doctors and interns of Bangladesh Medical College Hospital"" was held on 14-6-2022. The speaker was Prof. Dr. Md. Tarek Alam, Professor and Head, Dept. of Medicine, BMC.

- The inaugural ceremony of "Training on Teaching Methodology and Assessment" was held on 15.1.2022 in BMC. Prof. Dr. Deen Mohd. Noorul Huq, Chairman, Governing Body, BMC graced the occasion as honorable Chief Guest. It was chaired by Prof. Dr. Paritosh Kumar Ghosh, Principal, BMC.

- CME on "Effective Teaching and Learning: Concepts & Characteristics" was held on 15.1.2022 in BMC. The speaker was Dr. Khondoker Ehsanul Arefin, Associate Professor, Dept. of Pediatrics, BMC. He is the Focal Person of this training workshop to coordinate with Directorate General of Medical Education (DGME).

- CME on "Educational objectives" was held on 30.1.2022 in BMC. The speaker was Prof. Dr. Khaled Noor, Professor, Dept. of Neonatology, BMC.

- CME on "Lesson plan" was held on 15.2.2022 in BMC. The speaker was Prof. Dr. Sharmeen Yasmeen, Professor and Head, Dept. of Community Medicine, BMC.

- CME on "Effective delivery of lecture" was held on 28.2.2022 in BMC. The speaker was Dr. Mainul Alam Chaklader, Associate Professor, Dept. of Community Medicine, BMC.

- CME on "SGT presentation" was held on 15.3.2022 in BMC. The speaker was Prof. Dr. Md. Dabir Hossain, Professor, Dept. of Medicine, BMC.

- CME on "Principles and Methods of Assessment" was held on 30.3.2022 in BMC. The speaker was Prof. Dr. Zafor Md. Masud, Professor and Head, Dept. of Oncology, BMC.

- CME on "SAQ abd MCQ" was held on 2.4.2022 in BMC. The speaker was Prof. Dr. Md. Mizanur Rahman, Professor and Head, Dept. of Ophthalmology, BMC.

- CME on "OSCE and OSPE" was held on 11.5.2022 in BMC. The speaker was Prof. Dr. Syed Khalid Hasan, Associate Professor, Dept. of Surgery, BMC.

- CME on "Structured Oral Examination (SOE)" was held on 17.5.2022 in BMC. The speaker was Dr. Sadia Saber, Assistant Professor, Dept. of Medicine, BMC.

- CME on "Integrated Teaching" was held on 28.5.2022 in BMC. The speaker was Dr. Mahfuja Rahman, Professor (CC), Dept. of Biochemistry, BMC.

- CME on "Effective Use of Teaching Materials" was held on 15.6.2022 in BMC. The speaker was Dr. Sultana Jebinnaher, Associate Professor, Dept. of Gynae and Obtetrics, BMC.

- CME on "Integrity of Medical Education" and "Educational Management" was held on 25.6.2022 in BMC. The speakers were Prof. Dr. Sharmeen Yasmeen, Professor and Head, Dept. of Community Medicine, BMC and Prof. Dr. Md. Tarek Alam, Professor and Head, Dept. of Medicine, BMC.

Participation in the International Conferences/Seminars/Workshop/ Congress/ Meetings:

- Dr. Rezwanur Rahman, Associate Professor, Dept. of Nephrology, BMC attended the 59th Annual Nephrology Congress organized by European Renal Association (ERA) held from 19-22 May, 2022 in France.

- Dr. Muhammed Akhtaruzzaman, Associate Professor, Dept. of Cardiology, BMC attended international scientific symposium "SPACE-2022" held from 17-21 July in Istanbul, Turkey.

- Dr. Mohammad Aftab Halim, Assistant Professor, Dept. of Neuromedicine, BMC attended international scientific symposium "SYNAPSE-2022" held from 15-19 July in Istanbul, Turkey.

New Appointments in BMC:

- Dr. Md. Nazrul Islam Bhuiyan, Associate Professor and Head, Dept. of Urology
- Dr. Ananya Das, Lecturer, Dept. of Pharmacology and Therapeutics
- Dr. Afrin Khandaker, Lecturer, Dept. of Anatomy

Prepared by:
Shahana Akter Dalia
Senior Admin. Assistant
Bangladesh Medical College

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