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Editorial

Routine immunization of health care workers- A stitch in time saves nine

Yasmeen S

Health care workers (HWCs) are at greatest risk of acquiring infectious diseases as a result of their occupational environments and prolonged time of contact with infectious cases knowingly or unknowingly.[1] It has always been considered as an occupational hazard and unfortunately many would just shrug it off as just part and parcel of being a HCW no matter how much serious is the disease. However, this risk can be significantly reduced with combination of standard Infection Prevention and Control (IPC) practices and routine vaccinations among the HCWS. In addition, routine vaccination of HCWs will also reduce their risk of becoming source of vaccine preventable diseases (VPD).[1]

In general, healthcare workers include physicians, nurses, emergency medical personnel, dental professionals and students, medical and nursing students, laboratory technicians, pharmacists, hospital volunteers, and administrative staff. [2] Among the occupational diseases of the HCWs some are VPDs such as influenza, pneumonia, hepatitis -B, measles, mumps, rubella, pertussis, varicella, typhoid, meningitis, tetanus and as newer addition COVID-19. Most VPDs still carry a significant risk of resurgence and have caused outbreaks in recent years. Recommendations for vaccination for HCWs and general populations differ from country to country and vaccine coverage varies widely for each microorganism and for each country making hospitals and clinics vulnerable to outbreaks.[3,4]

It is generally expected by the patients that they will not contract potentially life-threatening and preventable illnesses from their healthcare providers while they remain under their care. But unfortunately undiagnosed, asymptomatic and carrier state of diseases in HCWs are sources of nosocomial infections among patients in clinical settings. It is the responsibility of health care providers to ensure a safe and healing environment for the health care seekers both sick and healthy. After all, sum of steps taken by the providers to avoid and cease transmission of a dangerous virus or bacteria to the sick or healthy is consistent with the fundamental principle of the medical profession- No maleficence, meaning "Do no harm".[5] On the contrary, unvaccinated HWCs face a high risk of infection themselves when working with patients who may carry these preventable illnesses and which could be carried back to their own family, co-workers and local community.

WHO recommends to assist countries to develop national policies for the vaccination of HCWs. For recommended vaccines, all HCWs should have documented proof of immunity or immunization. This should be required as a condition of employment and enrollment into training. The recommended vaccines by WHO and CDC for HCWs are- Hepatitis-B, Hepatitis-A, Influenza, MMR, BCG, Meningococcal, Pneumococcal, Polio, Tetanus, Pertussis, Diphtheria, Typhoid, Yellow fever and Varicella.[2,6] Many developed countries have already implemented routine national vaccination programme and vaccines in the schedule vary from country to country. In most of the low and middle income countries routine vaccination program is not yet established. Some of the barriers for introducing routine vaccination for HCWs in low and low middle income countries are related to issues like- regulatory policy and immunization schedule, lack of fund, vaccine hesitancy, myths, limited knowledge about vaccine safety, limited resource for supply and operation, manpower and logistics.[7] There is lack of data and evidence based information about the actual load of vaccine preventable diseases among the HCWs in terms of morbidity, mortality and disability. Rate of vaccination among them is still insignificant and undetermined. Some sporadic studies were conducted in some selected centers which could not draw any inference. Health care workers have various categories and some are vaccinated by their own cost (except COVID vaccine) and interest; very few are vaccinated with initiative by the institutional authority.

Recent experience of pandemic of COVID-19 affected people of all strata within short period of time particularly the frontline health workers on the first hand.[8] We paid a high death toll of health professionals mostly doctors in many countries including Bangladesh. We lost about 200 doctors in Bangladesh with additional deaths of nurses, paramedics, technicians and other health workers. Many of our professionals died and are dying at their very young age between 40-50 years due to sudden heart attack and stroke which may be due to post COVID complications. But best part is both mortality and morbidity and severity have reduced greatly and recovery rate increased with less complications due to COVID-19 vaccination. In Bangladesh there is no routine national vaccination programme for HCWs. This recent pandemic has given rise an issue of equity in providing other recommended vaccines to HCWs of other LIC & LMIC as the tool of occupational safety, and occupational right. In many developed countries HCWs have already been vaccinated with recommended vaccines of WHO long before invention of COVID-19 vaccine.[9] It created a new area of research to explore how routine vaccination provides a protective role over COVID-19 severity.

Lessons learned from worldwide COVID-19 vaccination programme could be an evidence based intervention model where we found significant reduction of new cases and increase of recovery rate as two important tools for control of this disease. Now it is assumed that pandemic is transforming to endemic to occasional epidemic.[10] Newer generations COVID vaccines and other vaccines are under trial. Many more epidemiologically important vaccines are being used irregularly and under trial like- Dengue vaccine, Malaria vaccine, Nipah virus vaccine, HIV vaccine, Ebola vaccine etc.

Regarding Bangladesh, we are optimistic as we have a very successfully running EPI program and newly added COVID-19 vaccination program. An inbuilt system of supply, store and delivery of vaccine is already prevailing very well. A decision to vaccinate a worker should be based on the activities they perform rather than their job title. Equity and social justice to be done while vaccinating the HCWs. Achieving and sustaining high vaccination coverage among healthcare personnel will help to save lives, reduce disease burden and shrink health-care costs.[11] Capacity building for manufacturing vaccine should be addressed to attain self-reliance and reduce dependency on external funds.

We already have scarcity of health workforce and COVID-19 pandemic further aggravated shortage of skilled workforce. Now policy maker must decide whether vaccination of the HCWs will be mandatory, voluntary or both. Routine vaccination of HWCs adds resiliency to health systems by protecting the workforce. So adjustment of fund, supply chain management, monitoring, operational support, advocacy, awareness and global partnership will play pivotal role in implementing a sustainable routine national vaccination program for HCWs in LIC and LMIC including Bangladesh.

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Original Article

Prevalence and Antimicrobial Susceptibility Pattern of *Salmonella* Typhi & *Salmonella* Paratyphi isolated from clinical samples of Ibn Sina Medical College Hospital, Dhaka, Bangladesh

Siddiqua M[a], Alam AN[b], Akter S[c], Ahsan T[d], Sultana KN[e], Ferdousi RS[f]

Abstract

Background: Enteric fever is one of the serious blood stream infections caused by *Salmonella* Typhi & *Salmonella* Paratyphi.

Objective: The aim of this study was to find out the prevalence and antimicrobial susceptibility pattern of *Salmonella* Typhi & *Salmonella* Paratyphi isolated from clinical samples of Ibn Sina Medical College Hospital, Dhaka, Bangladesh.

Methods: All the blood cultures done at Microbiology department of Ibn Sina Medical College Hospital were considered for study purpose. Culture and Sensitivity test was performed using standard protocol using disk diffusion method.

Results: A total of 6677 blood culture were done during the period April 2018 to March 2020 of which 686 (10.27%) gave positive result for different types of organisms. *Salmonella* Typhi was positive for 540 (78.71%) samples followed by *Salmonella* Paratyphi 119 (17.35%) and other organisms were 27 (3.94%). Most effective drugs against *Salmonella* were found to be imipenem, ceftriaxone, cefixime and amoxyclav having sensitivity of 100%, 99.54%, 96.51% and 93.02% respectively. Lowest sensitivity was found in ciprofloxacin (5.77%). Ampicillin, Cotrimoxazole, Chloramphenicol and Azithromycin were found to be sensitive ranging from 61.35% to 83.31%. About one fourth positive samples 171(24.72%) were found to be multidrug resistance (MDR) *Salmonella*.

Conclusion: In the present study, *Salmonella* Typhi & *Salmonella* Paratyphi showed very good sensitivity to commonly use and locally available antibiotics. But the possibility of develop resistance cannot be rule out as evidence showed some good sensitive drugs developed resistance e.g. ciprofloxacin with time. This study thus emphasizes the need for continuous evaluation and judicious use of antimicrobials.

Keywords: *Salmonella* Typhi, *Salmonella* Paratyphi, blood culture, antimicrobial susceptibility.

Introduction:

Enteric fever is a severe bloodstream infection caused by the bacterial pathogens *Salmonella enterica* serovar Typhi and Paratyphi (commonly known as *Salmonella* Typhi and *Salmonella* Paratyphi). It is an important cause of morbidity and mortality in the developing world.[1] Typhoid fever is an endemic problem for Bangladesh, Indian subcontinent, South and Central America and Africa, has a potential to be epidemic. Despite the use of newly developed antibacterial drugs, multidrug-resistant bacteria cause enteric fever is one of the major health problems in Bangladesh, especially for the children.[2]

Globally, 14·3 million cases of typhoid and paratyphoid fevers occurred in 2017 which is about 44·6**%** decline from 25·9 million in 1990. Age-standardized incidence rate declined by 54·9**%** from 439·2 per 100 000 person-years in 1990 to 197·8 per 100 000 person-years in 2017. In 2017, *Salmonella* Typhi caused 76·3% of cases of enteric fever. Globally the case fatality rate was about 0·95% in 2017, with upper case fatality estimates among children and older adults particularly those who live in lower-income countries. Therefore, an estimated 135·9 thousand deaths from typhoid and paratyphoid fever reported globally in 2017, a 41·0**%** decline from 230·5 thousand (131·2-372·6) in 1990.[3]

Among the community-acquired bacterial bloodstream infections, *Salmonella* Typhi is account for 30% of the infections in Asia[4] and 10% in Africa,[5] whilst *Salmonella* Paratyphi A is a raising pathogen in Asia, which causes up to[7]

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35% of all enteric fever episodes in India and more than 60% in China.[6] Notably, paratyphoid fever is clinically indistinguishable from typhoid fever and the enteric fever is an important cause of acute undifferentiated febrile illness. The heterogeneity in the etiologies of febrile illness depends on geographic location, age group, diagnostic testing panel and seasonality.[8]

The unhygienic sanitary conditions and lack of or inadequate potable water has great role in increasing incidence of enteric fever in developing countries.[9] It has been recognized that food sources such as eggs, poultry and meat products are the major risk of transmission of enteric fever to humans. However, typhoid fever can be transmitted via fecal-oral route through contact with active, convalescent cases or chronic carriers.[10] So use of antimicrobials is necessary for the control of enteric fever caused by *Salmonella* species. Resistance to antimicrobials hinders in control measures which is mainly driven by the selective pressure caused by inappropriate use especially in developing countries like Bangladesh, where people do not have the minimal awareness of resistance, antibiotics and infections. Infections with drug-resistant microorganisms are associated with severity of the patient's illness, increased patient contact with healthcare personnel and length of stay in the hospital that leads to extra cost of health care, sudden or prolonged health complications including significant excess morbidity and mortality.[11] Sometimes is responsible for the cross-infection of hospitalized patients with such drug-resistant organisms.[12] Reports have been found regarding the plasmid mediated multidrug resistant *Salmonella* species to some commonly prescribed antibiotics such as ampicillin, chloramphenicol, co-trimoxazole in different countries of the world.[13] The resistance of *Salmonella* spp. to amoxicillin, fluoro-quinolone, chloramphenicol and co-trimoxazole has become a new challenge for the treatment of typhoid fever.[14] Furthermore, multidrug resistance (MDR) defined as resistance to ampicillin/amoxicillin, chloramphenicol and co-trimoxazole.[15] Hence, it is necessary to know the prevalence and susceptibility patterns of *Salmonella* spp. to conventional antibiotics for understanding antibiotics susceptibility profile of the isolates which will ultimately help to treat and prevent salmonella infection.[16] So, this study was to find out the prevalence and antimicrobial susceptibility pattern of *Salmonella* Typhi & *Salmonella* Paratyphi isolated from clinical samples of Ibn Sina Medical College Hospital, Dhaka, Bangladesh.

Material and Methods:

Study setting

This retrospective descriptive study was conducted in Microbiology Department of Ibn Sina Medical College Hospital, Dhaka. In this study all isolates of Salmonella were included from 6677 blood cultures conducted during the period of 01.04.2018 to 31.03.2020.

Sample Collection and Processing

Eight to ten ml of blood was collected from adult patients in Bactec Plus Aerobic/F culture vials whereas 1-3 ml of blood from children in Bactec Peds Plus/F culture vials with all aseptic precautions. Then, the vials were put in the Bactec machine (BD BACTEC FX40) where it was incubated at 37˚C and agitated continuously. The growth was indicated by alarm message on the computer screen. Then those positive samples were sub-cultured on blood agar and MacConkey's agar media for isolation & identification of *Salmonella* spp. According to manufacturer's instructions, any sample that did not generate any signal within 5 days of incubation was interpreted as no growth (negative). Specific identification of all culture positive samples were accomplished by sub-culture on Blood agar, and MacConkey agar media (OXOID CO. UK). Culture plates were incubated aerobically at 37^{0}C and examined after 18-24 hours of incubation. Gram's stain, biochemical and serological test were done for final identification.[17]

Antibiotic Susceptibility Test

Antibiotic resistance pattern of the isolates was performed by disc diffusion method according to Clinical Laboratory and Standards Institute (CLSI-2018) recommendations. Azithromycin (15µg), Amoxyclav (30µg), Ceftriaxone (30 µg), Cefixime (5 µg), Ciprofloxacin (5µg), Cotrimoxazole (25µg), Chloramphenicol (30µg), Imipenem (10µg), Ampicillin (10 µg) were used.[18] To perform the test, the inoculum was adjusted to the 0.5 McFarland standard and antibiotics discs were placed on the inoculum on the solidified Mueller-Hinton Agar plate and incubated at 37°C for 24 hours. The zone of inhibition was recorded in millimeter (mm). Isolates were considered as sensitive, intermediate or resistant on the basis of zone of inhibition following the criteria of CLSI guidelines.[18] Statistical calculation done by using MS excel.

Results:

Table 1: Frequency of growth in blood culture (n=6677)

Six thousand six hundred seventy seven (6677) samples for blood culture were done during a period of April 2018 to March 2020 of which 686 (10.27%) were culture positive and 5991 (89.73%) were culture negative (Table 1).

Blood culture	Number	Percentage
Positive growth	686	10.27
Negative growth	5991	89.73
Total	6677	100

Table 2: Frequency of Culture positive organisms (n=686)

Name of Pathogen	Number of isolates	Percentage
Salmonella Typhi	540	78.71
Salmonella Paratyphi	119	17.35
Others	27	3.94
Total	686	100

Among the culture positive samples *Salmonella* Typhi was 540 (78.71%) and *Salmonella* Paratyphi 119 (17.35%). Other organisms like *Escherichia coli*, *Pseudomonas* spp., *Klebsiella* spp. & *Acinetobacter* spp. were 27 (3.94%) as shown in Table 2.

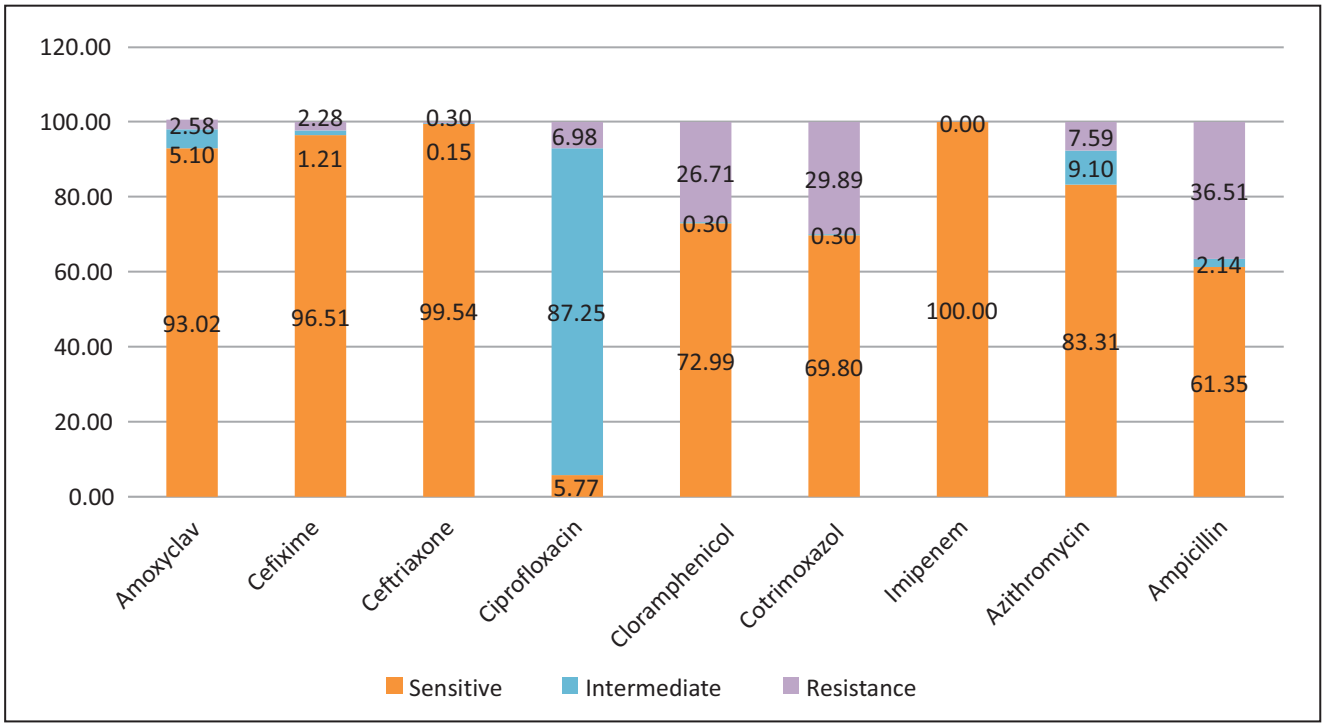


Figure 1: Antibiotic sensitivity pattern of *Salmonella* Typhi and *Salmonella* Paratyphi

Figure 1 showed, most effective drugs were found to be imipenem, ceftriaxone, cefixime and amoxyclav having sensitivity of 100%, 99.54%, 96.51% and 93.02% respectively. Lowest sensitivity was found in ciprofloxacin (5.77%). Ampicillin, cotrimoxazole, chloramphenicol and azithromycin were found to be sensitive ranging from 61.35% to 83.31%. Intermediate sensitivity to ciprofloxacin was found 87.25%.

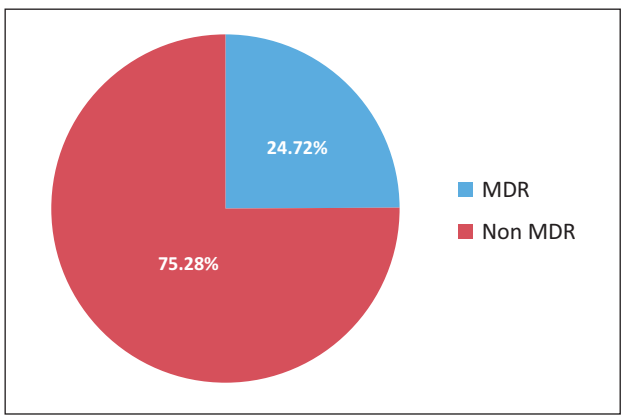


Figure 2: Percentage of multidrug resistant *Salmonella* Typhi & *Salmonella* Paratyphi

About one fourth positive samples 171(24.92%) were found to be resistant against ampicillin, cotrimoxazole and chloramphenicol which are considered as multidrug resistance (MDR) Salmonella (Figure 2).

Discussion:

Blood culture is a well-established procedure at laboratory for confirming cause for many infectious diseases especially enteric fever. In the countries like Bangladesh, all kinds of drugs including the antibiotics are sold over the counter and misuse of antibiotics has been found to be responsible for developing pool of resistant bacteria.[19] Thus culture and sensitivity test should be done to understand resistance status to commonly used antibiotic particularly against *Salmonella* spp.

The present study found that overall isolation of bacteria from blood culture as 10.27 % (Table: 1). One study with similar design done in Bangabandhu Sheikh Mujib Medical University (BSMMU) found bacterial isolation rate as 9.88%.[20] In other study from Bangladesh, recovery rate of bacterial pathogens from blood was found 11.6%.[21] Slightly higher isolation rate (20%) was reported from study done in Nepal.[22] Findings of those studies were in good agreement with the result of the present study.

The present study found *Salmonella* Typhi (78.71%) as most common isolates, followed by *Salmonella* Paratyphi 17.35% & others 3.94% (Table: 2). This finding was in accordance with other studies at home or abroad. *Salmonella* Typhi was the single most common pathogen (72.7%) among the recovered isolates reported in a study at Dhaka.[23] Study at BSMMU, Dhaka, found *Salmonella* Typhi and *Salmonella* Paratyphi isolation rate as 77.97 % and 22.02% respectively.[20] Higher isolation rate of *Salmonella* Typhi and *Salmonella* Paratyphi species is a

significant finding which point out that enteric fever is prevalent in Dhaka city might be due to improper sanitation system leading to gross faecal contamination of consumable water. Lower recovery was found in other study in Columbia, reported *Salmonella* Typhi recovery rate as 36.6%.[21]

In the present study, *Salmonella* Typhi & *Salmonella* Paratyphi showed very good sensitivity to commonly use and locally available antibiotics (Figure 1). Exceptionally, ciprofloxacin showed very low sensitivity (5.77%). The sensitivity towards the third generation of cephalosporin was found 99.54% for ceftriaxone and 96.51 % for cefixime. This finding was in accordance with the study conducted in India.[24] The sensitivity towards azithromycin was seen 83.31% in this study whereas higher sensitivity of azithromycin has been reported in India ranged from 96.3-100% and in Bangladesh 94.25%.[25, 26] Lower sensitivity of azithromycin found in this study might be due to misuse of the antibiotic, oral route of administration and broad-spectrum antimicrobial activity with minimal side effects. In this study *Salmonella* Typhi showed 100% sensitivity to imipenem which is similar to a study done in Pakistan.[27] Among the 2nd generation quinolone group drug, ciprofloxacin was used which showed very low sensitivity 5.77%. Most ciprofloxacin was found to be intermediate sensitive (87.25%). The resistance to ciprofloxacin has increased in our study as well as other reports.[28] As the susceptibility breakpoints of ciprofloxacin interpretative criteria for the MIC breakpoints were lowered from 1 to 0.06 μg/ml and zone diameter increased from 21 to 31 mm by CLSI, the susceptibility percentage of ciprofloxacin in our strains changed from about 92.54% to 5.53%. Similar results are reported from other regions where the susceptibility changed from 95% to 3% due to the revised CLSI guideline.[29]

In our study, we found that 24.72% isolates of *Salmonella* Typhi *&* *Salmonella* Paratyphi were multidrug resistant (Figure 2). This shows frightening increase of multidrug resistance organism in Bangladesh, also supported by a number of previous studies.[30] Similar pattern of increase in multidrug resistance has been observed in India too.[31] Over use of drug, misuse and inappropriate prescribing practices by physicians along with intrinsic microbiological plasmid-mediated transmission might be the major contributory factors.[32] In Bangladesh, huge population and rapid urbanization may facilitate the spread of resistant bacteria and gene leading to MDR in the country; same scenario was seen in other countries too.

Conclusion:

Our study confirms that about one fourth *Salmonella* strains were resistant to at least 3 drugs considered as MDR. Further, the concern about fluoroquinolone was the decreased in susceptibility as indicated by the intermediate susceptibility or resistance was increased in this study. Though imipenem, cefixime, and ceftriaxone showed good susceptibility, the possibility of antibiotic resistance with the irrational use of these antibiotics cannot be rule out. This study thus emphasizes the need for continuous evaluation and judicious use of antimicrobials. Further prospective studies are necessary to correlate the clinical outcome of treatment based on in vitro antimicrobial susceptibility patterns of *Salmonella* isolates in Enteric fever cases.

Conflict of interest: None

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Clinical and microbiological aspect of perianal abscess in adults: An experience of 75 patients

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Abstract

Background: Perianal abscess is the most common disease requiring an emergency surgical treatment.

Objective: The purpose of our study was to identify the risk factors, clinical features of different subtypes and microorganisms responsible for perianal abscess. We also compared the culture findings in patients with Diabetes Mellitus (DM) to those in patients without DM.

Methods: This cross sectional descriptive study was carried out at Bangladesh Medical College & Hospital, a tertiary teaching hospital in Dhaka, Bangladesh on 75 patients of perianal abscess from 2018 to 2020. All the bacterial culture and identification were done in the microbiology laboratory of same hospital following standard microbiological techniques. Data regarding sociodemographic variables, risk factors, clinical features and pattern of microorganisms were collected on semi structured questionnaire. Data analysis was done with SPSS version 18 software. Data were presented in descriptive frequency in tables and diagrams

Results: Out of 75 patients 58 (77.33%) were male and 17(22.66%) were female. About 38.66% of patients had DM, 18.66% needed more than 7 days of hospital stay and 18.66% had obesity. Among 75 patients 18 (24%) were found Subcutaneous, 48(64%) Intersphincteric and Submucous variety was found in 12(16%) patients. All 75 patients presented with pain and tenderness and majority with local swelling 82.66% and fluctuation 74.66%. *Escherichia coli* was the predominant organisms in both DM 58.62% and non-DM patients 76.08%.

Conclusion: Perianal abscess was found predominant among male. Diabetes Mellitus, obesity and longtime hospital stay more than 7 days were identified as major risk factors. Inter sphincteric variety of perianal abscess was found as a major variety of perianal abscess. A relatively large percentage of aerobic organisms especially *Escherichia coli* was detected in perianal abscess. Due attention is needed for public awareness to prevent and control the common health problems like perianal abscess.

Keywords: Perianal abscess, Subtypes, *E. coli.*

Introduction:

An abscess is a localized collection of infected fluid. There are strict anatomical definitions for the different anorectal abscesses; the preliminary management is same in most cases so the term "perianal abscess" is generally used. Infection of the cryptoglobular glands results about 90%of idiopathic perianal abscesses.[1,2] Most occur posteriorly and in the intersphincteric space, where the anal glands are located.[3] The annual incidence of perianal abscess is estimated between 14000 and 20000 people in the UK, resulting in about 12500 operations in the NHS each year.[4] The true incidence may be higher because in the community many patients are treated with antibiotics and some abscesses regress or discharge spontaneously.[5,6]

Perianal abscesses are twice as common in men as in women, with a mean age of 40 years in both sexes.[7,8] Known risk factors associated with developing an abscess include inflammatory bowel disease, HIV infection and smoking.[9] The most common presentations of abscesses are perianal (up to 60%) and ischiorectal swelling.[3,10]

The purpose of our study was to identify the risk factors, clinical features of different subtypes and microorganisms responsible for perianal abscess. We also compare the culture findings in patients with Diabetes Mellitus (DM)to those in patients without DM.

Materials and Methods:

This study was carried out at Bangladesh Medical College & Hospital, a tertiary teaching hospital in Dhaka, Bangladesh. A cross sectional descriptive study was done in a total of 75 patients who were attended Bangladesh Medical College

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Hospital, Dhanmondi, Dhaka from July 2018 to June 2020 were analyzed. Patients with perianal abscess were admitted in the department of surgery. All the bacterial cultures and identification of organisms were done in microbiology laboratory of the hospital following standard microbiological techniques.[11,12] Data were collected by using a semi structured questionnaire and analyzed with SPSS software version 18 software. Data were presented in descriptive frequency in tables and diagrams. We excluded patients with Crohn's disease or ulcerative colitis who known to have a higher risk of perianal abscess than the general population.[13,14] Patients who had fistulas with perianal abscess, perineal and scrotal soft tissue necrosis, or pilonidal abscesses, and who used antibiotic before culture were also excluded from this study.

Results:

Table 1: Age & gender distribution of patients with perianal abscess (n=75)

Variable	Male No. (%)	Female No. (%)
Gender	58 (77.33)	17 (22.67)
Age group	**No. (%)**	**No. (%)**
21-30 years	21 (36.20)	5 (29.41)
31-40 years	30 (51.72)	9 (52.94)
41-50 years	6 (10.34)	2 (11.76)
51-60 years	1 (1.72)	1 (5.88)

This table shows out of 75 patients with perianal abscess 58 (77.33%) were male and 17(22.67%) were female. In male the highest percentage (51.72%) was found in 31-40 years' age group, followed by 21-30 years' age group (36.20%). In female, majority 52.94% were in 31-40 years' age group.

Table 2: Risk factors associated with perianal abscess (n=75)

Risk factors	No. (%)
Length of stay >7 days	14 (18.66)
Past history of abscess/Fistula in-ano	8 (5.3)
DM	29 (38.66)
Pregnancy	0
Recent surgery	1 (1.33)
Steroid therapy	1 (1.33)
Alcohol use	0
Malignancy	2 (2.66)
Trauma	0
History of IBD	2 (2.66)
Obesity	14 (18.66)
Hyperthyroidism	2 (2.66)
Chronic renal failure	4 (5.33)

Table 2 shows that about 38.66% of patients have DM, 18.66% of patients needed more than 7 days of hospital stay and 18.66% has obesity.

Table 3: Types of perianal abscess (n=75)

Types	No.	%
Subcutaneous	15	20
Intersphincteric	48	64
Submucous	12	16
Total	**75**	**100**

Table 3 shows that majority 64**%** of the pelvic abscess were Intersphincteric type followed by subcutaneous 20**%** and submucous 16**%**.

Table 4: Clinical features of perianal abscess n=75

Clinical features	No. (%)
Pain	75 (100)
Local swelling	62 (82.66)
Fluctuation	56 (74.66)
Fever	12 (16)
Discharge/pus	26 (34.66)
Erythema	10 (13.33)
Tenderness	75 (100)

Among 75 patients presented with pain and tenderness with local swelling 82.66%, fluctuation 74.66%, discharge/pus 34.66%, erythema 13.33% and fever 16% as shown in Table 4.

Table 5: Variation of clinical features among Subcutaneous subtypes of perianal abscess **(**n=15**)**

Clinical features	No. (%)
Pain	15 (100)
Local swelling	15 (100)
Fluctuation	13 (86.66)
Discharge/pus point	10 (66.66)
Fever	4 (26.66)
Erythema	6 (40)
Tenderness	15 (100)

Table 5 shows that among patients with subcutaneous variety all presented with pain, local swelling and tenderness. Patients presented with fluctuations 86.66%, discharge 66.66%, 40% with erythema and 26.66% with fever.

Table 6: Variation of clinical features among Inetrsphincteric subtypes of perianal abscess **(**n=48**)**

Clinical findings	No. (%)
Pain	48 (100)
Local swelling	38 (79.16)
Fluctuation	34 (70.83)
Discharge or pus point	17 (35.41)
Fever	7 (14.58)
Erythema	4 (8.33)
Tenderness	41 (85.41)

Table 6 shows all of Inetrsphincteric subtypes were presented with pain (100%), local swelling (79.16%), tenderness (85.41%), fluctuation (70.83%), discharge or pus point (35.41%), fever (14.58%) and erythema (8.33%).

Table 7: Variation of clinical features among submucous subtypes of perianal abscess (n=12)

Clinical features	No. (%)
Pain	12(100)
Local swelling	4 (30.76)
Fluctuation	3 (23.07)
Discharge or pus point	8 (30.76)
Fever	3 (23.07)
Erythema	3 (23.07)
Tenderness	5 (38.46)

Table 7 shows all of submucous variety presented with pain, tenderness 38.46%, local swelling 30.76%, discharge or pus point 37.77%, and fluctuation, erythema and fever 23.07%.

Table 8: Pathogens isolated from perianal abscess

Pathogens	DM (n = 29)	Non-DM (n = 46)
Escherichia coli	17 (58.62)	35 (76.08)
Klebsiella spp.	2 (6.89)	1 (2.17)
Staph. Aureus	6 (34.48)	5 (10.86)
No growth	4 (13.79)	5 (10.86)
Total	**29 (100)**	**46 (100)**

This table shows *Escherichia coli* was the predominant organisms in both DM 58**.**62**%** and non**-**DM patients 76**.**08**%**, followed by *Staph***.** *aureus* and *Klebsiella* spp**.**

Discussion:

Successful eradication of anorectal suppuration requires an in-depth understanding of anorectal anatomy. At the level of the dentate line, the ducts of the anal glands empty into the anal crypts. Some 80% of the anal glands are submucosal in extent, 8% extend to the internal sphincter, 8% to the conjoined longitudinal muscle, 2% to the intersphincteric space, and 1% penetrate the internal sphincter.[15,16]

Ninety percent of all anorectal abscesses result from nonspecific cryptoglandular infection whereas the remainder result from other causes. According to the cryptoglandular theory championed by Parks,[17] abscesses result from obstruction of the anal glands and ducts. Obstruction of a duct may result in stasis, infection, and formation of an abscess.

In our study 75 patients were diagnosed as perianal abscess. Among them 58(77.33%) patients were male and 17(22.67%) were female. Highest percentage (51.72%) of perianal abscess was found in male 31-40 years' age group and 36.20% was found in 21-30 years' age group (Table-1). Female are less sufferer than male in this study. Several other studies have reported this male preponderance.[18,19]

This study showed that the most common associated conditions were DM 38.66%, then obesity 18.66%, CRF 5.33%, malignancy 2.66% and history of IBD 2.66%. Post-operative recovery of majority of patients was uneventful and 18.66% patients needed more than seven days for discharge (Table-2). Long time hospital stay was mostly due to sepsis and pain. Mehmet Ulug et al shows that, DM 22.2%, obesity 8.6% and malignancy 6.1% were the most common conditions associated with perianal abscess.[20]

Here we found the subcutaneous variety 24%, intersphincteric variety 64% and sub mucous variety 16% (Table-3). All patients in this study presented with pain and tenderness with local swelling 82.66%, fluctuation 74.66%, discharge/pus 34.66%, fever 16% and erythema 13.33% (table-4). The commonest complains of sub variety group were pain, tenderness and local swelling in subcutaneous type of perianal abscess and pain, discharge in other two types (Table-5,6,7). A similar findings is found in another study.[21]

Escherichia coli were detected both in DM patients 58.62% as well as in non-DM patients 76.08%(Table-8). Most aerobic and anaerobic organisms isolated from perianal abscess as found in study are of GIT and skin flora origin.[22] The result of our study supported that GIT-derived organism, such as *Escherichia coli* was the most predominant organism isolated from patients. A study done in Taiwan where they found *Escherichia coli* were the predominant organisms in non-DM patients.[23] Another study showed similar findings.[20] The second most organisms in DM patients in this study was *Staph. aureus* and third one was *Klebsiella* species. In non-DM patients *Staph. aureus* and *Klebsiella* species were also found with low percentage than DM patients in our study.

Conclusion:

This study suggests that most of the patients of perianal abscess were male. DM, obesity and longtime hospital stay more than 7 days were identified as major risk factors. Intersphincteric variety of perianal abscess was found as a major variety of perianal abscess. A relatively large percentage of aerobic organisms especially *Escherichia coli* was detected in perianal abscess. In view of significant burden on health resources, the policy makers and stakeholders are urged to raise their voice for public awareness to prevent and control the common health problems like perianal abscess.

Conflict of interest: The authors declare that there is no conflict of interests regarding the publication of this paper.

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Evaluation of histological pattern of Lupus Nephritis with biochemical features in a selected tertiary care hospital: An experience of 50 cases

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Abstract

Background: Lupus Nephritis is histopathologically evident in most patients with Systemic Lupus Erythematosus (SLE) even those without clinical manifestations of renal disease. The presentation of renal disease in SLE is variable, ranging from clinically silent nephritis to rapidly progressive crescentic glomerulonephritis with acute renal failure. Biochemical assessment is very important for diagnosis SLE, activeness of the diseases and for the follow up of the lupus patients. Assessment and management of patients with suspected Lupus Nephritis is greatly facilitated through evaluation by renal biopsy.

Objectives: To evaluate the histological findings of renal biopsy with biochemical features among patients with lupus nephritis.

Methods: This cross-sectional study was carried out at department of Medicine and Nephrology of Bangladesh Medical College Hospital during the period of 2011 to 2015. Total 50 cases were selected by purposive sampling who were both old and newly diagnosed cases of SLE. Informed consent was taken from the patients. All demographic, relevant biochemical, and histopathological findings of renal biopsy were documented in a preformed structured questionnaire. Data were directly analyzed by SPSS version 16.0. For relationship among the variables $p<0.05$ was considered as statistically significant.

Results: Majority of patients (58.0%) were in 21- 30 years age group and were female (90%).Male:female was 1:9. Most common histopathological class of LN was Class-IV (58%), followed by Class-V (20%) and class III (16%). Nephrotic range proteinuria found in class III, IV, V. Class IV were presented commonly nephrotic range proteinuria, class V were presented with hematuria. ANA, anti dsDNA was significant in class-V.

Conclusion: Early diagnosis and prompt institutional care and guideline of appropriate supportive therapy can make a favorable outcome in SLE patient. The emphasis in SLE related glomerular disease prevention programs must be on early identification of patients at risk and appropriate treatment by means of clinical, biochemical, pathological and renal biopsy clarification.

Keywords: Systemic lupus erythematosus, lupus nephritis, glomerulonephritis, biochemical renal biopsy.

Introduction:

Systemic Lupus Erythematosus (SLE) is a chronic, usually lifelong potentially fatal autoimmune disease characterized by unpredictable exacerbation and remission with variable clinical manifestations. Patients with SLE have a spectrum of glomerular disease, different glomerular injury identified within the general category. Severe Lupus Glomerulonephritis is responsible for most of the morbidity and mortality in this disease. The importance of lupus nephritis to practicing nephrologists is that, although rare, it is a serious disease whose prognosis can usually be improved dramatically by treatment, but for which the treatment is potentially toxic, prolonged, complex, and difficult to plan and carry out. Lupus is defined by its clinical picture, together with antibodies directed against one or more nuclear components, particularly anti-double stranded DNA (dsDNA). It is best regarded as a syndrome, in which a variety of immunologic events may lead to a similar final common pathway, and thus present a similar clinical picture.[1]

William Osler was the first one who described nephritis as a component of systemic lupus erythematosus (SLE). Despite great improvements in the diagnosis and treatment of SLE in the past 50 years, nephritis remained the leading cause of death among patients with SLE. Today, lupus nephritis is responsible for growing percentages of cases with end-stage renal failure that need dialysis or renal transplantation.[2] Lupus nephritis has been extensively

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studied during the last 20 years and renal biopsy results have been classified according to WHO and other institutes. The WHO classification system considers six histopathological classes and their subtypes for renal involvement in SLE patients.[3]

The clinical diagnosis of SLE depends on careful and very thorough history of patients, assessment of the presenting clinical features, examination of all the organ systems and selected investigations. Lupus nephritis can mimic almost any morphologic pattern of glomerulonephritis and it is emphasized that the diagnosis of SLE is not based on morphologic features. SLE is usually diagnosed according to the widely accepted criteria of the American College of Rheumatology.[4]

Lupus nephritis, one of the most serious SLE, usually arises within 5 years of diagnosis. Lupus nephritis is histopathologically evident in most patients with SLE, even those without clinical manifestations of renal disease. The symptoms of lupus nephritis are generally related to hypertension, proteinuria and renal failure.[5]

Studies of human leukocyte antigens (HLA) reveal that HLA-A1, B8, DR2 and DR3 are more common in persons with SLE than in the general population. A genetic predisposition is supported by the 40% concordance among monozygotic twins.[6]

Autoimmunity plays a major role in the pathogenesis of lupus nephritis. The immunologic mechanisms include production of autoantibodies directed against nuclear elements. The characteristics of the nephritogenic autoantibodies associated with lupus nephritis are as follows: Antigen specificity directed against nucleosome or double-stranded DNA (dsDNA) - Some anti-dsDNA antibodies cross-react with the glomerular basement membrane, Higher-affinity autoantibodies may form intravascular immune complexes, which are deposited in glomeruli.

Autoantibodies may bind to antigens already located in the glomerular basement membrane, forming immune complexes in situ. Immune complexes promote an inflammatory response by activating complement and attracting inflammatory cells, including lymphocytes, macrophages, and neutrophils.[7]

Assessment and management of patients with suspected lupus nephritis is greatly facilitated through information obtained by renal biopsy. A number of changes occur in kidney in the patients with lupus nephritis. The pathologic findings of lupus nephritis are extremely diverse and may occur in all four renal compartments: glomeruli, tubules, interstitium, and blood vessels.

On renal biopsy, most frequent finding is class IV lupus nephritis, followed by class V, class III, class II respectively.[8] Prevalence of male lupus is more common in class IV and V than in other classes. Lupus nephritis class I and II may occur in the absence of clinical abnormality. Class V is characterized by nephrotic syndrome which often is persistent, but renal function impairment develops slowly and is rarely severe.[9] Haematuria, massive proteinuria, low albumin, low complement and renal insufficiency are more marked in proliferative lupus nephritis than other histopathological classes.[10]

Considering the above-mentioned facts and unavailability of data about this disorder and its subtypes in our geographical region, we decided to evaluate the biochemical and histopathological findings among patients with lupus nephritis.

Materials & Methods:

This cross-sectional study was carried out at the department of Medicine and Nephrology, Bangladesh Medical College Hospital, Dhaka during the period of Jan 2011 to December 2015. Fifty patients were selected purposively who were diagnosed cases (old and new) of SLE with >4 ARA (American Rheumatism Association) criteria. Inclusion criteria of patients of SLE (with one or more criteria) were: Urinary Total Protein UTP > 0.5 gm / 24 hour/1.73m^2 body surface area; Urinary Active Sediment-R.B.C and R.B.C cast; Renal insufficiency evidence by serum creatinine ≥1.5 mg/dl; Clinically suspected RPGN or Rapidly Progressive Glomerulo Nephritis). Among exclusion criteria: Clinically SLE not having renal biopsy; Patient having bleeding disorders (according to BT, CT report); Bilateral small kidneys or single kidney; Previously diagnosed patient of SLE having treatment with MMF (Mycophenolate Mofetil) or pulse cyclophosphamide. Informed consent was taken from the patients.

A pre-structured questionnaire was filled up by the physicians. Patients' data such as age, sex, clinical presentation, biochemical finding and histopathological result of kidney etc. were documented in the questionnaire. Patients were monitored after hospital admission, during hospital stay and outcome assessed time to time. Data were presented by tables and diagrams with descriptive frequency. Data analysis was done by using SPSS version 16.0. "p" value <0.5 considered as statistically significant.

Results:

Table 1: Socio-demographic characteristics of the patients (n=50)

A) Age Group	Frequency	Percentage
<20	6	14
21-30	29	58
31-40	10	20
41-50	03	06
>50	01	02
Mean ± SD: 26.7±11.6 Years		
B) Sex	Frequency	Percentage
Male	05	10
Female	45	90
Total	50	100

Age range of the study population was 18-52 years. Majority of patients (58%) belonged to age group 21-30 years. Mean age was 26.7±11.6 Years (Table 1A). Out of 50 cases 45 (90%) were female and 5 (10%) were male as shown in Table-1B. Male female ratio was 1:9.

Table 2: Histopathological classes of LN (according to WHO histopathological classification system)

Histopathological classes	Number of patients	Percentage
Class I	0	0
Class II	3	6
Class III	8	16
Class IV	29	58
Class V	10	20
Class VI	0	0
Total	**50**	**100**

Majority (58%) of the lupus nephritis cases were histopathologically classified as class-IV, followed by class V (20%) and class III (16%). No class I and class VI patients were found as shown in Table 2.

Laboratory findings of lupus nephritis patients:

Table 3: Correlation of laboratory findings and WHO classes (I-VI) of lupus nephritis

Laboratory findings	**Histopathological classes**				**Total**
	II (n=3)	III (n=8)	IV (n=29)	V (n=10)	50
UTP (≥ 3 gm/ 24 hour)	0	4 (50)	27 (93.10)	6 (60)	37 (74)
Serum creatinine ≥ 1.5 mg/dl	1 (33.33)	0	21 (72.4)	6 (60)	28 (56)
ANA(Anti-nuclear antibody)	1 (33.33)	5 (62.5)	15 (51.72)	10 (100)	31 (62)
Anti ds DNA	1 (33.33)	4 (50)	18 (62.02)	9 (90)	32 (64)
Haematuria	0	3 (37.5)	7 (24.13)	9 (90)	19 (38)
Hypocomplementaemia	0	3 (37.5)	7 (24.13)	6 (60)	16 (32)
Hypoalbuminemia	1 (33.33)	1 (12.5)	9 (31.03)	9 (90)	20 (40)

Table 3 shows most of the patients (93.10%) of class-IV were presented with nephrotic range proteinuria. About 90% patient of class -V had hematuria. Most of the patients (50%) of class- III and 60% of class V patients were presented with Nephrotic range proteinuria. ANA and Anti ds DNA both were 90% in class-V. No renal impairment (serum creatinine) was found in class-III but 33.33% of class-II, 72.40% of class-IV, and 60% patients of class -V had renal impairment. The *p*-value is .000198. The result was found statistically significant at $p < .05$.

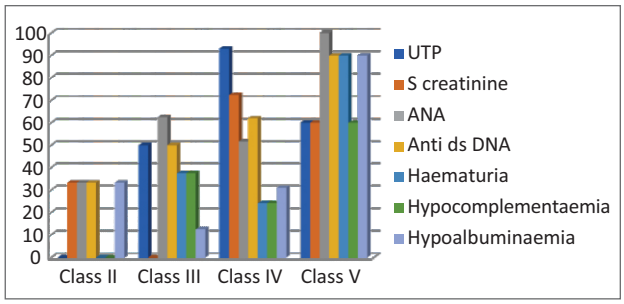


Figure 1: Spectrum of nephrotic range proteinuria and renal insufficiency in different classes of LN

Fig 1 shows Nephrotic range proteinuria and renal insufficiency were mainly in class -IV, V. Study demonstrated that 50% of class-III, 93.10% of class -IV, and 60% of class -V patient had Nephrotic range proteinuria. Renal insufficiency observed in 33.33% of class-II, 72.4% of class -IV, and 60% of class-V patients.

Discussion:

The objective of this study was to evaluate the histopathological finding of renal biopsy to biochemical findings of lupus nephritis patients. These issues may be particularly relevant for observational studies that use particular biochemical manifestation, histopathological findings in which sources of bias may be sufficiently large to either obscure a real difference in rates or create an apparent one.

In this study majority of LN cases were in young age group 21-30 years (58%), next group of patients (20%) observed in 31-40 years of age group and mean age was 26.7 ± 11.6 years (Table 1A). Findings are consistent with other study at home and abroad. Study in a tertiary center of Bangladesh, by Huq MZ[11] reported that mean age was 28.2 ± 7.2 years. Majority of the patients were in 3rd decade (51.6%). Another study at BSMMU in 2006 showed mean age of the Lupus Nephritis patients was 25.5±8.8 years.[12] Similar studies were carried out in Singapore[13] and China[14] showing the mean age of the patient 35.4±8.2 years and 33±14 years respectively.

In this study, out of 50 cases 45 (90%) were female and 5 (10%) were male (Table 1B). Male female ratio was 1:9. Huq MZ[11] reported male: female ratio of 1:7.5. Okpechi IG et[15] al in 2012 in their study in South Africa showed male: female as 1:5.3, You SJ et al in 2009, in a study in Korea showed M: F as 1:12.[16] This study corroborating previous study from Iran and Korea. But present study differs with the study carried out in Singapore showing a male: female ratio of 1:4 and study carried out by Parichatikanond P et al 1986 where male female ratio was 1:19.[17] This difference could be due to racial and geographical variation of Lupus Nephritis.

In his study that most common histopathological class was class IV, the next common classes were class III (20.0%) and class V (18.3%) respectively. In 1991 Halland A M. et

al[18] in their study found class IV: 62.7%, class III: 25.4%, class II: 11.7% and class V: 7.8%. Parichatikanond P et al[17], in 1986, in their study found class IV: 58.6%, class II: 17.9%, class V: 12.9%, class III: 9.9%. You SJ, et al[16] in 2009, in Korea, found class IV: 44.8%, class III and V: 22.4% both, class II: 10.4%. Similar frequencies of WHO classification were found in Khoo J J et al[19] where 65.7% of their cases belonged to WHO class IV. Hiramatsu et al found the relative frequency of each class were: Class IV: 60%, Class III: 17%, Class II: 13%, Class V: 10%.19(p= 0.000.[20]

Patient with class -IV, V lupus nephritis typically presented with most severe biochemical features; virtually all had proteinuria and heamaturia. Renal dysfunctions were typical. Most of the Class V patient had nephrotic range proteinuria and haematuria with minimal Hypocomplementaemia and Hypoalbuminemia. In this Study demonstrated that ANA and Anti dsDNA were significant in class V. Patient with class III lupus nephritis presented with proteinuria, haematuria and significant positive ANA and Anti ds DNA but no renal impairment. Patient with class II lupus nephritis presented with minimal renal impairment and positive ANA or Anti ds DNA but no haematuria or hypocomplementaemia. One-Way ANOVA test shows The *f*-ratio value is 12.31746. The *p*-value is .000198. The result is significant at $p < .05$ (Table 3). Findings are consistent with the result of other study. [21] A study in tertiary centre of Bangladesh shows that Anti-ds DNA was positive among all (100%) patients and antinuclear antibody was positive among 19 (63%) patients.[22] After evaluation of renal biopsy, 2 (6.7%) was found in Class-II LN, 9 (30%) patients had Class -III LN, 12 (40%) had Class IV LN 4 (13.3%) had Class -V LN. Among all patients 6 (20%) had ≥3 g proteinuria.[22] Another study demonstrated that dominant feature of renal lupus is proteinuria. Microscopic hematuria is almost always present, but never in isolation and macroscopic hematuria is rare. Antinuclear antibodies, particularly those against dsDNA are strongly associated with the presence of nephritis (40 to 90%). Treatment may rapidly eliminate anti-ds DNA antibodies from the circulation, while the positivity on the fluorescent antinuclear antibody (FANA)test remains.[23]

Finally considering the findings of this study, it is evident that some of the biochemical parameters were associated with histopathological classes of lupus nephritis and these parameters could be used to identifying patient with proliferative lupus nephritis in resource limited centers where the performance of a biopsy is not possible or where renal biopsy is contraindicated. In this study, from observation of biochemical findings of different histopathological classes of lupus nephritis it was evident that class -II patients had minimal clinical and renal findings, proteinuria was in non- nephrotic range and renal function was almost normal. But class-IV, V patients were presented with most severe clinical and biochemical findings.

Our study design raises a number of important methodological issues, including patient selection, sample size and the prospective evaluation of association between histopathological findings of renal biopsy with biochemical findings among patients with SLE, all of which may exert a powerful influence on the results. Most of the published studies lupus nephritis have focused on individual problems in isolation, such as clinical presentation, grading, or laboratory parameters. These studies have used a range of different designs; furthermore, methods of patient selection, diagnostic criteria, timing, and duration of follow-up vary considerably between studies, and therefore it is hardly surprising that the reported result of these studies also varied. But our study conducted in point of time and result correlated with other international, national study. An important strength of our study is place and duration. Bangladesh Medical College Hospital is a large tertiary care teaching hospital, situated in the metropolitan city of Dhaka. Huge number of patients admitted or transferred from rural areas of the country in this center with varied presentation and diverse clinical scenario.

Among the limitations, it was a single center based study with small sample size. A large scale study would be needed to reach to a definitive conclusion regarding histopathological finding and biochemical finding of lupus nephritis.

Conclusion:

This study was carried out with an aim to observe the association of histopathological pattern of lupus nephritis with biochemical findings. Early diagnosis and prompt institutional management with appropriate supportive therapy can make a favorable outcome in SLE patient. Although it is common that the persons with SLE are at high risk for future glomerular injury and still need to develop better measurement protocol to minimize and to prevent the negative consequences of this disease. The emphasis in SLE related glomerular disease prevention programs must be given priority for early identification of patients at risk and appropriate treatment by means of clinical, pathological, biochemical and renal biopsy clarification.

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Original Article

Evaluation of Dengue virus serotypes by molecular test (RT-PCR) among the NS1 positive patients in a tertiary care hospital in Dhaka city

Hoque MM[a], Shourov MMH[b], Giti S,[c] Khan AA[d]

Abstract

Background: Dengue fever is an acute febrile illness caused by the dengue virus, which is transmitted to humans by mosquito vector *Aedes aegypti*. The four dengue viruses, DEN-1 to DEN-4, are immunologically related, but do not provide cross-protective immunity.

Objectives: Evaluation of Dengue virus serotypes by molecular test (RT-PCR) among the NS1 positive patients in a tertiary care hospital in Dhaka city.

Methods: This is a descriptive type of cross sectional study conducted in Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment from 01-04-2021 to 30-09- 2021. A total of 100 patients were selected who were tested positive by Dengue NS1 ICT method. Selected patients were re-tested by Dengue RT-PCR tests for comparison of the efficacy of the test procedures and further serotype identification. FTD Dengue Differentiation RT-PCR kit (Fast-track Diagnostics, Luxembourg) was used for species identification among the selected patients. A real-time one-step RT-PCR was performed using two sets of consensus primers. Among 94 RT-PCR positive samples all were of DEN-3 serotypes. Proper aseptic techniques were strictly followed whiles taking the blood samples from patients and further processing and test procedures.

Results: Out of 100 cases 59 (59%) were male and 41 (41%) were female and the male Most common clinical presentations were acute onset of fever (100%), followed by retro-orbital pain (91%), arthralgia (52%), generalized weakness (93%), and rash (58%). Duration of fever was mostly 2-5 days. Leucopenia was detected in all patients (100%). Platelet count was decreased in 79 (79%) cases. Only 24 patients had raised haematocrit level (24%). Among 100 NS1 ICT positive cases, 94 were positive in dengue virus nucleic acid detection by RT-PCR (94%) with the accuracy of 94%. The PCR-positive samples were further tested for all four dengue serotypes.

Conclusion: This study reflects that 2021 Dengue epidemic in Bangladesh was caused predominantly by DEN-3 serotype. RT-PCR technique can be used as a most sensitive and reliable method for dengue diagnosis along with the specific serotypes.

Keywords: Dengue virus, NS1, RT-PCR.

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Introduction:

Dengue virus (DENV) belongs to the family Flaviviridae, genus Flavivirus, and is transmitted to humans by Aedes mosquitoes, mainly Aedes aegypti. This virus has four serotypes (DENV-1, DENV-2, DENV-3, and DENV-4).[1] In the year 2021 there was significant increase in number of cases of dengue occurring throughout the country and even from the rural areas though the case fatality rate (CFR) was not very high. Dengue virus infections may be asymptomatic or may lead to undifferentiated fever, dengue fever, or dengue haemorrhagic fever (DHF) with plasma leakage that may lead to Dengue Shock Syndrome (DSS).[2]

The pathogenesis of severe dengue is due to the involvement of different immune factors. The epidemiology of dengue in South East Asia is undergoing a change in the human host, the dengue virus and the vector bionomics.[3,4] All four DENV serotypes have emerged from the forests of South-East Asia.[5] Infection with one dengue serotype elicits immunity to that serotype but does not provide long-term cross-protective immunity to the

remaining serotypes. Subsequent infection with a different serotype results in the binding of the new virus to cross reactive non-neutralizing antibody from the previous infection facilitating the uptake by mononuclear phagocytes enabling amplified viral replication. The resulting increase in viral load then drives an immunopathogenic cascade and the resultant exaggerated cytokine response leads to a transient increase in micro vascular permeability.[6,7]

DEN-1 and DEN-2 serotype were prevalent during last few years in Bangladesh. Continuous monitoring of dengue virus serotype is important for prevention and control of sudden epidemic by other serotype.[8] Each of the four serotypes has progressed into multiple genotypes. The viruses are perpetuated 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.[9]

The diagnosis of dengue is mainly based on ICT or ELISA, detecting either nonstructural protein-1 (NS1) antigen or IgM antibody capture in countries where dengue is prevalent.[10] The patients with dengue fever have high levels of NS1 protein in their serum after onset till 1-7 days. Therefore, NS1 could be useful diagnostic indicator for acute dengue fever.[11] However, anti-dengue virus IgM is produced during both primary and secondary infection. After 3-4 days of infection, IgM rises rapidly and is usually identified after 5-6 days. Its titre reaches the peak at about 14 days of infection, and then declines to undetectable levels over 2-3 months. The molecular methods like reverse transcriptase polymerase chain reaction (RT-PCR) for diagnosis is promising for early detection with its serotypes. This test has been approved by WHO in dengue bulletin 2009.[12] Primary infections usually results in milder illness, while more severe disease occurs in cases of repeated infection with different serotypes.[13] This study was conducted to evaluate Dengue virus serotypes by molecular test (RT-PCR) among the NS1 positive patients in a tertiary care hospital in Dhaka city.

Materials & Methods:

This is an observational, descriptive and cross sectional study conducted in Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment from 01 April 2021 to 30 September 2021. A total of 100 patients were selected who were tested positive by Dengue NS1. ICT Kit for NS1 Antigen Detection (CMC Medical Devices, Spain) was used. Selected patients were re-tested by Dengue RT-PCR tests for comparison of the efficacy of the test procedures and further serotype identification. FTD Dengue Differentiation RT-PCR kit (Fast-track Diagnostics, Luxembourg) was used for species identification among the selected patients. A real-time one-step RT-PCR were performed using two sets of consensus primers, one primer set targeting a region of the nonstructural protein 5 (NS5) genes to detect all flavi viruses and the other primer set targeting a region of the capsid gene to detect all DEN serotypes. Among 94 RT-PCR positive samples all were of DEN-3 serotypes. RT-PCR done using a protocol developed from Centers for Disease Control (CDC) DENV- 1-4 Real-Time RT-PCR assay.[14] Proper aseptic techniques were strictly followed whiles taking the blood samples from patients and further processing and test procedures.

Results:

Table 1: Socio-demographic characteristics of the patients

Table 1a: Age distribution of the patients (n=100)

Age (years)	No. of patients (%)
≤20	18 (18)
21-30	50 (50)
31-40	20 (20)
41-50	12 (12)
Total	100(100)

Mean ± SD age is 35.7 (±6.23) years

Among 100 patients 50% patients were from 21-30 years' age group followed by 20% (31-40 years), 18% (≤20 years) & 12% (41-50 years). Mean age is Mean ± SD is 35.7 (±6.23) years.

Table 1b: Gender distribution of the patients (n=100)

Sex	Frequency (%)	M:F
Male	59 (59)	1.4:1
Female	41(41)	
Total	100 (100)	

Out of 100 cases 59% were male and 41% were male. Male and female ratio was 1.4:1.

Table 1c: Distribution of patients according to residence (n=100)

Residence	No. of patients (%)
Rural	15 (15)
Urban	85 (85)

Percentage of Urban people was higher (85%) than rural people (15%).

Table 2: Clinical symptoms of disease among respondents (n=100)

Clinical symptoms	No. of patients (%)
Acute onset of fever	100 (100)
Retro-orbital pain	91 (91)
Generalized weakness	93 (93)
Headache	79 (91)
Photophobia	74 (74)
Rash	58 (58)
Backache/Arthralgia/Arthritis	52 (52)
Myalgia	45 (45)
Vomiting	27 (27)
Anorexia	58 (58)

Most common clinical presentations were acute onset of fever (100%), followed by retro-orbital pain (91%), arthralgia (52%), generalized weakness (93%), and rash (58%). Duration of fever was 2-5 days in maximum cases. Leucopenia was detected in all patients (100%). Platelet count was decreased in 79 (79%) cases. Only 24 patients had raised haematocrit level (24%) as shown in Table 2**.**

Table 3: Distribution of the patients according to case definition of Dengue syndrome **(**n=100)

Types	Number of patients	Percentage (%)
Dengue Fever	88	88.0
Dengue Haemorrhagic Fever	12	12.0

Table 3 shows that 88% were Dengue fever and 12% were Dengue haemorragic fever.

Table 4: Dengue viral RNA detection by RT PCR method **(**n=100**)**

Sample tested	NS1 positive **(**n=100**)**	Accuracy rate of RT-PCR (%)
RT-PCR positive	94	94.0%
RT-PCR negative	6	

Table 4 shows 94% patients were RT-PCR positive and 6% were RT-PCR negative.

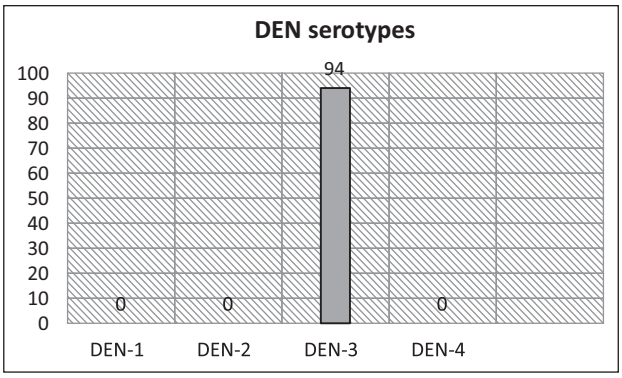


Figure 1: Assessment of Dengue virus serotypes by molecular test (n=94)

The PCR-positive samples were further tested for all 4 dengue serotypes (Figure 1).

Discussion:

In this study maximum numbers of patients (50%) were between 21-30 years of age group, next (20%) were between the age group of 31-40 years. Out of 100 cases 59% were male and 41% were male (Table 1a). Male and female ratio was 1.4:1 (Table 1b). Large numbers of respondents came from urban area 85%, followed by rural area 15% in (Table 1c). In a study, a total of 200 adult positive dengue cases of various grades were studied. Among these 152 (76%) were male and 48 (24%) were female. Male to female ratio was 3.17:1. The age range of the patients was 18 to 60 years and the mean age 39±12.5 years.[15] The global prevalence of dengue has grown dramatically in recent years. Not only is the number of cases increasing as the disease is spreading to new areas, but explosive outbreak of the disease is occurring as its epidemiological pattern is gradually changing.[16] During the 2019 epidemic, the mean age of hospitalized patients with serologically confirmed dengue in Dhaka was around 29 years.[17] In 2020, 62.0% of confirmed cases among patients aged 10-70 years admitted to a Dhaka hospital were 16-30 years old. The adult predominance may be because dengue in childhood is either asymptomatic or causes few symptoms and consequently hospitalization is not required.[18]

Dengue in Bangladesh is most commonly reported among adults and older children, consistent with other relatively low incidence countries in the region.[19] However, measles, which is one of the principal differential diagnoses for dengue, is among the most important causes of death among children under five years of age in Bangladesh. Therefore, dengue may frequently be misdiagnosed as measles, leading to under-reporting among younger children.[20] The capital, Dhaka, consistently reports the highest number of cases, with few notifications from elsewhere since 2010. In this study maximum patients hailing from urban area. Bangladesh is one of the world's most densely populated countries. Current population density is 964 people per square kilometer and there are more than three million births per year.[21]

Poor city management with an absence of proper waste disposal, sanitation, drainage systems, and water supply, together with the use of unprotected water reservoirs creates suitable habitats for Aedes aegypti and Aeded albopictus. Mosquito breeding sites, in combination with unrestricted mosquito–human contact due to the absence of window and door screens, enhance transmission. The urban poor, about 35.2% of the total population of the six major cities (Dhaka, Chittagong, Khulna, Rajshahi, Barisal and Sylhet) live in slum areas. The slums are overcrowded settlements without access to piped water and people store water in temporary containers like drums and earthen jars in which Aedes aegypti lays eggs.[22]

In this study among 100 cases of NS1 positive, 94 cases showed RT-PCR positive giving an accuracy of 94.0% (Table 4). The RT-PCR positive samples were further tested for all 4 dengue serotypes differentiation. Among 94 RT-PCR positive samples all were of DEN-3 serotypes (Figure 1).

In most of the previous epidemics occurring in different regions of Bangladesh, not all four serotypes of dengue virus had been identified simultaneously. In few epidemics these multiple serotypes were found co-circulating as detected by real time RT-PCR. Previously, ELISA assay used for dengue virus serotype identification failed to detect multiple serotypes in acute viraemia; therefore, the aforementioned method should be used as a tool for the rapid identification and serotyping of DENV.[22] Result of this study was dissimilar with another study findings observed that on Real time RT-PCR, Dengue virus (DENV) was detected in 83.33 % (n=10) patients**.** Among them Serotype dengue**-**4 **(**DENV**-**4**)** was detected in 40% (n=4) patients, DENV-2 in 30% (n=3) patients, DENV-1 in 10% (n=1) and DENV-3 in 20% (n=2) patients.[23] The negative RT-PCR results in 06 cases in this study may be attributable to the reasons like detection sensitivity rate of the RT-PCR assay, loss of sample integrity due to storage of the sample in -20 degree Celsius freezer or nucleic acid disintegration.[24] In a study in Bangladesh reported RT-PCR method giving an accuracy of 98.87%. Out of 89 NS1 positive cases 88 were RT-PCR positive. Among the RT-PCR positive cases, DEN-1, DEN-2 or both DEN-1 and DEN-2 were found in 46.7%, 51.1% & 2.2% cases respectively. No cases of DEN -3 or DEN- 4 were detected.[8]

A seroprevalence study in 2012 found that 80% of individuals in Dhaka had evidence of past infection with dengue however, as individuals can get infected more than once by different serotype, so, this result doesn't assure protection from the infection and/or disease. Infection with other serotype (DEN-3 or DEN-4) might have potential risk of large epidemics.[25]

The enormous expansion of dengue infection are rapid population growth, urbanization with inadequate public health systems, lack of vector control, climatic variability and rainfalls, and increased travel (especially air travel) to endemic areas. Due to aforementioned factors, there is an increase in the reportable cases of dengue infection in different countries with more severe forms of the disease.[26]

Conclusion:

Dengue, an acute systemic viral infection has gradually become one of the leading causes of morbidity and mortality in tropical and subtropical areas in the last few decades. Global expansion due to international travel, climate change with distribution from urban to rural settings make the dengue virus as one of the prioritized neglected tropical diseases (NTDs). This study reflects that 2021 Dengue epidemic in Bangladesh was caused predominantly by DEN-3 serotype. RT-PCR technique can be used as a most sensitive and reliable method for dengue diagnosis along with the specific serotypes. Continuous surveillance is crucial for early warning of emergence of new serotype in the circulation and public health preparedness.

Conflict of interest: No conflict of interest.

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Original Article

Frequency of Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency in women with complicated pregnancy and its outcome- an experience of 30 cases

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Abstract

Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest human enzymopathy, affecting estimated 470 million people worldwide. Researchers have found that there is a correlation between G6PD deficiency and adverse pregnancy outcome like miscarriage or spontaneous abortion in pregnant women. This enzymopathy may be one of the risk factors for complicated pregnancy.

Objectives: To assess the frequency of G6PD deficiency among pregnant mother with complicated obstetric history. We also evaluated its consequence on pregnancy outcome.

Methods: This was a cross sectional type of descriptive study. The study population included 30 pregnant women, having complicated obstetric history. Exclusion criteria were women with TORCH infection, diabetes mellitus, thyroid dysfunction and heart disease. Sampling technique was purposive type of non-probability sampling. Erythrocyte G6PD level was measured by Spectrophotometric method using kit of Randox. Hemoglobin concentration, TC of RBC and Reticulocyte count were measured by standard laboratory techniques.

Results: About 5 (16.67%) of study population had G6PD deficiency and among them 3 delivered live, healthy baby but unfortunately other 2 cannot. The hemoglobin concentration and total count of RBC were lower in G6PD deficient female but reticulicyte count was normal.

Conclusion: This study revealed that G6PD deficiency may be a contributory factor for complicated pregnancy. The postulated cause may be hemolysis associated with G6PD deficiency.

Keywords: G6PD deficiency**,** complicated pregnancy, hemolysis

Introduction:

A complicated pregnancy refers to any pregnancy in which mother or infant is at increased health risk. The majorities of women experience uncomplicated pregnancies but between 10-15% of women suffer from complications.[1]

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Factors associated with complicated pregnancy includes anemia, hypertension, pre-eclampsia, eclampsia, upper urinary tract infection etc. The unfavorable fetal outcome may be in terms of two or more consecutive spontaneous abortions, early neonatal deaths, intrauterine fetal death (IUD), intrauterine growth retardation (IUGR), still birth and congenital abnormalities.[2]

G6PD is the initial enzyme in the alternate pathway of glucose metabolism. It plays an important role in hexose monophosphate shunt, which is an important glucose oxidation pathway. It leads in the formation of reduced Nicotinamide Adenine Dinucleotide Phosphate (NADPH) and pentose (ribose5-phosphate). NADPH attenuates oxygen radicals that continuously emerge during the physiological process. G6PD deficiency is an enzymatic abnormality due to the mutation of the G6PD gene and thus decreased the enzyme activity.[3,4]

According to Beutler[5] in the eastern hemisphere, G6PD enzyme deficiency has the highest prevalence and frequency. It is an X linked disorder which primarily affects male. But may also fully express in homozygous female.[6] The common features of G6PD deficiency is hemolytic anemia and neonatal jaundice. The diagnosis of

G6PD enzyme deficiency is established when G6PD enzyme activity is < 60%. At this level the clinical signs become evident.

World Health Organization (WHO) classified the different G6PD variants based on the measurement of the enzyme activity and also the severity of hemolysis.[4,5,7,8]

The classification is described below:

Class I : Severe deficiency (<10% activity) with chronic hemolytic anemia

Class II : Severe deficiency (<10% activity), with intermittent hemolysis.

Class III : Moderate deficiency (10-60% activity), hemolysis with significant oxidant stress.

Class IV : No enzyme deficiency or hemolysis, no clinical sequelae.

Class V : Increased enzyme activity

G6PD deficiency generally does not result in remarkable clinical symptoms. However, upon exposure to oxidants it can be leading to clinical features. Currently, the observation of clinical symptoms resulting from G6PD deficiency is only directed towards hemolytic anemia.[7]

Investigators from different countries showed that there may be a relationship of G6PD deficiency with miscarriage or spontaneous abortion, stillbirth, IUD.[9, 10, 11] Giorgio et al [10] found that pregnant women with G6PD deficiency had history of stillbirth in 20% cases and miscarriages in 3.4% cases and few had IUD. Animal model study with G6PD deficiency reveals intra- or extra uterine fetal death and abnormal fetal delivery.[12] This was confirmed by Longo,[13] who proved that G6PD could distort placental development resulting in fetal death.

Some recent study proved that several antioxidant enzymes play role in organogenesis during intrauterine development. Some dominant members of this group are superoxide dismutase (SOD), glutathione peroxidase (GSHPX), and catalase. To function properly, glutathione peroxidase (GSHPX) and catalase require NADPH, which is a product of glucose 6 phosphate dehydrogenase activity.[14,15] In G6PD deficient pregnant women there is diminished action of glutathione peroxidase (GSHPX) and catalase, resulting an increase in hydrogen peroxide (H_2O_2) which in turn induces formation of hydroxyl radical (OH^-). This OH^- leads to damage of the important cellular components which plays a vital role in maintaining cellular integrity and survival of tissue.[16]

The importance of G6PD in normal embryonic development is becoming established day by day. In placental syncytiotrophoblast, concentration of G6PD enzyme is lower than other trophoblastic cells. It causes oxygen pressure to be increases three times than normal resulting oxidative stress. This trophoblastic change occurs at about 10 to 12wks of gestational age. Therefore, spontaneous abortion may occur in female who suffers from G6PD enzyme deficiency.[15, 16, 17] According to Jalan Anil [19] the G6PD gene is located in the telomere region chromosome X (Xq28). It can be attributed to the occurrence of repeated abortion. Result of the study showed that 50-70% of spontaneous abortion is that of unknown cause [19].

Materials and Methods:

This was a cross sectional type of descriptive study. For this, 30 multi-gravid pregnant women, were selected from the Out Patient Department (OPD) of Obstetrics and Gynaecology in BSMMU, Dhaka. The inclusion criteria included gestational age of or more than 8 weeks; ever experienced miscarriage, pv bleeding, intra- or extra uterine fetal death, stillbirth; early fetal death, with no TORCH (toxoplasma, rubella, cytomegalovirus or herpes) infection; no hormonal abnormalities (diabetes mellitus or thyroid) and no heart diseases; and not alcoholic or cigarette smokers. The exclusion criteria were the age below 20 or more than 35yrs, primigravida, experienced miscarriage in gestational age less than 8 weeks., Rh negative mother, smokers, pregnant women having jaundice, diabetes mellitus, thyroid diseases, history of high fever (>100^{0}F) in present pregnancy were excluded.
5ml of blood samples were taken from ante-cubital veins, for estimation of hematological tests and other tests. The Erythrocyte G6PD level was determined by spectrophotometric method by using kit of Randox [20] and Hb concentration [21], TC of RBC[22] and reticulocyte count [22] were estimated by standard laboratory technique.

Results:

Table 1: Distribution of pregnant women according to age group (n=30)

Age group (years)	Number	Percent
20 -25	9	30
26-30	16	53.33
31-34	5	16.67

Table 1 shows majority of the women 15 (53.33%) from age between 26 to 30 years followed by 9 (30%) of the pregnant women from group 20 to 25 years and rest 5 (16.67%) were from age group 31 to 34 years.

Table 2: Distribution of study subject according to Erythrocyte G6PD level (n=30)

G6PD level (MU/10^{9}E)	Number	Percent
Normal (245 -299 MU/10^{9}E)	25	83.33
Below normal (<245 MU/10^{9}E)	5	16.67

Table 2 shows that among 30 samples, only 5 (16.66%) women had below normal G6PD level (enzyme G6PD activity was< 60%).

Table 3: Distribution of pregnant women according to pregnancy related complications (n=30)

Complications	Women with normal G6PD level (n=25)		Women with below normal G6PD level (n=25)		p-value
	No.	Percent	No.	Percent	
Pre-eclampsia	7	28	3	60	0.386^{ns}
Eclampsia	3	12	2	40	0.380^{ns}
Severe anemia	5	20	3	60	0.196^{ns}
UTI	17	68	4	80	1.000^{ns}
PV bleeding	7	28	1	20	1.000^{ns}

p-value obtained by Fisher Exact test, ns= not significant

Table 3 gives an idea about pregnancy related complications. The adverse effects like pre-eclampsia (60%), eclampsia (40%) and severe anemia (60%) are more in G6PD deficient pregnant women. About 68% women with normal G6PD level and about 80% women with deficient group had UTI. Per vaginal (PV) bleeding during pregnancy was more in non deficient group (28%) than the deficient group (20%).

All p values are non-significant because of small sample size.

Table 4: Distribution of pregnant women according to fetal outcome in previous pregnancies. (n=30)

Fetal outcome	Women with normal G6PD level (n=25)		Women with below normal G6PD level (n=5)		p-value
	10	Percent	2	Percent	
Live birth	19	40	5	40	1.000^{ns}
Miscarriage	5	76	1	100	0.540^{ns}
Intrauterine death	11	20	3	20	1.000^{ns}
Stillbirth	6	44	4	60	0.869^{ns}
Early neonatal death		24		80	0.056^{ns}

p-value obtained by Fisher Exact test, ns= not significant

Table 4 shows complications like miscarriages, IUD, stillbirths, early neonatal deaths are more common among G6PD deficient group compared to normal G6PD group, though they are statistically non- significant.

Table 5: Distribution of G6PD deficient pregnant women according to their present pregnancy outcome. (n=5)

Present pregnancy outcome	No.
Full term healthy baby delivered by C/S	2
Pre term baby delivered by C/S	1
Died after birth	1
Stillbirth	1

Table 5 shows the fetal outcome of present pregnancy of G6PD deficient women. Among 5, two of them gave birth of healthy baby, one mother had pre term delivery but baby is alive. One baby died 2 hours after delivery and another mother experienced stillbirth.

Table 6: Distribution of study population according to their hematological parameters like Hemoglobin, Erythrocyte and Reticulocyte levels

Heamatological parameters	Women with normal G6PD level (n=25)		Women with below normal G6PD level (n=5)	
	Normal	Below normal	Normal	Below normal
Hemoglobin (g/l) Mean ± SD	21	4 11.04 ±1.17	2	3 10.16±1.91
Erythrocyte (10^{12}/L) Mean ± SD	17	8 4.14±0.49	3	2 3.95±0.46
Reticulocyte (%) Mean±SD	25	0 0.99±.43	5	0 1.6±.65

Mean Hb. concentration (11.04 ±1.17gm/dl), erythrocyte (4.14±0.49X10^{12}/L) is more in pregnant women with normal G6PD enzyme level. But mean reticulocyte count (1.6±.65%) is more in deficient group as shown in Table 6.

Discussion:

The purpose of the study was to analyze the erythrocyte G6PD level in pregnant women who had complicated obstetric history. Also hemolytic status of these subjects was assessed by measuring Hb concentration, TC of RBC, and reticulocyte count.

In this study, about 16.66% of pregnant women with complicated obstetric history had Erythrocyte G6PD enzyme deficiency. Hb concentration and TC of RBC were lower in those who have less G6PD activity. But 2 of them had normal Hb and and 3 of them normal RBC count. Similar type of findings were also reported by Suhartati et al and Misra et al.[11, 19] Low levels of Hb and erythrocyte count indicate hemolysis which is suggestive of G6PD deficiency. In addition, upper normal reticulocyte count may be the result of compensatory increase in erythropoiesis in response to hemolysis. Hemoglobin and erythrocyte counts influenced the G6PD activities assays. In addition, it has been suggested that deficiency of this enzyme G6PD leads to hemolysis of RBC which showed changes of some of the hematological parameters. Therefore, lower values of hemoglobin concentration and total count of RBC with upper normal reticulocyte count are the consequences of G6PD deficiency depending on the hemolytic status. [11,15,]

Pregnancy related complications like pre-eclampsia (60%), eclampsia (40%) and severe anemia (60%) are more in G6PD deficient pregnant women in this study. Also there is increased percentage of adverse fetal outcome like

miscarriage, IUD, stillbirth in the deficient group. Some researchers found that, as there is less generation of NADPH by erythrocytes, which is a regulatory enzyme of pentose phosphate pathway, in pregnant women G6PD deficiency. This subsequently results in destruction of RBC.[11] In G6PD deficient pregnant women, increased oxidative stress and a disrupted antioxidant system causes placental lipid peroxidation resulting in decreases synthesis of placental hormone. This ultimately leads to the development of pregnancy related complications such as pre-eclamsia, miscarriage, early fetal death, fetal growth retardation.[11,13.]

Some other investigators suggested that superoxide radicals have a potential role in synthesis of prostaglandin F2α (PGF2 α) in human endometrial stromal cells. As PGF2α is a powerful inducer of uterine contraction, the increased rate of PGF2α production by oxidative stress in the deciduas may contribute to spontaneous miscarriage and other complication in G6PD deficient pregnant women.[23] Similar type of observation also experienced by Giovanni et.al.[24] that increased oxidative stress causes increased production of reactive oxygen species (ROS) in red cell. This ROS induced damage to lipid and proteins may cause destruction of red cell membrane and hemolysis in pre-eclampsia.[25,26]

Poor pregnancy outcome like miscarriage and IUD has many patho-physiological explanations. One hypothesis is that, Oxygen derived free radicals act as a teratologic threat to the fetal tissues. Some experts suggested that G6PD deficiency is a contributory factor for bad obstetric history. They also showed that complicated pregnancy with associated reduced activity of erythrocyte G6PD, causes generation of less NADPH by erythrocytes.[11] Increased oxidative stress and a disrupted antioxidant system may be involved in a variety of pregnancy complications such as eclampsia, preterm labour, fetal growth retardation, and miscarriage etc. [25,26]

According to Jaumiaux et al[15] syncytiotropoblast is responsible for placental hormones synthesis which is vulnerable to oxidative stress due to G6PD deficiency. If antioxidant defense is hampered as occurs in G6PD deficiency, extensive rise of oxygen tension in the normal placenta during establishment of maternal circulation may be a factor in the pathogenesis of miscarriage and pre-eclampsia.

Various possible explanations made by different investigators as mentioned earlier like increased oxidative stress, disrupted antioxidant system, increased production of ROS, increased lipid peroxidation of placenta, defective placental hormone synthesis etc are also in favor of this enzyme deficient state as a contributory factor for complicated pregnancy. However, due to small sample size, individual role of them was not possible to measure in this study.

Conclusion:

This study reveals that pregnant women with G6PD deficiency may be one of the risk factor for complicated pregnancy like pre-eclampsia, miscarriage and fetal death. In addition, hemolysis may aggravate the complications during this group of pregnancy. Further studies using molecular analysis should be carried out to the patients with G6PD deficiency to raise awareness and improve the life quality of G6PD deficiency pregnant women.

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Review Article

Marfan's syndrome and pregnancy: Pre-conceptional to post-partum management

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Abstract

The management of a patient with Marfan's syndrome in pregnancy requires attention to specific issues to ensure safe motherhood. It comprises a multidisciplinary approach and involves cardiologists, geneticists and feto-maternal specialist. An overall idea regarding important management issues will help the supervising doctor to take necessary decisions regarding timely referral if judged necessary. This review article has been inspired by a 28-year-old second gravida presenting at 16 weeks of pregnancy with typical features of Marfan's syndrome with acute retention of urine and concomitant uterovaginal prolapse (Photographs are provided with patient's consent). Collaboration with Cardiology revealed prolapsed anterior mitral leaflet (MVP) with noncoaptaion of Tricuspid Valve and mild Pulmonary hypertension (PASP 43.1 mm of Hg) with normal Aortic root diameter (27mm) and Ejection Fraction 66% at rest. The patient had an uneventful antenatal period with vaginal delivery of a healthy female child at term. The uterine descend spontaneously corrected after delivery. She was advised LARC Cu-T after 6 weeks and annual echocardiography for follow-up.

Introduction:

Marfan's syndrome (MFS) is an autosomal dominant condition with typical skeletal and other features including long bone overgrowth, high arched palate, thoracolumbar scoliosis, ectopia lentis/lens dislocation and aortic root dilatation. MFS is caused by a mutation in the gene for MFS (FBN1) on chromosome 15q21, encoding the extracellular matrix protein **fibrillin-1**resulting in decreased elastin content in vessels[1,2]. Unfortunately, MFS often remains undiagnosed prior to pregnancy and is recognized only after life-threatening complications occur in pregnancy or after the delivery. The article is designed to include an overview of Marfan's syndrome including diagnostic features/criteria, clinical directions for the detection and monitoring of evolving/pre-existing cardiovascular features ; such as aortic dilation, aortic dissection and concomitant secondary pulmonary hypertension. Pre-conceptional optimization of cardiac status by surgery if indicated/ aortic root replacement) is advised is selected Marfan's patients, as an aortic root diameter of 4cm and beyond with or without concomitant significant pulmonary hypertension is an absolute contraindication of pregnancy necessitating the need for strict contraception. Careful monitoring of blood pressure including the need for beta-blockers to prevent superimposed pre-eclampsia is a must. Moreover , the risk of sub-acute bacterial endocarditis (SBE) and endocarditis prophylaxis in case of any invasive procedure needs to be emphasized. Assessment of risk of Venous thromboembolism(VTE) in pregnancy with Marfan's syndrome with or without mitral valve prolapse and subsequent institution of appropriate thromboprophylaxis as judged by the VTE risk score Both ante partum and post-partum) is needed to prevented related morbidity/ mortality. The role of synchronous routine antenatal screening of common pregnancy complications; such as pregnancy –induced hypertension, diabetes,anaemia and Urinary tract infection (UTI) should not be overlooked.

Addressing the issues of connective tissue laxity evident as uterine descent in pregnancy, pelvic girdle abnormalities or kyphoscoliosis and its impact on vaginal birth and regional anaesthesia during operative delivery involves anesthesiologist and physiotherapist. Regarding fetal impact, fetal inheritance as an autosomal dominant trait poses both diagnostic challenges and ethical issues. Surveillance for detection of intra-uterine growth restriction has heightened significance with strict emphasis on growth centile monitoring andDoppler wave form study of Umbilical artery and Middle cerebral artery as pregnancy advances. Careful planning of delivery may include mode of delivery and maternal and or fetal safety of the proposed route. Lastly, post-partum issues include cardiac risk reduction and PPH prevention strategies. Choice and safety of appropriate personalized contraceptive methods cannot be overemphasized.

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Discussion:

The diagnosis of Marfan's is primarily clinical based on the Ghent criteriapublished in 1996, later revised to take into account many individuals with MFS who do not have the FBN1 mutation and there is no rapid and efficient testing for FBN1 mutations (Table 1)[3,4]. In the United States alone, estimated prevalence of MFS is 1 in 5,000, affecting both genders equally[2,5.]Recently, heterozygous mutations have also been identified in the gene encoding tissue growth factor-β receptor 2 (*TGFBR2*) on chromosome 3p24.2–25[6] with resultant increased transforming growth factor-β (TGF-β) activation. MFS segregates as an autosomal dominant trait in ~70% of families and the remainder of cases is caused by de-novo mutations.

Cardiac complications:

Majority (80%) of MFS patients have some form of cardiovascular involvement, including aortic dilatation, aortic regurgitation and mitral and tricuspid valve prolapse with or without regurgitation [2,3.] Although in the past life expectancy was reported to be greatly reduced, significantly better life expectancy due to improved medical and surgical treatment has been recently described. The leading cause of morbidity and mortality in MFS is aortic dissection (AoD).[3,4.]

In summary, the rates of aortic complications reported in prospective studies appear to reach an average 4.0%[4] and is 2–6% in large retrospective reports including 1,142 pregnancies[4,5]. Progressive aortic root dilatation and an aortic dimension of > 4 cm are associated with increased risk. The expected rate of Aortic dissection (AoD) ranges from 1% in women with aortic root diameter <40 mm to as much as 10% in high-risk patients:aortic root diameter >40 mm, rapidly evolving dilatation or history of previous dissection of the ascending aorta[5]. Despite the rare occurrence of AoD in women with MFS with a normal size aorta[6,7,8,9], an event-free pregnancy cannot be guaranteed in these women.

Although in women with minimal cardiac involvement and an aortic root <4.0 cm, pregnancy is concluded to be relatively safeby Goland *et al.* [3]Rossiter *et al.*[8],Pyeritz *et al.* [10], Stella et al [11], Meijboom *et al.* [12.]Goland *et al.* in a review of 39 cases of pregnancy related complications described AoD in 29, involving the ascending aorta (19 cases), descending aorta (8 cases) or both (2 cases), 8 of these women were undiagnosed with MFS prior to the occurrence of aortic complications. Five patients developed an AoD before week 20 of gestation (13-20 weeks), 18 patients at 24-40 weeks, and 6 after delivery. One patient developed an extension of distal dissection at 1 week PP, chronic dissection remained unchanged in two patients and intracranial hemorrhage occurred PP in two cases. Nineteen of the patients were diagnosed with dilatation of aorta prior to pregnancy and four had a history of aortic surgery.[3]Pyeritz *et al.*[10] showed only a low risk for maternal complications and death in a retrospective analysis of 105 pregnancies in 26 patients with MFS and a prospective follow-up of 10 patients who had minimal or no pre-existing cardiovascular disease. Rossiter *et al.* [8]prospectively evaluated 45 pregnancies in 21 women with MFS and reported AoD in only 2 cases (4.4%) while the rest who had aortic diameter <4.0 cm tolerated pregnancy well. More recently, Lipscomb *et al.*[9]reported the outcome of 91 pregnancies in 36 women with MFS and described AoDs in pregnancy in 4 (4.4%) with two others requiring aortic surgery following delivery. Meijboom *et al.* [10]followed prospectively 127 women with MFS and compared aortic root diameter changes during 33 pregnancies with those of 22 matched childless women. During 6.4 years of follow-up, no significant difference in growth of the aortic root was obtained and only one woman with previous type A dissection developed type B dissection during her 2nd pregnancy. Yuan *et al.* [13]published a literature review of 27 cases of postpartum dissection which occurred from day 1 to day 42 and 41% of them accounted for MFS. Based on this information it seems advisable to extend the follow up of women with MFS for 3-6 months post-partum.

Aortic dissection can be acute, chronic (evolving over 2 or more weeks), recurrent, dynamic/evolving with distal extension, progressive requiring Aortic root replacement surgery even in pregnancy and complicated by intracranial hemorrhage/SBE. Acute aortic dissection should be suspected if a woman in late pregnancy presents with severe chest or inter-scapular pain, particularly if associated with systolic hypertension, different blood pressure in each arm, and an early diastolic murmur of aortic regurgitation. AoD can be of two types: A (Involving the ascending aorta, commoner and having an acute presentation) and B (involving descending aorta , causing renal/mesenteric is chemia, usually chronic). Although AoD occurs in most women during 24-40 weeks and post-partum, it may also occur at any time of gestation[9].An average increase/growth of 3 mm (0–7 mm) in aortic root diameter has been naturally observed during pregnancy in MFS, which decreases postpartum, but without complete recovery at 5 years follow-up.Multiparity, larger preconceptional aortic diameter, and greater rate of aortic growth during pregnancy, and no β-blocker therapy and irregular follow-up during pregnancy, prior history of aortic surgery are known risk factors for AoD and adverse obstetric outcome. Therefore it is important to measure the aortic root in pregnancy and monitor the growth of the aortic root between 24-40 weeks and post-partum and ensure compliance regarding beta –blockers in pregnancy. Baseline aortic root more than 40 mm or any root dilatation of more than 3 mm from the base line are suspects. The American guidelines (ACCF/AHA) recommend monthly or bimonthly echocardiographic measurements of the ascending aortic dimensions in women with aortic dilatation during pregnancy and the first weeks after delivery.[3,7,10]

ß-blockers in pregnancy:

A number of studies have demonstrated that ß-blockers slow the growth of the aortic root and significantly reduce rates of aortic dissection and death.[14] However, a recent meta-analysis of all prospective trials demonstrated that although β-blockers were effective in aortic root growth rate reduction in patients with MFS, they had no influence on rate of dissection and final aortic size. The applicability of these findings to pregnancy, which is associated with

changes in the aortic wall and enhanced risk of dissection, needs to be studied in more detail, but on the basis of available information, the prophylactic use of ß-blockers during pregnancy seems to make a good clinical sense. The use of selective β receptor blockers is recommended during pregnancy at a dose titrated to reduce heart rate by at least 20 bpm with a close follow-up to detect intra-uterine growth restriction[15]. A favorable effect of angiotensin receptor blockers (ARB) leading to a reduction in rate of progressive aortic root dilation in patients with MFS has been reported. The use of ARBs in pregnancy, however, is contraindicated because of potential toxicity to the fetus[16], therefore, ARB's should be switched to β-blockers as soon as contraceptives are stopped and pregnancy is planned. As high blood pressure may increase the risk of aortic complications, strict blood pressure control is recommended for all pregnant women with MFS. The use of nitroprusside for acute AoD during pregnancy may lead to thiocyanate toxicity to the fetus, thus, the gestational use of nitroglycerine or hydralazine plus β-blockers to control blood pressure is preferred.

VTE and MFS:

Thrombotic events are relatively rare in Marfan's patients, indicating a possible protective function for TGF-β activation, potentially through prevention of lipid lesion formation.[17] However, contrasting evidence exists of increased risk for hypercoagulability and endothelial dysfunction in Marfan's syndrome, both of which may contribute to thromboembolism formation. Bridges, et al. noted increased prothrombotic factor VIII von Willebrand Factor antigen levels in Marfan patients secondary to endothelial injury caused by impaired tensile strength in blood vessels.[16] In the same study, increased thrombomodulin levels, which promote anticoagulation, were also noted and may serve to balance the hypercoagulability of elevated factor VIII levels. Endothelial injury and dysfunction are known to promote thrombus formation which can contribute to pregnancy-induced hypertension/Pre-eclampsia and thromboembolism in pregnancy. Wilson, et al. explored the close association between fibrillin and endothelial cells, indicating a possible functional role for fibrillin in the endothelium. The study demonstrated impaired flow-mediated vasodilation, possibly due to dysfunctional mechanotransduction and reduced large-artery distensibility as a result of decreased fibrillin levels [19]. Furthermore, Wilson, et al. and Chung, et al investigated endothelial dysfunction in patients with Marfan syndrome through various mechanisms (e.g. reduced expression of endothelial nitric oxide synthase (eNOS) and Akt, decreased cyclic guanosine monophosphate (cGMP) in the aorta, diminished acetylcholine signaling). In acquired/hypoxic Pulmonary arterial hypertension (PAH), Alpha enolase 1 (ENO1) regulates metabolic reprogramming. An overexpression of ENO1 due to metabolic shift toward increased glycolysis observed in pulmonary artery smooth muscle cells (PASMC) promotes a synthetic, de-differentiated, and apoptotic-resistant phenotype via the AMPK-Akt pathway explaining progressive PAH after the inciting stimulus.[20]

Anaesthetic considerations:[21-22]

Considerations of anaesthesia particularly general anesthesia **(**G/A**)** in a patient of Marfan syndrome should take into account the followings**:**

- Airway problems related to difficult intubation due to high arched palate,potential cervical spine (C1/2) ligamentous instability and Temporomandibular Joint (TMJ) laxity & potential dislocation with laryngoscopy
  - Cardiovascular dysfunction associated with Valvular disease (Aortic incompetence AI, MR, MVP),Aortic arch aneurysm, potential for aortic rupture &prior risk of dissection ,MIs secondary to medial necrosis of the coronary arterioles and arrhythmias & conduction defects
  - Respiratory dysfunction due to kyphoscoliosis, pectuscarinatum/excavatum & restrictive lung disease, pulmonary hypertension, corpulmonale, potential for spontaneous pneumothorax , emphysema
  - Ocular considerations: lens dislocation, retinal detachment, glaucoma
  - Potentially difficult positioning during regional anesthesia
  - Ruling out the entity ofduralectasia

Therefore the goals during anesthetic intervention are to minimize increase in aortic wall tension through avoidance of sustained increase in systolic BP during G/A, establish airway with minimal cervical spine movement, maintain hemodynamic goals of associated valvular lesions, provision of lung protective ventilation considering restrictive lung disease & potential bullae, careful positioning (lax joints & potential peripheral nerve injury) and optimizing post-operative pain (neuraxial or regional preferrably) .

Mode of delivery and analgesia:[23-26]

- If the patient has no symptoms & aortic root diameter is < 4cm → no special considerations & vaginal delivery can be allowed unless there is any obstetric indication for a ceasarean delivery.
- If aortic root dilatation/AI → multidisciplinary management with cardiology,cardiac surgery and high-risk obstetrics team, though some authorities recommend cesarean section for aortic diameter > 4.5cm and allow labor if > 4cm&< 4.5cm.
  - Issues in pregnancy are the airway might be more difficult than in non-pregnant counterpart
  - Neuraxialanaesthesia/analgesiais good option for vaginal delivery & cesarean section;considering very early epidural to reduce shear forces on aorta during labour.
  - Drug therapy to prevent tachycardia &using labetalol as the preferred antihypertensive drug to maintain systolic BP less than120mmHg.

- Avoidance of ergotamine post -partumas it may precipitateabrupt elevation of blood pressure.
- Presence of Dural ectasia (ballooning or widening of the dural sac associated with herniation of nerve root sleeves)is not an absolute contraindication to epidural placement but higher risk for failed block and dural puncture with consequent Post dural puncture headache (PDPH).

Genetic testing:

While Marfan syndrome can be diagnosed based on clinical features/Ghent diagnostic nosology alone, genetic testing of the FBN1 gene and exclusion of phenotypically similar Marfanoid conditions, like Loeys-Dietz syndrome and vascular Ehlers- Danlos syndrome, is important. Some clinical features of Marfan syndrome may develop with time while some features may not emerge at all. Genetic testing can help to confirm the diagnosis where clinical diagnostic criteria cannot be fulfilled but is highly suspected and thereby guide management. It is recommended that an individual bearing FBN1 gene disease-causing variant should be evaluated annually by a cardiologist and ophthalmologist. Additionally, people that have a clinical diagnosis of Marfan syndrome due tophenotypical similarity may actually have a variant in a different gene identified only through genetic testing. Confirming the genetic variant in the FBN1 gene versus a different gene is important as it can impact medical care. Some of the related conditions such as vascular Ehlers-Danlos have dilatation of arteries other than the aorta, needing periodic angiography of selected vessels in addition to echocardiography. Additionally, other similar conditions have different surgical recommendations regarding timing of repair aortic aneurysm. Women with Loeys-Dietz syndrome have a risk of aortic dissection and uterine rupture during pregnancy and directly after childbirth. Pregnancy with vascular Ehlers Danlos syndrome is uniquely associated with obstetric complications include spontaneous uterine rupture during labor, cervicovaginal laceration, and spontaneous rupture of blood vessels and the colon. Once the underlying genetic variant in an individual with Marfan syndrome has been identified through genetic testing, this allows the rest of the family members to have tested for the same variant. Screening thosefamily members helps to detect MFS and related features, like aortic aneurysms and dissection.[26-28]

Table 1: Ghent diagnostic nesology

System	Major criteria	Minor criteria
Skeletal	At least 4 of the following features: Pectus carinatum Pectus excavitum requiring surgery ULSR <0.86 span: height >1.05 Wirst and thumb sings Scolliosis >20º or spondlisthesis Reduced elbow extension (<170°) Pes planus Protrusion acetabulae	Two of the major features, or 1 major feature and 2 of the following: Pectus excavatum Joint hypermobility High palate with dental crowding Characteristic face
Ocular	Lens dislocation (ectopia lentis)	Flat cornea Increased axial length of globe (causing myopia) Hypoplastic iris or cilliary muscle (causing decreased miosis)
Cardiovascular	Dilatation of aortic root	Mitral valve prolapse Dilatation of the pulmonary artery, below age 40 Calcified mitral annuas, below age 40 Other dilatation or dissection of the aorta
Pulmonary	None	Spontaneous pneomothorax Apical blebs
Skin/integument	None	Striae atrophicae Recurrent or incisional hernia
Dura	Lumbosacral dural ectasia	None
Genetic findings	Parent, child or sibling meets these criteria independently Fibrillin 1mutition known to cause marfan syndrome Inheritance of DNA marker haplotype inked to marfan syndrome in the family	None
Having one of the features listed constitutes a major criterion or minor criterion for all systems except the skeletal system, where more than one feature is needed. ULSR, upper to lower ratio		

Obstetric complications and neonatal outcome:

Pregnancy in women with MFS has been shown to be associated with a high rate (up to 40%) of obstetric complications, such as cervical insufficiency, premature deliveryodds ratio (OR) 2.15 (1.60-2.89) (both iatrogenic and spontaneous sequel toprelabour rupture of membranes), pregnancy-induced hypertension/pre-eclampsia,antepartum haemorrhage, operative vaginal delivery (forceps or ventouse), post-partum haemorrhage, post partum cardiac arrhythmia OR 10.64 (5.49-20.61), pneumothorax OR 51.95 (6.18, 437.10) and associated adverse neonatal outcome e.g. intrauterine growth restriction, small for gestational age fetus OR 2.06 (1.24-3.43)and neonatal mortality[29-35].Preconception counseling should take these risks into consideration and appropriate pregnancy care in tertiary centers should be considered. Each of these obstetric complications need to be addressed individually irrespective of the diagnosis of MFS. Indications for caesarean section OR 1.91 (1.53-2.38) may be obstetric or due to evolving cardiac conditions/ progressive aortic root dilatation, Aortic root diameter>40mm or deteriorating Left Ventricular function. For the affection of the baby, fetal echocardiography may be used at 24 weeks to diagnose cardiac manifestations of MFS in the fetus. An inverse relationship between birth weight and maternal height also exists. **Marfan disease of the uterine vasculature** is a unique histopathologic change found in the hysterectomy specimen of patient of Marfan syndrome suffering from secondary Postpartum Haemorrhage (PPH).[36] This is characterized by degenerative vascular changes characteristic of Marfan's syndrome with unexpected affection of large number of small muscular arteries with marked aneurysmal dilatation.

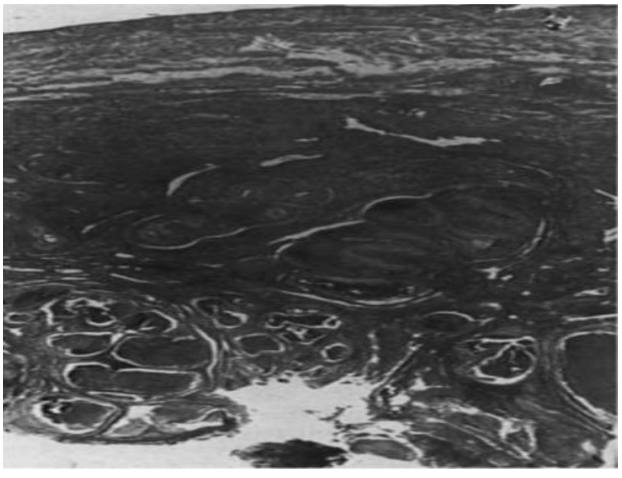


Fig. 1: Microscopic section of urine wall full thickness, spiral arteries progressively thin walled and dilated toward inner aspect. Magnification x 5-5.

Conclusion:

Compilation of facts and recommendations for the optimum management of individual patients of MFS planning pregnancy and their subsequent antenatal,intrapartum and postpartum care is the goal of this review article. Through guarded advice and timed investigation and attention to every details by multidisciplinary team, it would be possible to achieve safe maternity along with cardiac safety.

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Pelvic abscess following postpartum endometritis after caesarean section: A rare case report

Jebunnaher S

Abstract

Caesarean section is one of the most commonly performed operations in women worldwide, with gradually increasing trend especially in high and middle income countries. Pelvic abscess following postpartum endometritis is very rare complication associated with caesarean section. Here a case of post-partum endometritis with pelvic abscess was presented that developed after emergency caesarean section even with prophylactic antibiotic coverage. She had also uncontrolled diabetes, hypothyroidism and pregnancy induced hypertension. As patient showed clinical evidence of wound and puerperal infection, on 6th POD wound swab report revealed staphyloccous infection. As intervention with repeated and multiple antibiotic did not improve patient's condition, USG was done and she was diagnosed as endometritis with pelvic abscess. USG guided aspiration of 150 ml pus was done and following that day patient improved dramatically.

Keywords: Postpartum endometritis, Pelvic abscess, Caesarean section.

Introduction:

Endometritis is inflammation of the uterine lining. Bacterial infections during labour and the puerperium are among the leading causes of maternal morbidity and mortality worldwide.[1,2] Postpartum endometritis is the most common infectious complications following childbirth and This infection is more common after cesarean section than with vaginal delivery.[3]

Pelvic abscess is a life threatening collection of infected fluid in the Pouch of Douglas (POD), fallopian tube, ovary or parametrial tissue. It occurs in less than 1% patients with endometritis.[4] Pelvic abscess responds well to adequate antibiotic treatment.[5] Due to variable presentation, it requires early recognition, diagnosis, immediate hospitalization, and treatment regardless of the size of the abscess.[6] The incidence of pelvic abscess has declined with prophylactic antibiotics, however severe outcomes are still deemed to occur.[4]

Here we are presenting a case of post-partum endometritis with pelvic abscess that develops after an emergency caesarean section even with prophylactic antibiotic coverage.

Case Presentation:

Mrs. Morsheda, 35 years old lady, admitted with 38 weeks' pregnancy with rupture membrane for 3 days. She was a multiparous lady and also diabetic. During admission, she was on oral hypoglycemic drug, but her blood sugar was completely uncontrolled. Insulin was started as part of treatment. She also had hypothyroidism and Pregnancy induced hypertension (PIH). Prophylactic antibiotic (Cephalosporin) was given after admission. She was mildly anaemic and one unit of blood transfusion was given. As there had no spontaneous labour pain, induction was given with oxytocin but labour did not progress. During this time her Cardiotocography (CTG) was non-reactive & there was no progress of labour. So decision for caesarean section was taken with the consent from the patient.

In the post-operative period her blood sugar was uncontrolled. From 4th POD she developed severe lower abdominal pain which was unusual and treated with analgesic but condition did not improve. Two days thereafter on 6th POD we found discharge from the wound which was greenish, purulent and offensive in nature. Wound swab report revealed staphyloccous infection. At the same time, she was also having purulent offensive per vaginal discharge. High vaginal swab also taken for culture but reveled no growth as she was already on Inj Ceftriaxon. Due to high fever and wound infection her antibiotic was changed to Inj. Meropenem, Clindamycin and Gentamycin. Later on as per culture sensitivity report Inj. Linazolid was added. Even with parenteral antibiotic patient did not improve, so her USG was done which reveled thick collection (suggesting abscess) in the Pouch of Douglas (6.5X 8 cm), collection also noted in the pelvis along with bowel loops and hepatorenal angle (Figure: 1,2). Uterus was edematous with fuzz contour. Mild to moderate collection was noted in the uterine cavity. So she was diagnosed as endometritis with pelvic abscess. As the patient did not improve with parenteral antibiotic alone, USG guided aspiration was done. About 150 ml pus aspirated through posterior fornix from POD. Following that day patient improved dramatically.

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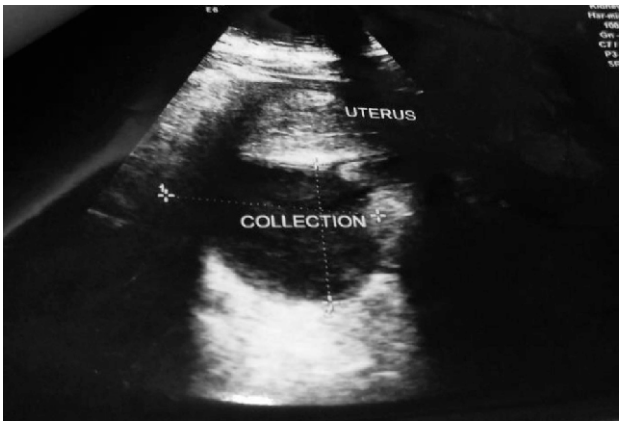


Figure 1: USG showing collection in Pouch of Douglas

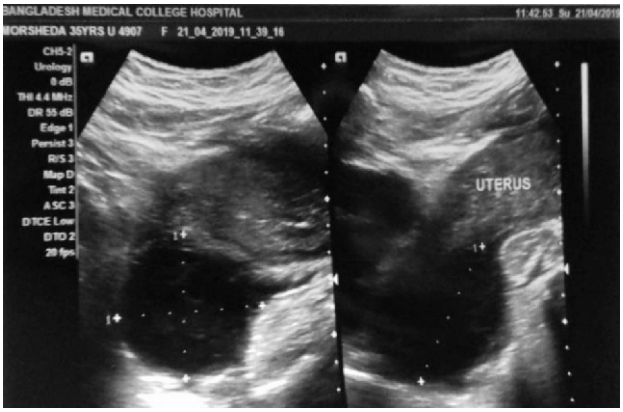


Figure 2: USG showing collection in Pouch of Douglas

Discussion:

Number of complications are associated with caesarean section. Post-partum pelvic abscess is a very rare complication occurring in <1% of post-partum endometritis which is < 0.1% of all cesarean section deliveries.[7]

This particular complication often creates a diagnostic dilemma, causes significant maternal morbidities and requires complicated and varied treatment approaches ranging from radiological imaging guided aspiration of pus to laparotomy and even hysterectomy. [7-9]

Incidence of postpartum endometritis is affected mainly by the mode of delivery. In vaginal deliveries the rate is 7.6%. In caesarean section (before labor starts). 13.8% and after unscheduled caesarean section (done after labor starts) it is 22.5%.[10]

Patients with post caesarean metritis often form a parametrial phlegmon, which develops as an area of induration within the leaves of broad ligaments. This is caused by cellulitis of adjacent caesarean section wound. This phlegmon rarely suppurates and forms an abscess.[9] The risk factors of post caesarean pelvic abscess are diverse and include- prolonged labour, Premature rupture of membrane (PROM), multiple vaginal examination, delivery by emergency caesarean section, low socioeconomic status, BMI >30, uncontrolled diabetes etc.[9,11]

Al-Abdullah N et al.[12] reported in their study high BMI is another risk factor for developing pelvic abscess following caesarean section. In their study they also showed that women who delivered by emergency caesarean section have a five times higher chance of developing pelvic abscess than those with elective caesarean section. They also focused that women with DM have twice the risk of developing pelvic abscess following caesarean section compared to woman without DM. Other risk factors are pelvic inflammatory disease, congenital anomalies of genital tract. Asymptomatic bacterial vaginosis is another important risk factor for post-surgical vaginal cuff cellulitis and abscess formation.[11]

In our patient she had multiple risk factors like uncontrolled DM, low socioeconomic status, anaemia, poor hygiene etc. More importantly, she had prolonged rupture of membrane and repeated vaginal examination was done and her emergency caesarean section was done due to fetal distress. Though she received prophylactic antibiotic several doses before her operation but could not prevent the development of pelvic abscess. This could be explained by the fact that antibiotic prophylaxis might not have covered the pathogens responsible for the abscess formation. Moreover, our patient had multiple risk factors specially uncontrolled diabetes. Some studies showed that emergence of more virulent pathogen such as ESBL Klebsiella, which is a global threat and might require a change in institutionally recommended antibiotic prophylaxis.[13-15] Muin et al.[4] reported presence of Gardnerella vaginalis, Mycoplasma hominis and Ureplasma in pelvic abscess following caesarean section. Yamaguchi et al. considered Mycoplasma hominis is the primary causative organism in post caesarean pelvic abscess.[16] Prophylactic antibiotic reduced the risk of endometritis by approximately 60%.[17]

Diagnosis of post caesarean pelvic abscess is often a challenge. Patient may have undulating fever, tender uterus, leukocytosis, elevated ESR, CRP. Profuse, malodourous vaginal discharge may be present.

In our patient her initial symptom was lower abdominal pain which was unusually severe. She was treated with analgesics but not improving. After two days, she developed high fever with copious, purulent, offensive vaginal discharge. Injectable ceftriaxone with metronidazole was started. Even after 48 hours she had high fever. Subsequently she developed purulent discharge from the cesarean section wound. Her antibiotic was changed according to the culture sensitivity report.

Most cost effective imaging technique to require to confirm the diagnosis is ultrasonography. Computed tomography scans are performed where there is doubt about the diagnosis or location of the abscess. We did ultrasonography to confirm the diagnosis.

Treatment of pelvic abscess may vary. Many of the cases respond to antibiotic alone and some may require surgical intervention. Once diagnosed, a combination of parental antibiotic should be started to treat the mixed aerobic and anaerobic organism. The gold standard antibiotics regimen is the combination of metronidazole or clindamycin with aminoglycoside, penicillin or 3rd generation cephalosporins. Broad spectrum parenteral antibiotics should have started promptly and continued 24 to 48 hrs after the patient become afebrile. However, 25% of the patient fails to respond to conservative treatment.[5] The success rate of broad spectrum intravenous antibiotics alone in women with pelvic abscess ranges between 34% to 88%.[18] It has been shown that the size of the abscess correlates with need for surgical intervention and duration of hospital stay.[19] In tubo-ovarian abscess, every 1 cm size was associated with an increase in inpatient duration by 0.4 days. The average abscess size for drainage / surgery was 7.7 cm; abscesses greater than 8 cm were associated with increased complication rates as in intra-abdominal rupture.[20]

Potential route for drainage are transvaginal, transrectal, transabdominal, and transgluteal under radiographic guidance. [20] Unless abscesses are located at the apex of the vaginal vault or in the subcutaneous tissues of the caesarean incision, they are hardly accessible by palpation and only localizable in the pelvis through ultrasound or CT imaging.[6] In our case only parenteral antibiotic did not help, so needed USG guided aspiration of pus. Recent evidence suggests that it is acceptable and beneficial for the patient to perform primary surgical drainage along with appropriate antibiotic coverage. It decreases the length of hospital stay and improves the fertility outcomes. CT, MRI or USG guided drainage with antibiotics is the procedure of choice and has success rate of 80-90% [21]

Aim of writing this case is to show an unusual development of severe post caesarean pelvic abscess despite prophylactic antibiotic. The points to consider are the appropriate choice of antibiotics according to culture and sensitivity, and individual risk factors.

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Case Report

Gall bladder tuberculosis: A case report on a rare disease

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Abstract

Gall bladder tuberculosis is a rare disease even in tuberculosis endemic regions. Clinical features are non-specific and similar to that of chronic cholecystitis or gall bladder malignancy. Laboratory findings of gall bladder tuberculosis are also non-specific. Hence preoperative diagnosis is difficult and diagnosis is mostly histopathological following cholecystectomy. Here we present a female patient with repeated attacks of biliary colic who underwent cholecystectomy for gall stone disease and post-operative histopathology revealed features consistent with tuberculous infection of gall bladder. She was given anti-tubercular drug therapy for nine months following cholecystectomy with uneventful recovery on follow-up.

Introduction:

Intra-abdominal tuberculosis is a common entity in a tuberculosis endemic region like Bangladesh. But gall bladder tuberculosis is extremely rare.[1] The first case of gall bladder tuberculosis was reported by Gaucher[2] in 1870 and since then only a few cases have been reported in literature. Gall bladder is infected by tuberculosis by haematogenous route or as a component of intra-abdominal tuberculosis.[3,4] Clinical features and laboratory findings of gall bladder tuberculosis are non-specific and similar to that of chronic cholecystitis or gall bladder malignancy. Hence preoperative diagnosis is rare and diagnosis is mostly histopathological following cholecystectomy. Laboratory investigations are not very helpful; may reveal an elevated ESR and a positive Mantoux test. Chest radiology may reveal concurrent pulmonary tuberculosis or old healed pulmonary lesion. Ultrasound and Computed Tomography findings are variable. Treatment includes administration of standard four drugs anti-tubercular therapy for six to nine months following cholecystectomy. In patients diagnosed pre-operatively, anti-tubercular therapy is to be administered first followed by cholecystectomy.

Case Presentation:

A 27 year old female patient from Narayanganj was admitted with upper abdominal pain for 3 months. The patient had been suffering from intermittent mild to moderate colicky right upper abdominal pain which occasionally radiated to the back; usually aggravated on taking heavy meals and subsided on medication. Pain was associated with occasional nausea.

She did not complain of any fever, weight loss, chronic cough or jaundice. She had a previous attack of Acute Cholecystitis with Pancreatitis. She was conservatively treated and discharged with the advice of follow-up after 1½ months for Interval Cholecystectomy.

On admission the patient was non-anaemic, non-ecteric; pulse was 68 b/min, BP was 100/60 mm Hg, temperature was normal. On per-abdominal examination, abdomen was soft, mildly tender over right hypochondriac region. Systemic examination revealed normal findings.

On laboratory investigations her total WBC count was 5,740 /cumm, Neutrophil 76%, Lymphocte 20%, Monocyte 03%, Eosinophil 01%, Basophil 0%, Haemoglobin 9.80 gm/dl, ESR 110 mm in 1st hour. Biochemical investigations revealed Random Blood Sugar 5.2 mmol/L, Serum Creatinine 0.7 mmol/L, Total Bilirubin 0.6 mg/dL, ALT 27 U/L, Alkaline Phosphatase 209 U/L, Prothrombin time 17.20s, INR 1.43. Her ultrasound of whole abdomen revealed contracted gall bladder with multiple bright echogenic structures within the lumen of gall bladder casting posterior acoustic shadow. Her chest radiology showed normal bilateral lung fields.

Patient was prepared for elective laparoscopic cholecystectomy. Per-operatively gall bladder was found to be thick-walled, contracted with moderate adhesion with omentum and liver. Patient's post-operative recovery was uneventful. Post-operative histopathology of gall bladder revealed multiple granulomas composed of epithelioid cells, lymphocytes, macrophages and multi-nucleated giant cells in the mucosal region with foci of early caseation necrosis. Features were suggestive of granulamatous inflammation, histologically consistent with tuberculosis.

Patient was sputum negative for acid fast bacilli. She was treated with nine-month anti-tubercular therapy with four drugs (Isoniazide, Rifampicin, Pyrazinamide, Ethambutol) for two months and two drugs (Isoniazide, Rifampicin) for seven months.

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Discussion:

Tuberculosis continues to be an important health problem. In spite of effective drug treatment 2.5 to 3 million people die of this disease every year.[5] The global incidence of tuberculosis is growing at approximately 1.1% per year and the number of new cases is 2.4 percent per year.[6] About 1/3rd of the current global population is infected with tuberculosis asymptomatically, of whom 5-10% will develop clinical disease during their lifetime.[7] The rise of tuberculosis has been linked to the spread of AIDS and the evolution of new multi-drug resistant strains.

Gall bladder disease is multifactorial and depends on various host and environmental factors including sex, weight, diet, age, rapid weight loss, diabetes and consumption of cholesterol lowering drugs. Gall bladder disease occurs when bile contains excess of cholesterol or bilirubin, but not enough bile salts; or when the gall bladder does not empty completely.[8] Whether tuberculosis does cause these alterations, and at which level, remains to be proven.

Gall bladder is relatively resistant to infection by Mycobacterium. Previous authors have suggested the cause of rarity of gallbladder tuberculosis is high alkalinity of bile and bile acids which inhibits the growth of tubercle bacillus.[9] Tuberculous infection spreads to gallbladder either by haematogenous or lymphatic spread from nearer foci or serosal spread from peritoneal lesion or canalicular dissemination.[10] Most of the previous reported cases were associated with gall stone. Around 70% of gall bladder tuberculosis cases are accompanied by gallstones. Cystic duct obstruction leading to low bile acid concentration in bile and damage of gallbladder mucosa due to gall stones are supposed to be the causes of gallbladder tuberculosis in cases reported with coexistent gall stones.[11]

A correlation between gallstone disease and abdominal tuberculosis has also been established. Intestinal tuberculosis involving terminal ileum and ileo-caecal junction affects the absorption of bile from the intestine into blood circulation. Interruption of entero-hepatic circulation is accompanied by decrease in concentration of bile salts and phospholipids. This reduces the solubility of cholesterol, leading to precipitation of cholesterol and gallstone formation.[12]

Though our patient was a 27-year-old female, gall bladder tuberculosis mostly occurs in female over the age of 30 years.[13] Clinical features of gall bladder tuberculosis are non-specific and may present with symptoms such as abdominal pain, which may or may not be confined to the right hypochondrium; jaundice, weight loss, fever, vomiting, and abdominal mass[9]. Presentation may also mimic that of carcinoma of gall bladder,[13] acute cholecystitis[10] or with a persistent port site sinus after laparoscopic cholecystectomy.[14] Our patient presented with features consistent with chronic cholecystitis.

It is difficult to establish a pre-operative diagnosis of gall bladder tuberculosis. Laboratory investigations may reveal an elevated ESR and a positive Mantoux test, though they are not consistent and are non-specific.[9] Ultrasound imaging may reveal an enlarged gallbladder with wall thickening, soft tissue mass or a nodular lesion.[15] Computed tomographic findings are also variable and include thickening of the gallbladder wall, gallbladder mass and micronodular lesions of the gallbladder.[16] Positron emission tomography may be false positive for malignancy in patients with gallbladder tuberculosis.[17] Chest radiology and sputum for acid fast bacilli may be relevant in patients with concurrent pulmonary tuberculosis. Computed tomographic findings combined with clinical manifestations may guide a possible approach to diagnose gallbladder tuberculosis preoperatively. Confirmed diagnosis of gallbladder tuberculosis can only be established on histopathological examination of the resected specimen.

In a patient diagnosed with gallbladder tuberculosis preoperatively, the treatment includes administration of anti-tubercular drug therapy for six to nine months; four drugs, HRZE, for two months and two drugs, HR, for another four to seven months[18]. The presence of gallstones or repeated attacks of cholecystitis warrant cholecystectomy following anti-tubercular therapy.[18] Patients who have recently completed the anti-tubercular treatment for other sites can be subjected to cholecystectomy for symptoms and gallstones. Postoperative diagnosis based on histopathology following cholecystectomy will require anti-tubercular therapy with four drug regimen for six to nine months. If patient has already received anti-tubercular therapy, then second-line anti-tubercular therapy should be administered.[12,13]

Conclusion:

The vast paradigm of Tuberculosis infection continues to be an important health issue worldwide. Whether tuberculous cholecystitis is not commonly encountered or not commonly recognized remains a debatable question. The difficulty in establishing a pre-operative diagnosis due to non-specific clinical features and lack of pathognomic findings in imaging or other modalities of investigations is a challenge. Awareness among surgeons needs to be improved with a high index of suspicion regarding the possibility of gallbladder tuberculosis in endemic regions and patients with active or previous history of pulmonary or extra-pulmonary tuberculosis.

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Bilateral pneumothorax with pneumomediastinum in a severe COVID-19 diabetic patient: A case report from a semi-urban primary care center in Bangladesh

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Abstract

COVID-19, since its recognition in 2019, has presented to physicians with a wide range of complications.Amongst them, pneumothorax and pneumomediastinum have been a rarer one and have been traditionally observed with preexisting lung disease and patients on mechanical ventilation or, any risk factor that may lead to barotrauma.This case report delineates grave consequence of severe COVID-19 pneumonia, pneumothorax and pneumomediastinum in an apparently, previously healthy diabetic lady with no known existing lung disease. The patient was immediately referred to higher center, tube thoracostomy was done, but unfortunately she subsequently developed acute respiratory distress syndrome and expired after 2 days.

Keywords: COVID-19, pneumothorax, pneumomediastinum.

Introduction:

COVID-19 is a highly pestilent viral pneumonia caused by SARS-COV-2. Since Its emergence in December 2019, COVID-19 till 26 December, 2021 has infected more than 278 million cases and just under 5.4 million deaths have been reported globally.[1] Spontaneous pneumothorax and pneumomediastinum are very rare in COVID-19, specially, if the patient has no history of pre-existing lung disease and not on mechanical ventilation. Estimated incidence of pneumothorax is 1% of hospitalized severe COVID-19 patients and 2% of patients requiring ICU care.[2]Being the majority of the patients were male with a high mortality in patients having both pneumothorax and pneumomediastinum. Though the exact mechanism is unknown, but COVID-19 associated diffuse alveolar injury, intractable cough, ischaemia, pneumatocele rupture, mechanical ventilation are some of proposed mechanisms. Diabetes Mellitus , systemic hypertension and ischaemic heart disease were the most common comorbid conditions associated with COVID-19 pneumothorax and pneumomediastinum [1].Here we present a case of Severe COVID-19 associated spontaneous pneumothorax and pneumomediastinum in a non-ventilated diabetic patient and its deadly consequence.

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Case Presentation:

Mrs.X, 35 years old diabetic COVID-19 positive lady from Muradnagar, was admitted in Debidwar Upazila Corona Isolation Unit with the complaints of fever and cough for 5 days and progressive dyspnoea for last 2 days. On examination, she was dyspnoeic, tachypnoeic, restless; her oxygen saturation in room air was 84%, random blood sugar was 22.4 mmol/L, BP-130/80 mm Hg. Immediately oxygen supplementation via Non-rebreather mask, dexamethasone, enoxaparin in prophylactic dose, remdesivir, insulin infusion was started. The patient's condition was steadily improving and oxygen saturation was maintained with 15 L of oxygen, but suddenly after 3 days she developed severe respiratory distress with chest pain and oxygen concentration was 72% in 15 L of oxygen. Immediate resuscitation was done; dexamethasone was switched to methylprednisolone. The patient was referred to higher center, but she refused to leave health complex hospital.

Looking at patient's chest radiograph and clinical findings we had a suspicion that the patient may have pneumothorax. A HRCT scan chest was performed from another nearby hospital equipped with CT facilities. Patient's chest radiograph, HRCT chest and other routine investigations are attached below.

Chest X-ray PA view (Fig-1) was suggestive of accentuating of bronchovascular markings in both side.

Routine investigations revealed that, Hb-14g/dl, WBC–18300/cumm, Neutrophil-94%, Lymphocyte-4%, Monocyte 1%, Creatinine 0.68mg/dl, Ferritin 2698 ng/ml, Procalcitonin 0.068 ng/ml, CRP 96mg/L, Troponin I 0.012 ng/ml.



Fig. 1: Patient's initial chest radiograph showing accentuating of bronchovascular markings.

HRCT scan (Fig-2a & 2b) of chest was suggestive of moderate pulmonary inflammation along with multifocal ground glass opacities, bilateral and consolidation in right middle lung field, COARDS category IV, 65% lung field involved along with bilateral pneumothorax and pneumomediastinum with pleural thickening.

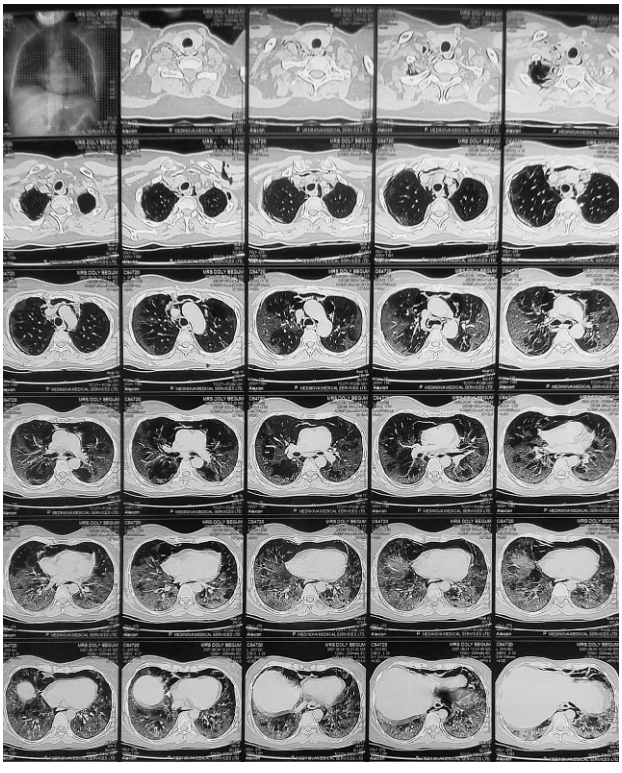


Fig. 2a: HRCT shows diffuse ground glass opacities, with bilateral consolidation



Fig. 2b: HRCT shows bilateral pneumothorax and pneumomediastinum

Immediately patient was transferred to higher center after proper counselling, tube thoracostomy was done, high flow nasal cannula was initiated, but unfortunately patient expired.

Discussion:

The commonest symptoms encountered in COVID-19 are fever, cough and dyspneoa. Radiological imaging plays an important role in diagnosing and following up the COVID-19 patients as standard rRT-PCR has a variable sensitivity and is influenced by many factors. Classical CT scan findings are patchy ground glass opacities in bilateral lower zonal infiltrates mostly in posterior-basal segmental distribution.[3]

Pleural effusion, pericardial effusion, lymphadenopathy, cavitation, pneumothorax, Hydropneumothorax, pneumomediastinum, giant bullae are some of the possible but least reported findings in COVID-19 pneumonia.[3,4] Secondary spontaneous pneumothorax has been reported to complicate COVID-19 pneumonia like its predecessors SARS and MERS.[5] It has been assumed that about 1% of hospitalized patients with COVID-19 may develop pneumothorax even in the absence of previous lung disease and mechanical ventilation.[2] COVID-19 associated diffuse alveolar injury, violent cough, rupute of emphysematous bullae or blebs, any other pre-existing chronic lung disease, invasive ventilation all may contribute to the development of pneumothorax.[5,6,7] Pneumomediastinum can be spontaneous, traumatic or, with chronic respiratory diseases like chronic

obstructive pulmonary disease, bronchiectasis etc. Although harmless, pneumomediastinum may be life-threatening if trapped air causes pressure effect over the mediastinal structures leading to tension pneumothorax, subcutaneous emphysema and cardiac tamponade which are life threatening.[8,9] Macklin phenomenon can best explain the pathophysiology, in which large pressure gradient between lung alveoli and parenchyma result in escape of air into broncho-alveolar sheath and subsequently pleual space.[8,9,10] In concomitant pneumothorax and pneumomediastinum, tube thoacostomy, 100% oxygenation, complete bed rest, antibiotics and analgesics are the mainstay of treatment.[10] Tube thoracostomy with a closed circuit with viral filter, needle aspiration and conservative careful observation all have been tried, but majority of the patients had undergone tube thoracostomy, specially who had mediastinal compressive symptoms. Our patient had no known pre-existing lung disease, neither was on ventilation, but unfortunately developed spontaneous pneumothorax and pneumomediastinum. Though all the possible measures had been taken, but unfortunately it was too late and we lost her. We should keep in mind that, in COVID-19, pneumothorax and pneumomediastinum should be considered as a possible aetiology of acute decompensation if not addressed timely life can be endangered.

Conclusion:

Pneumothorax and pneumomediastinum are rare, but not uncommon complications of severe COVID-19 patients, specially, in diabetic and hypertensive ones. When these complications develop, it's a life threatening situation despite all possible available measures. So, physicians must be very cautious when there is acute desaturation in a severe COVID-19 patient, keeping these possibilities in mind that may help in early and prompt intervention to save the life of the diseased.

Conflicts of interest: Nothing to declare.

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College News

College Events:

- The National Mourning Day was observed on 46th death anniversary of Father of Nation Bangabandhu Sheikh Mujibur Rahman in Bangladesh Medical College and Hospital on 15th August 2021. Teachers, doctors, nurses, students of BMC & H and officials & staffs of BMSRI participated in that event.
- 50th Victory Day of Bangladesh was celebrated in Bangladesh Medical College and Hospital premises on 16th December 2021. Teachers, doctors, nurses, students of BMC & H and officials & staffs of BMSRI participated in that event
- Commencement ceremony of newly admitted students of BM-35 was held on 1st August, 2021 in virtual platform due to COVID-19 pandemic. Total 120 students were admitted in the session of 2020-2021. Hon'ble Minister, Ministry of Agriculture, Government of Peoples' Republic of Bangladesh Dr. Md. Abdur Razzak MP, Chairman, E.C, BMSRI was present as Chief Guest of this ceremony.

Seminar/Workshops:

- Webinar on "Reciprocity of COVID-19 and Non-Communicable Diseases-Lessons and Challenges in Bangladesh" was held on 30-9-2021. The speaker was Prof. Dr. Sharmeen Yasmeen, Head of the dept. of Community Medicine, BMC.
- Seminar on "Updated Management of Stroke" and "Surgical Options of Stroke Patients" was held on 30-10-2021. The speakers were Dr. Mohammad Aftab Halim, Assistant Professor of Neuromedicine, BMC and Dr. Muhtamim Chowdhury, Assistant Professor of Neurosurgery, BMC.
- Seminar on "The Other Side of the Coin-Maternal Deaths during Childbirth: Can We Prevent it?" was held on 9-12-2021. The speaker was Dr. Monira Parveen, Consultant, UNICEF, Bangladesh.
- Seminar on "COVID-19 and Mental Health" was held on 22-12-2021. The speaker was Dr. Arman Ibne Haq, Assistant Professor and In-Charge of the dept. of Psychiatry, BMC.

Obituary:

Architect Mosharraf Hussain Mohammad Shahjahan, honorable member of BMSRI, died due to old age related complications on 14th September, 2021.

New Promotions in BMC:

Dr. Muhammed Akhtaruzzaman, Associate Professor, Dept. of Cardiology .

Dr. Kazi Nazneen Sultana, Associate Professor, Dept. of Biochemistry.

Dr. Iqbal Mahmud, Registrar, Dept. of Nephrology.

Dr. Faysal Ahmed, Registrar, Dept. of Orthopedics.

New Appointments in BMC:

Dr. Rabab Sultana, Assistant Professor, Dept. of Oncology.

Dr. Ashiq Mahmud, Registrar, Dept. of Urology .

Dr. Tamanna Mallik, Lecturer, Dept. of Biochemistry.

Dr. Farhana Sultana, Lecturer, Dept. of Biochemistry.

Dr. Nuren Jannat Nowrin, Lecturer, Dept. of Physiology.

Dr. Nuzrat Naz, Lecturer, Dept. of Pathology .

Dr. Nishat Tasnim Lupin, Lecturer, Dept. of Forensic Medicine.

Dr. Rozina Hoq, Dept. of Pathology.

Dr. Murtaza Zakiul Abrar, Lecturer, Dept. of Pathology.

Dr. I M Al-Hosain Parvez, Dept. of Anatomy.

Dr. Md. Mazed Hossain Jitu, Lecturer, Dept. of Anatomy.

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