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Emergence of Zika Virus: A Public Health Emergency of Global Concern

Sobhan F ^a

At present one of the greatest concerns in medical science is the reemergence of Zika virus. The comeback of the pathogen has raised global alarm because of its rapid geographical spread and causal relationship with complications, previously unknown. Although the infection is benign in most people, it is reported to be associated with two uncommon conditions: microcephaly in newborn babies and Guillain Barre Syndrome. This has led the World Health Organization (WHO) to declare the current Zika outbreak a Public Health Emergency of International Concern.¹

Emergence of Zika virus and transmission

Zika virus is an arbovirus of the Flaviviridae family, which is related to West Nile, dengue, chikungunya, yellow fever and Japanese encephalitis viruses.² It was first identified in 1947 in the Zika Forest of Uganda being isolated in a rhesus monkey that had been placed in a cage on a sentinel platform in the forest by the Virus Research Institute. Different species of the female Aedes mosquito, mainly *A. aegypti* and *A. albopictus* are responsible for infection in humans.³

Sexual transmission of Zika virus is possible. Other modes, like perinatal transmission and blood transfusion are currently being investigated.⁴

Globalization of Zika virus

For over six decades, Zika virus spread slowly and unremarkably from the Zika forest in Uganda to other parts of Africa and South East Asia. In 1952, it was identified in humans in Uganda and United Republic of Tanzania.⁴ By 1981, only 14 cases had been reported. Most of the infections were asymptomatic, mild, and resolved in a few days. The first large outbreak was reported in 2007, from the Pacific island of Yap in Micronesia. Around 73% of the island population had been infected. In 2013, the virus spread to French Polynesia, where an estimated 28,000 cases occurred in a population of 270,000. The epidemic rapidly spread to Cooks Island and Easter Island. In 2015, the virus made its way to Brazil and was associated with the occurrence of a large number of microcephaly in babies born to mothers who had contracted the infection during pregnancy. Brazil is the epicenter of the recent epidemic which is rapidly spreading across South and Central America, a number of islands in the Caribbean, the Virgin Islands and Mexico.³

The globalization of the Zika virus was made possible by the widespread presence of the Aedes mosquitoes in various parts of the world and increased human travel

across borders. El Nino and global warming have also been cited, as these cause hot winters and summers which favor the spread of the virus.⁵ It is difficult to predict the ultimate intensity and extent of spread.

Potential Complications

Although most Zika virus infections are characterized by subclinical or mild influenza like illness, the virus is associated with potential neurological and autoimmune complications. Prenatal Zika infection has been linked to adverse pregnancy and birth outcomes, notably microcephaly and other serious brain anomalies. A dramatic increase in the number of babies with microcephaly born to mothers infected with Zika virus has been reported from Brazil in May 2015. Apart from microcephaly, this virus has been associated with outbreaks of Guillain Barre syndrome in French Polynesia and South America.^{4,6-9} In November 2015, the Ministry of Health in Brazil confirmed the relationship between Zika virus and microcephaly outbreak.¹⁰ The association with microcephaly was also confirmed by the Centre for Disease Control and Prevention in the United States.¹¹

Zika's association in certain geographical areas with coexistent dengue and chikungunya infections in humans has raised questions about the potential roles of these other viruses as cofactors for the more serious complications of Zika.⁷

Control

Zika infection is self-limited and short in duration making treatment with antiviral drugs challenging and unjustifiable.⁷ Again, development of vaccine is a lengthy process, and question remains as to whether one can be developed and tested for efficacy before the current outbreak subsides.

In the present context, reducing transmission through vector control measures remains the mainstay.

WHO has given detailed guidelines for the prevention of infection: reducing mosquitoes through source reduction (removal and modification of breeding sites) and reducing contact between mosquitoes and people.⁴

Sexual transmission of Zika virus is possible. People who have been infected should practice safer sex using condoms.

Pregnant women's partners living in or returning from Zika affected areas should practice safer sex or practice abstinence throughout pregnancy.

Travelers returning from Zika affected areas should be kept under surveillance.

2016 Olympic and Para Olympic games in Brazil

Brazil is going to host the much awaited Olympic and Para Olympic games 2016, in Rio de Janeiro. Brazilian Government has deployed over 200,000 staff to educate and assist the public in a massive mitigation operation ahead of the Rio Olympics to help educate the population and assist in cleaning areas of stagnant water.¹² This is a commendable step which will reduce apprehension among the visitors.

The Future

Despite growing knowledge about the virus, questions remain regarding the viruses' vectors and reservoirs, pathogenesis, genetic diversity and potential synergistic effects of co-infection with other circulating viruses.

Closely following on the heels of chikungunya and ebola outbreaks, the current Zika outbreak highlights the need for more aggressive and prompt global action to defend against emerging pathogens. It is likely that changes in vector characteristics, globalization and climate changes has put the world at risk for further outbreaks from other known viruses. This calls for a global coordinated system to avert the global health threats.

Dr. Farzana Sobhan, M.Sc (UK), MBBS
Associate Professor, Dept. of Community Medicine
Bangladesh Medical College and
Assistant Editor, Bangladesh Medical College Journal
Email: f_sobhan@yahoo.com

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Health Problems and Health Seeking Behaviour among the Elderly Population of Urban Slum Dwellers

Farah S^a, Karim M^b, Rahman T^c

Abstract

Background: A health condition involves a state of complete physical, mental and social well being. It involves functioning of the body systems, absence of disease and disability. Change in socio-economic status and various health problems adversely affect an individual's way of life during old age. The fast ageing of populations around the world is presenting challenges for developed and developing countries.

Objective: The objective of the study was to assess the common health problems and health seeking behaviour of elderly people in urban slums of Dhaka city.

Methods: A cross sectional study was carried out in Moghbazar (urban) slum area of Dhaka city during February 2014 to April 2014. Interviewing and clinical examination of 1041 elderly subjects of 61 years of age and above was done. The sample was selected by purposive sampling technique. A pre structured, pretested questionnaire was used to get detailed information. The data analysis was done by using SPSS software.

Results: Majority 604(58.0%) were from the age group of 61-69 years. Their mean age was 61.77 years; (SD± 6.038). Most of the study subjects had three health problems 375(36.0%), followed by four problems 335(32.1%) and two problems 182(18.6%). The most frequent health problem was low back pain, comprising 48.2% followed by hypertension in 36% of the older persons. Difficulty in vision and anaemia ranked third and fourth affecting 35.5% and 35% older persons. Among the employed respondents, 625(60.0%) respondents were absent from work place, among them more than fifty percent respondents were absent for =5 days due to sickness. Around 982 (94.3%) respondents were taking some kind of treatment. Among them most 341(34.7%) of the respondents were taking treatments from hospital.

Conclusions: Geriatric health care services should be promoted and integrated to the national health care system and urban based health care services should also address the old people living in slums on priority basis.

Keywords: Health problems, health seeking behaviour, slum dwellers, elderly.

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Introduction:

The process of aging is lead by the decline in fertility reinforced by increasing longevity due to falling mortality in older ages.¹ It produces unprecedented changes in the age-structure of all societies, notably the historic reversal in the proportions of younger and older persons. In the turn of 21st century, population aged 60 and above is increasing

at an accelerated rate and most of the rapid growth is projected in developing countries.²⁻⁴ The health of the citizen is very crucial to the nation's economic growth. It is not gainsaying that improvement in the health sector is an improvement in the socio-economic development of a nation. A healthy population is likely to be a productive population and a productive population will lead to a growing economy.⁵ Several social and biological determinants have been postulated as having direct or indirect influences on health. Age has been identified as one of the important determinants of health. Gender is another and as such there has been increasing attention to the role of gender in influencing health behaviour and healthcare.⁶

Socio-economic condition of the most of the elderly people are not good due to poverty, wage discrimination, want of essential goods and commodities, shelter and compulsory retirement from job when age limit is attained.⁷ A small proportion (around 6%) of the total population of Bangladesh constitutes the elderly population, but the

a. Dr. Shayela Farah; MPH, MBBS
Assistant Professor, Department of Community Medicine
Dhaka Community Medical College

b. Dr. Mohoshina Karim; MPH, MBBS
Lecturer, Department of Community Medicine
Dhaka Community Medical College

c. Dr. Tanjila Rahman; MPhil, MBBS
Assistant Professor, Department of Microbiology
Dhaka Community Medical College

Correspondence to:

a. Dr. Shayela Farah
Assistant Professor, Department of Community Medicine
Dhaka Community Medical College
Moghbazar, Dhaka-1217
E-mail:shayelafarah@yahoo.com

absolute number of them is quite significant (about 7.2 million) and the rate of their increase is fairly high.⁸ Old people need health care because old age is associated with pain and ill-health.⁹ Worldwide the increase in the proportion of elderly is in response to improvement in health technologies and life expectancy of people.¹⁰ Health seeking behaviour is directly related to the availability and accessibility of health facilities apart from motivations and ability of the individual to seek medical treatment.¹¹ The World Health Organization and Moe S, et al. (2012)¹⁰, highlighted that aging process and problems related to elderly should be better understood so that effective elderly health prevention can be planned and implemented. The purpose of this study was, therefore, to assess the health problems and health seeking behaviour of elderly people in urban slums of Dhaka city with special focus on gender distribution.

Methodology:

The present study was a descriptive type of cross sectional study conducted in urban slums of Moghbazar attached to Dhaka Community Medical College and Hospital. The study was conducted during February 2014 to April 2014. All the elderly (1041) aged 61 years and above were included for the study to assess the health problems and health seeking behaviour. Elderly individuals who were critically ill, age less than 60 years and unable to comprehend questions were excluded. Data were collected by face to face interview and clinical examination. The information was collected by under graduate 4th year students MBBS students and other faculty members of Dhaka Community Medical College. Written informed consent was obtained from all the participants. Information on socio demographic variables, existing health problems and health seeking behaviour were recorded using pre-tested and pre designed questionnaire. Subjects were clinically evaluated based on the steps given by the 'Hand book on Health Care of the Elderly: A Manual for Physician in Primary and Secondary Health Care Facilities'¹² i.e. by their reported illness (Existing diagnosis), medication held by the subjects, history and clinical examination. The physical equipments used were stethoscopes, B.P. Apparatus, Snellen's Chart, Sahil's haemoglobinometer and glucometer to assess the morbidity status of the elderly. Blood pressure was measured in lying down position using mercury type sphygmomanometer twice in each individual at an interval of 30 minutes. Elderly with systolic blood pressure of 140 mm hg or more and / or diastolic blood pressure of 90 mm of hg or more were considered as hypertensive. Snellen's chart (E chart) was used to assess the visual acuity. Collected data were checked, verified & then entered into the computer. Data analysis was done by software SPSS (Statistical Package of Social Science, version-17).

Limitation of study: A limitation in the study was that it was not possible to verify certain responses to queries on

age, literacy levels, occupational levels, economic status and health problems.

Results:

Socio-demographic characteristics of the study subject: Out of 1041 respondents, majority 604(58.0%) were from the age group of 61-69 years. Their mean age was 61.77 years; (SD± 6.038). Majority of the geriatrics respondents 624(59.9%) were male and 417(40.1%) were female. Regarding educational status, 820(78.8%) were illiterate and only 221(21.2%) partially or fully completed primary level of education. Among the respondents who were currently at work, 144(13.8%) were unemployed. Most of them (n=897, 86.2%) were employed like domestic work, day labor, rickshaw/van puller, small business and others. The average monthly family income of the respondents were 7202.43SD ±2969.90 taka. Majority 616(59.2%) respondents were from nuclear family.

Table 1: Distribution of study subjects according to number of morbidities (n=1041)

Multiplicity of health problems	Male (n=624)	Female (n=417)	Total (n=1041)
Only one problem	07(1.1%)	08(1.9%)	15(1.5%)
Two problems	82(13.1%)	100(24%)	182(18.6%)
Three problems	125(20%)	250(60%)	375(36.0%)
Four problems	135(21.6%)	200(48%)	335(32.1%)
Five problems	59(9.5%)	75(18%)	134(12.7%)

Table-1 shows that the most of the subjects had three health problems 375 (36.0%), followed by four problems 335 (32.1%) and two problems 182 (18.6%).

Table 2: Type of health problem among male & female geriatric peoples (n=1041)

Variables	Male (n=624) No (%)	Female (n=417) No (%)	Total (n=1041) No (%)
Low back pain	286 (45.8%)	216 (51.8%)	502 (48.2%)
Hypertension	223 (35.7%)	150 (36%)	373 (36%)
Difficulty in vision	110 (17.6%)	260 (86%)	370 (35.5%)
Anaemia	115 (18.4%)	250 (60%)	365 (35%)
Dental problem	220(35.3%)	110(26.4)	330 (32%)
Arthritis	85 (13.6%)	179 (43%)	264 (25.3%)
Hearing loss	109 (17.5%)	98 (23.5%)	207 (20%)
Gastric ulcer	96 (15.4%)	93 (22.3%)	189 (18.1%)
Common cold	86 (13.8%)	75 (18%)	161 (15.4%)
Diabetes	75 (12%)	62 (15%)	137 (13.4%)
Skin disease	65 (10.4%)	52 (12.5%)	117 (11.2%)

Table-2 shows that most frequent health problem was low back pain, comprising 48.2% of the problems followed by hypertension in 36% of the older persons. Difficulty in vision and anaemia ranked third and fourth affecting 35.5% and 35% older persons. Arthritis comprised of the fifth morbidity affecting 25.3% of the study population. A significantly higher proportion of elderly people suffered from hearing loss (females: 23.5% vs. males: 17.5%), gastric ulcer (females: 22.3% vs. males: 15.4%), common cold (females: 18% vs. males: 13.5%), diabetic disease (males: 35.3% vs. females: 26.4%), while skin disease (females: 12.5% vs. males: 10.4%) was observed more in female.

Table 3: Distribution of the respondents by absent from work place due to sickness (n=897)

Absent from work place due to sickness	Frequency	Percent
Yes	625	69.7
No	272	30.3
Number of days lost due to sickness	Frequency	Percent
=5 days	348	55.6
6-10 days	188	30.3
11-15 days	63	10.0
16-20 days	13	2.0
21-25 days	1	0.1
26-30 years	5	0.9
>30 days	7	1.1
Mean = 17.10; (SD = ± 13.328)		

Table-3 shows that out of 897 employed respondents, 625(60.0%) respondents were absent from work place, among them more than fifty percent respondents were absent for =5 days due to sickness.

Table 4: Treatment seeking behaviour of geriatric people (n= 1041)

Taking any treatment	Male (n=624)	Female (n=417)	Total
Yes	554 (53.2%)	428 (41.1%)	982(94.3%)
No	38 (3.6%)	21 (2.1%)	59(5.7%)
Place of treatment			
Hospital	225 (22.9%)	116 (11.8%)	341(34.7%)
Pharmacist	144 (14.7%)	135 (13.7%)	279(28.4%)
NGO	126 (12.8%)	112 (11.2%)	238(23.8%)
Clinic	37 (3.7%)	22 (2.2%)	59(5.9%)
Private physician	24 (2.4%)	17 (1.7%)	41(4.1%)
Ayurbada	11 (1.1%)	13 (1.3%)	24(2.4%)

Table 4 shows that around 982 (94.3%) respondents were taking some kind of treatment. Among them most 341(34.7%) of the respondents were taking treatments from hospital and the other treatment place of the respondents were listed in Table 4.

Discussion:

The gender differences in the social consequences of health and illness include how illness affects men and women, including health-seeking behaviour, the availability of support networks, and the stigma associated with illness and disease. Morbidity among elderly people has an important influence on their physical functioning and psychological well-being. Many elderly have several disorders at the same time. The incidence of diseases increases with age.¹³ The study subjects had three health problems 375(36.0%), followed by four problems 335(32.1%) and two problems 182(18.6%). While Singh JP, et al.¹⁴ mentioned that majority of the study subjects had three morbidities (32.5%), followed by four morbidities (31.25%) and two morbidities (23.50%) in an urban slum area of Nagpur, Central India. The most frequent health problem was low back pain, comprising 48.2% of the problem followed by hypertension in 36% of the older persons. Difficulty in vision and anaemia ranked third and forth affecting 35.5% and 35% older persons. Arthritis comprised of the fifth morbidity affecting 25.3% of the study population. A significantly higher proportion of elderly people suffered from hearing loss (females: 23.5% vs. males: 17.5%), gastric ulcer (females: 22.3% vs. males: 15.4%), common cold (females: 18% vs. 13.5%), diabetic disease (males: 35.3% vs. females: 26.4%), while skin disease (females: 12.5% vs. males: 10.4%) was observed more in female. This observation is more close to Odaman OM et al. (2014)¹ study where elderly females (64.1%) and males (61.3%) complained of this health related problems. Thus, the findings in this study have tended to agree with those of Abduraheem (2007)¹⁶ and Sharma, et al. (2012)¹⁷ that arthritis, hypertension, body pains, joint pain, general body weakness, fatigue, poor eye sight, fever, irritability, nervous tension, depression, headaches and decreased mobility were the health related problems of the elderly. Regarding sickness absenteeism, 625(60.0%) respondents were absent from work place, of them more than fifty percent were absent for =5 days. Near ninety five percent of the respondents were taking some kind of treatment, of them 554(53.2%) were male and 428(41.1%) were female. Among them 341(34.7%) were taking treatments from hospital followed by 279(28.4%), 238(23.8%) from pharmacist and NGO. In developing countries, men seek treatment more frequently at formal health services, whereas women are more likely to self-treat or use alternative therapies. This has been explained by factors, such as multiple roles of women which limit their activities mainly to the domestic sphere and make it difficult for them to go to clinics during opening hours. By contrast, traditional healers or community shops are easier to access

and will often accept delayed payment or payment in kind or delayed. Traditional healers also provide explanations in ways that are easily understood, in contrast to the more scientific explanations of clinic staff.¹⁸ A study conducted in Shimla hills located in North India where nearly two third (65.8%) respondents were seeking treatment for their health problems. Majority of the older person preferred allopathic medicine (81.2%) followed by ayurvedic medicine (11.3%) and homeopathic medicine (7.3%).¹⁹ These findings were more or less similar in the present study. Hoeven MVD et al. (2012)²⁰ conducted a study at Karachi city; where 98% patients saw doctors for their ailment and this is much higher than a study from South Africa where 67% urban and 69% rural population never visit a traditional healer. No country can be properly regarded as sound when the generality of the people are poor in health. So all efforts need to be supported by appropriate gender and age specific research which can help reduce gender disparities in health among older persons.

Conclusion:

The burden of old age related morbidity increased with advancement of age possibly as a consequence to progressive multi-organ degeneration and lowered immunologic status involving one body system after another. There is a need for promotion of healthy lifestyles and behavioural changes through conduction of community-based health education program. This in turn leads to tackling the chronic health problems among ageing population by decrease the prevalence of many morbidities and also decreasing co-morbidities. Screening programs for chronic diseases, especially for diabetes and hypertension, is highly recommended among elderly population. There is also a need for satisfactory living condition for elderly; satisfy psychosocial needs, increase recreational activities for elderly involvement of elderly in doing useful activities.

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Mycobacterial Infection of Laparoscopic Port-Wounds: a Cross-sectional Study

Talukder MRR^a, Rahman MZ^b, Morshed M^c, Iffat T^d

Abstract

Background: As the sphere and incidence of laparoscopic surgery is widening fast, the incidence of annoying port-site infection is also increasing.

Objective: The objective of this study was to find out the frequency of laparoscopic port wound infection caused by Mycobacterium and to share our experience in overcoming this problem.

Methods: This cross sectional study was done on 948 patients operated with laparoscopic cholecystectomies to find out the number of tuberculosis infection at the port wounds from March, 2010 to February, 2016 in Bangladesh Medical College Hospital. Patients who developed and reported with wound infections within 3 months following cholecystectomy were studied. Suspected cases were confirmed by laboratory examinations. All patients with port wound infections received prophylactic broad-spectrum antibiotics pre- and post-operatively.

Results: Twenty eight (28) out of these 948 cases developed port-site infection (PSI) and 10 of them had tuberculous Mycobacterial infection and 2 had non-tuberculous Mycobacterial infection. The non-tuberculous cases initially did not respond to conventional anti-tubercular treatment, but they responded after addition of Clarithromycin.

Conclusion: As the incidence is emerging gradually in increasing numbers, we have to concentrate our focus on cases of non-healing post-operative wounds, which could be a case of atypical or non-tuberculous Mycobacterial wound infection and has to be dealt with accordingly.

Keywords: Laparoscopy, Mycobacterium, Laparoscopic port-wound.

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Introduction:

Tuberculosis is a major health problem in developing countries.¹ In Bangladesh the prevalence/disease burden in 2008 was 659,586 persons.² Various Mycobacteria produce cutaneous infection, but surgical wound infection is rare.^{3,4} No surgical wound is completely immune to infections. Despite the advances in the fields of antimicrobial agents, sterilization techniques, surgical techniques, and operating room ventilation, port-site infections (PSIs) still prevail. Incidence of surgical site infection (SSI) after elective

laparoscopic cholecystectomy is less than that after open elective cholecystectomy due to shorter length of incision.⁵ The emergence of rapid growing atypical mycobacteria with multidrug resistance, which are the causative organism in most of the cases, has further compounded the problem. PSIs are preventable if appropriate measures are taken preoperatively, intra-operatively and postoperatively. PSIs can often be treated non-surgically, with early identification and appropriate management. Macrolides, quinolones and aminoglycosides antibiotics do show promising activity against the atypical mycobacteria.⁶

Laparoscopic port-wound infection by both tuberculous and non-tuberculous Mycobacterium has become an annoying matter of concern now-a-days, as the wounds are often quite stubborn to be healed. Though the incidence is not very common, when it occurs, it creates a lot of concern, both on the part of the surgeon as well as the patients and their whole family. Often, it becomes very difficult to convince the patients and their party that it is not a hopeless condition and healing is not beyond our capability. Very often they lose patience and switch over from the original clinician to others and ultimately become badly confused. As a result, some of them even try to trace out, whether the treating surgeon or the hospital concerned has done any fault during the surgery or its subsequent managements. In this study we tried to explore the frequency of port wound

- a. Dr. Md Reza-Ur-Rahman Talukder; FCPS, MBBS
Associate Professor, Department of Surgery
Bangladesh Medical College & Hospital, Dhaka, Bangladesh
- b. Dr. Md. Ziaur Rahman; MBBS
Registrar, Department of Surgery,
Bangladesh Medical College & Hospital, Dhaka, Bangladesh
- c. Dr. Monjur Morshed; MBBS
Assistant Registrar, Department of Surgery,
Bangladesh Medical College Hospital, Dhaka, Bangladesh.
- d. Dr. Tanjim Iffat, MBBS
Honorary Medical Officer, Department of Surgery,
Bangladesh Medical College Hospital, Dhaka, Bangladesh.

Correspondence to:

- a. Dr. Md. Reza-Ur-Rahman Talukder
Associate Professor, Department of Surgery,
Bangladesh Medical College & Hospital, Dhaka-1207, Bangladesh
Email: drreza_talukder@yahoo.com

infection by mycobacterium after laparoscopic cholecystectomy operations.

Methods:

This cross sectional study was done on 948 patients operated with laparoscopic cholecystectomies to find out the number of tuberculosis infection at the port wounds from March, 2010 to February, 2016 in Bangladesh Medical College Hospital. Patients who developed or reported with wound infections within 3 months following cholecystectomy were studied. Diagnostic criteria included (i) Discharge from the wounds, (ii) Swelling, redness and shininess in the wounds, (iii) fever, (iv) raised ESR, (v) histological examination of the curetted granulation tissue from the affected wounds, (vi) Z-N staining of the discharged fluid, (vii) culture and sensitivity of the discharge.

All patients were briefed about the laboratory examinations, its possible outcomes and possible managements. We have mainly emphasized on the mycobacterial infections of the port-wounds, as these are the matter of concern for the laparoscopic surgeons, at home and abroad. All patients in this study received prophylactic broad-spectrum antibiotics -pre and post operatively.

Results:

Table 1: Distribution of port wound infection

Type of infection	No.	%
Port-wound mycobacterial infection	12	43
Non-specific port infection	16	57
Total	28	100

Twenty eight (28) cases out of 948 laparoscopic cholecystectomies developed port-wound infection. Out of 28 cases, 12 (42.87%) were established by histopathology of the wound curettes and Z-N staining of the wound smear, to have Mycobacterial infection. Out of these 12, only 2 cases were settled to have atypical Mycobacterium of non-tuberculous variant.

Table 2: Distribution of the post-operative Laparoscopic port-wound Mycobacterial infection (n=12)

Age (years)	Sex No.		Presentation pattern/ Wounds			Per operative gall bladder findings	
	M	F	fever	discharge	abscess	normal	inflamed/ deformed
<20	1			1			1
21-30		1		2		1	
31-40		2	1	4	4		2
41-50	3	2		1	1	2	3
51-60	2			1	2		2
61-70	1			1			1

Table 2 shows that age range was 19 to 68 years (mean=44.6 years.); 9 (75%) of them were within 50 years and 3 (25%) were above 50 to 70 years; 7 were male and 5 were female; discharge and abscess were common features; 9 were inflamed and 3 were normal in appearance.

Table 3: Time interval and port-site affected

Time interval from date of surgery	Number of patients	Port-site affected	
		umbilical	other ports
1-3 weeks	4	2	
3-6weeks	6	2	2
6-9weeks	1	3	1
9-12weeks	1	2	

Time of interval from date of surgery to development of infection was mostly 3-6 weeks (6/12 cases, 50%) followed by 1-3 weeks for 4 cases (33.3%) and 6-9 weeks & 9-12 weeks for 1 case each. But, when healing started, the wounds were gradually filling up following anti-septic dressings. None required secondary stitching.



Figure 1 (a): Right hypochondriac port-wound Mycobacterial infection



Figure 1 (b): The same patient viewing all the 4 laparoscopic ports

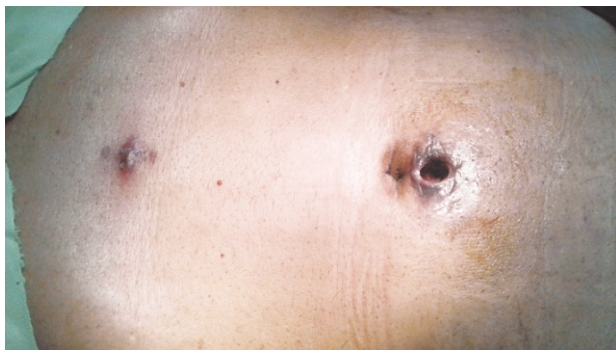


Figure 2: Infra-umbilical and epigastric port-wound mycobacterial infections.

Description of port wounds: Almost all cases presented with odourless, sero-sanguinous discharge from their laparoscopic port-wounds (9 from the umbilical port-wounds, 2 from epigastric and 1 from the right hypochondriac port-wounds) (Table-3). Its edges were shiny, having no sign of healing, rather some of the wounds were extending into the surrounding subcutaneous tissues (Fig. 1 and Fig. 2). None of the wounds were painful.

Table 4: Healing period from time of presentation

Healing period	Number of patients
1-3weeks	1
3-6weeks	5
6-12weeks	5
>12weeks	1

All the wounds were very stubborn to heal, even after starting anti-tubercular treatment. Ten cases healed within 3 to 12 weeks. Addition of Clarithromycin orally along with the conventional 4 drugs combination (Rifampicin, Isoniazide, Ethambutol, Pyrazinamide) gave very good response in majority of (10 out of 12) these cases.

In all cases, the anti-tubercular treatment was continued for 9months and that proved to be sufficient. After instituting anti-TB treatment, all the wounds started healing within 2weeks. But complete healing took 4-12 weeks. Two cases (16.67%) had recurrence within 3 weeks of healing, but ultimately healed within next 2-3 weeks.

There was no definite relation to job or social class and all received anti-TB vaccines in their childhood, except the three cases who were >60 years of age, could not provide definite history of vaccination. None of the 12 affected patients who developed tuberculous infection had any definite history of tuberculous exposure.

Discussion:

Though the surgical site infection (SSI) in case of Laparoscopic Cholecystectomy (LC) is much less (2.95%) than in open cholecystectomy (OC) (12%), it is one of the

three most common post-operative complications.⁷ The other two are haemorrhage and biliary leakage. In our series, though non-specific infection of the wound was not of much concern, tuberculous wound infection (though not very common) happened to be very much annoying, as it was quite difficult to manage.

Though in one series, Neri V et al⁸ found encouraging result in prophylactic use of topical Rifampicin ointment, we could not try it because of non-availability of the agent in our pharmaceutical market.

In another series, Sunil Sethi et al could trace out *M.fortuitum*, *M.cholerae* and *M.flavescens* (non-tuberculous Mycobacterium) to be the frequent cause of mycobacterial laparoscopic port-wound infections.⁹ But in our series, we could only detect atypical Mycobacterium in some, which responded to conventional 4 drugs combination (Rifampicin, INH, Ethambutol, Pyrazinamide) plus oral Clarithromycin for prolonged period. In their series, they found special efficacy of Ofloxacin against *M.flavescens*. In our study, addition of Clarithromycin to the conventional 4 drugs combination gave especially good response on prolonged use.

Although the frequency and precipitating factors for SSI following open cholecystectomy have been widely studied in the past, its prevalence following laparoscopic cholecystectomy, especially the incidence of Mycobacterial infection, have not yet been thoroughly evaluated. But the available data so far indicates a very low incidence.¹⁰ Overall, the port-site infection incidence is 5.07%.¹⁰ Jawein Met al, in a mega study, over 2 years, in 5140 cases of cholecystectomies, revealed port-site infection rate of 4.41% vs 1.08% in open vs laparoscopic cholecystectomies respectively.¹¹

As most of the infections occurred in the sub-umbilical or umbilical port wounds, role of umbilical flora could be an important factor, though we could not establish it, as random umbilical swab study for AFB were negative in serial 50 cases. But a few cases (n=3) had bile spillage during extraction of gall bladder through the umbilical port, which could have contaminated the wound.

Laparoscopic port-site Mycobacterial infection, though rare, it often occurs due to nosocomial infection and the likely source could be the instruments or accessories,¹² especially if the same set is used by multi-disciplinary surgeons, e.g- general surgeons, gynecological surgeons, urological surgeons etc. Here we did not observe any definite difference in SSI with Mycobacterial infection, whether the wound got contaminated with spilled-off bile or not. Of course, we did not randomly study the bile from the gall bladder for AFB, but, routine histopathology of the gall bladder specimens did not reveal tuberculosis in any. Leo Francis Tauro¹² et al, in their article, definitely casted doubt on the sterilization procedures and efficacy of 2% glutaraldehyde over 20 minutes for re-usable laparoscopic instruments.¹³ As most of the laparoscopic instruments

are very costly and damageable to autoclave treatment, they are re-used after immersion in 2% glutaraldehyde for about 20 minutes and the laparoscopic camera is not even exposed to this agent, rather it is re-used after cleaning with 0.5% W/V chlorhexidine gluconate +70% isopropyl alcohol, which is highly doubtful whether it can really decontaminate the instruments.¹² In our perspective, we don't get the other effective, but non-damaging sterilization procedures like gamma-ray or ethylene oxide.

So, we think this aspect has to be seriously addressed to prevent nosocomial tuberculous infection of the surgical sites, especially as tuberculosis is still a major global health problem and as Bangladesh still stands at rank-6 amongst 20 leading TB burdened countries of the world.¹⁴

Though the case series (n=9) of MA Mazid et al¹⁴ responded well to conventional anti-TB therapy, but in our study, cases caused by atypical Mycobacteria, were mostly quite stubborn to respond to conventional 4 drugs-Rifampicin+INH+Pyrazinamide+Ethambutol. But as per consultation with infectious disease expert, addition of Clarithromycin to the regimen showed very good response and though it is empirical, we continued this antibiotic for the initial 2 months and then 2 drugs (Rifampicin+Isoniazid) for next 7 months (9months in total at least).

It is worth mentioning that all but 3 (who were uncertain of their immunization history) of the cases had anti-TB immunization in their childhood. So, we may have to believe that, conventional anti-TB immunization doesn't protect the individuals against atypical Mycobacterial infections, or its efficacy might have lost.¹⁴

The last point worth mentioning is that the presence of cholecystitis (acute or chronic) along with cholelithiasis definitely precipitates wound infection¹⁵ which also corresponds with our findings.

Conclusion:

Atypical Mycobacterial infection of the laparoscopic port wounds, as well as some of the laparotomy and non-laparotomy wounds, are emerging gradually in increasing numbers, which are often very difficult to deal with. It is not possible to reach to a conclusion by studying 12 cases only. As the incidence is emerging gradually in increasing numbers, we have to concentrate our focus on cases of non-healing post-operative wounds, which could be a case of atypical or non-tuberculous Mycobacterial wound infection and has to be dealt with accordingly.

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Effect of Neoadjuvant Chemotherapy in Harvesting Axillary Lymph Node Count in Patients with Locally Advanced Breast Cancer

Hasan S K^a, Rahman S A^b, Ahmed N^c, Chowdhury R A^d, Masud Z M^e, Parveen S A^f

Abstract

Background: There is a clinical impression that we retrieve fewer lymph nodes after neoadjuvant chemotherapy and that there is an association between the total number of lymph nodes retrieved and the number of diseased lymph nodes. Neoadjuvant chemotherapy has become a common treatment for patients with locally advanced and lymph node positive breast cancer.

Objective: To assess the impact of neoadjuvant therapy on the lymph node counts of women undergoing axillary dissection for breast cancer. We also looked for other variables that could be associated with lower lymph node counts.

Methods: An analysis of medical records of patients treated during 2010 to 2013 from Bangladesh Medical College and Hospital and private practice records identified 150 patients treated for invasive breast cancer who underwent level I and II axillary lymph node dissections. Among those 125 patients fulfilled the inclusion criteria. Women from the neoadjuvant chemotherapy group (n= 60) were compared with those from the primary surgery group (n= 65). The total number of lymph nodes harvested was considered as a continuous variable, but also dichotomized into two categories (<10 and =10). Its correlation with the different variables was analyzed.

Results: The median number of lymph nodes retrieved in the neoadjuvant chemotherapy group was 10.0 (range 2 to 23) compared with 11 (range 2 to 28) in the comparison group. In pathologic lymph nodes stage, 24 (40%) patients of neoadjuvant group were pN1 versus 9(14%) of primary surgery group. Total 49 (75.4%) patients of primary group had pathologic lymph node status pN2 where 18(30%) patients of neoadjuvant group had pN2 and pN3 6(9.23%) versus 2(3.3%) and P<0.00001.

Conclusions: This study suggests that administration of neoadjuvant chemotherapy to breast cancer patients' results in a reduced number of lymph nodes retrieved in the axillary dissection specimens. Our data demonstrate a variability in axillary lymph node retrieval, depending on the degree of lymph node disease and treatment with neoadjuvant chemotherapy. These findings support the idea that a more conservative surgical approach to the axilla should be considered in patients with a significant response to neoadjuvant chemotherapy

Keywords: Neoadjuvant Chemotherapy, Axillary Lymph Node, Breast Cancer

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- a. Dr. Syed Khalid Hasan; FCPS, MRCS
Assistant Professor, Department of Surgery
Bangladesh Medical College & Hospital, Dhanmondi, Dhaka
- b. Dr. Saber Amenur Rahman; MBBS
Assistant Registrar, Department of Surgery
Bangladesh Medical College & Hospital, Dhanmondi, Dhaka
- c. Dr. Nabila Ahmed; MBBS
Registrar, Department of Surgery
Bangladesh Medical College & Hospital, Dhanmondi, Dhaka
- d. Prof. Riaz Ahmed Chowdhury; FCPS
Department of Surgery
Bangladesh Medical College & Hospital, Dhanmondi, Dhaka
- e. Dr. Zafor Md. Masud; MPhil, FCPS
Associate Professor and Head, Department of Oncology
Bangladesh Medical College & Hospital, Dhanmondi, Dhaka
- f. Prof. Parveen Shahida Akhter; FCPS
Professor and Head, Department of Medical Oncology
National Institute of Cancer Research and Hospital (NICRH), Dhaka

Correspondence to:

- a. Dr. Syed Khalid Hasan; FCPS, MRCS, MBBS
Assistant Professor, Department of Surgery
Bangladesh Medical College & Hospital, Dhanmondi, Dhaka
Email: skhalidhasan@gmail.com

Introduction:

There is a clinical impression that we retrieve fewer lymph nodes after neoadjuvant chemotherapy and that there is an association between the total number of lymph nodes retrieved and the number of diseased lymph nodes. Traditional staging of the axilla in patients with locally advanced breast cancer (LABC) has involved a surgical level I and II or level I, II, and III axillary lymph node dissection (ALND). Breast cancer does not necessarily spread in an orderly manner, first to level I and then to level II and III, but rather may metastasize initially to level II or III by circumventing the lower level nodes. Therefore, a level I dissection alone would be considered inadequate surgical staging of the axilla.¹ A minimum of 10 lymph nodes is required in the ALND specimen for the dissection to provide accurate information for staging.^{2,3}

This recommendation is derived from a mathematical model developed by Kiricuta and Tausch in 1992 in which

they determined that the retrieval of 10 axillary lymph nodes was the cut off value to allow a 90% certainty of a true negative axillary status after ALND.²

Neoadjuvant chemotherapy has become a common treatment for patients with locally advanced and lymph node positive breast cancer. Neoadjuvant chemotherapy is able to downstage the number of involved axillary lymph nodes as an important parameter in the definition of the pathological complete response (pCR).⁴ Clinical observations suggest a lower lymph node yield after NC, which might be due to chemotherapy dependent parameters influencing detection rates. To our knowledge, only one retrospective study has addressed this question; it revealed that 13% of patients treated by neoadjuvant chemotherapy had fewer than 10 lymph nodes at axillary dissection compared with 3% in the operation-first group ($p < 0.003$).⁵

The primary goal of our study was to assess the impact of neoadjuvant therapy on the lymph node counts of women undergoing axillary dissection for breast cancer. We also looked for other variables that could be associated with lower lymph node counts.

Methods and Materials:

An analysis of medical records of patients treated during 2010 to 2013 from Bangladesh Medical College and Hospital and private practice records identified 150 patients treated for invasive breast cancer. Of these, 60 received neoadjuvant chemotherapy. The neoadjuvant chemotherapy consisted of a regimen containing either anthracyclin or taxol.¹

A control group of patients was derived retrospectively from the same records and included 65 women with invasive breast cancer treated initially by operation. All patients had modified radical mastectomy with a continuity level I and II axillary dissection.

A total of 60 neoadjuvant chemotherapy and 65 primary surgery patients were included. Male patients were excluded from the study, as were women known to have metastatic disease before operation. Patients treated with neoadjuvant hormone therapy were also excluded from both groups. Patient and tumor characteristics are listed in Table 1. Pathologic evaluation of histologic subtype, tumor size, lymph vascular invasion, and nodal staging were performed on the surgical resection specimens. When available, tumor type and grade, estrogen and progesterone receptors status, and *HER2/neu* status of the biopsy specimens were recorded before chemotherapy; if not available, results from the surgical specimens were recorded. Estrogen and progesterone receptors status was determined immunohistochemically, with a threshold of 10% of stained tumor cells considered positive. *HER2/neu* status was also evaluated by immunohistochemistry, with the fluorescence in situ hybridization (FISH) technique used when the immunohistochemical analysis was interpreted as equivocal. Results that remained doubtful were pooled with negative results for analysis.

All axillary lymph nodes retrieved from surgical specimens were analyzed. The contents of the axillary lymph node specimens were examined by blunt manual dissection; chemical dissolving of fatty tissue was not used in our center. After careful gross dissection of the specimen, each lymph node or a representative sample of larger lymph nodes was submitted for hematoxylin and eosin staining followed by microscopic evaluation.

Univariate comparisons were performed between patients who received neoadjuvant chemotherapy and those who underwent primary operations. Continuous variables were analyzed with Student *t*-test, and ordinal and categorical variables were compared with chi-square tests, respectively. To evaluate their independency, all variables that showed a difference in either one of the two sets of comparisons were introduced in a nominal logistic regression model, with the number of lymph nodes (fewer than 10 versus 10 or more) as the dependent variable. A "p" value less than 0.05 was considered significant.

Results:

Table 1: Patients' characteristics by pathologic evaluation of histologic subtype, tumor size, lymph vascular invasion, and nodal staging

Characteristics	Neoadjuvant group, N= 60	Primary surgery group, N= 65	P value
Mean age Y	45.65	47	0.326
Pre-menopausal	33	35	0.82
Post-menopausal	27	30	
Tumor stage			0.0002
To	0	1 (1.5%)	
T1	16 (26.66%)	6 (9.2%)	
T2	27 (45%)	52 (80%)	
T3	9 (15%)	6 (9.2%)	
T4	8 (13.2%)	0	
Grade			0.179
I	0	1	
II	35	46	
III	25	18	
HER2/neu			0.77
Positive	20	28	
Negative	35	38	
Not Done	5	7	
Lymphovascular invasion	25	30	NS
Receptor status			0.47
Positive	35	42	
Negative	25	2	

NS= Not significant

In Table 1 univariate comparisons showed that patients from the primary surgery group were older than the neoadjuvant patients (mean 47 versus 45 years). In TNM classification, there was significant difference between primary surgery group and neoadjuvant group, 52 patients had T2 tumor versus 27 patients, 6 patients had T3 tumor versus 9 patients. Regarding tumor grading 46 patients belonging to primary surgery group had grade II tumor versus 35 of neoadjuvant group. In primary surgery group 28 patients were HER2/neu positive versus 20 patients of neoadjuvant group and 42 patients of primary surgery group were ER and PR positive versus 35 patients of neoadjuvant group. Thirty patients of primary surgery group had positive lymphovascular invasion versus twenty patients of neoadjuvant group.

Table 2: Distribution of pattern of Lymph Node Pathology

Lymph node characteristics	Neoadjuvant therapy group N=60	Primary surgery group N=65	P value
Total nodes removed:			
Mean	10.5 ± 4.71	11.43 ± 4.09	0.326
Median	10	11	
Range	2- 23	2-28	
Positive nodes removed:			
Mean	2.6 ± 3.46	6.04± 3.22	0.251
Median	2	6	
Range	0 14	1- 20	
Negative nodes removed:			
Mean	8.06 ± 5.10	5.49± 2.93	0.124
Pathologic lymph nodes stage:			
pN0	16 (26.66%)	1 (1.54%)	<0.00001
pN1	24 (40%)	9 (13.8%)	
pN2	18 (30%)	49 (75.4%)	
pN3	2 (3.3%)	6 (9.23%)	

In Table 2, the total number of lymph nodes retrieved after neoadjuvant chemotherapy was 10.5 ± 4.71 versus 11.43 ± 4.09 ($P = 0.326$) without neoadjuvant chemotherapy. After neoadjuvant chemotherapy the number of positive nodes was 2.6 ± 3.46 versus 6.04 ± 3.22; $P = 0.251$ without neoadjuvant chemotherapy. The number of negative nodes with neoadjuvant treatment was 8.06 ± 5.10 and 5.49 ± 2.93 in primary surgery group.

In pathologic lymph nodes stage, 24 (40%) patients of neoadjuvant group were pN1 versus 9(14%) of primary surgery group. 49 (75.4%) patients of primary group had

pathologic lymph node status pN2 where 18(30%) patients of neoadjuvant group had pN2 and pN3 6(9.23%) versus 2(3.3%). $P < 0.00001$.

Discussion:

Neoadjuvant systemic chemotherapy may sterilize axillary metastases in approximately 25% of patients^{7,8} but it is not clear whether it can also affect the total number of lymph nodes harvested at axillary dissection. Similar to Newman and colleagues⁵ we obtained fewer lymph nodes in axillary dissection specimens of women treated by neoadjuvant chemotherapy compared with those treated by primary operation. Indeed, comparisons between both the total number of lymph nodes harvested and the ratio of patients exhibiting fewer than 10 axillary lymph nodes were significantly different in the two groups. After neoadjuvant chemotherapy, microscopic examination of lymph nodes may reveal accumulations of histiocytes and display considerable lymphoid depletion, fibrosis, and hyalinization.^{9,10} So we can suppose that lymph nodes may shrink or disappear secondary to lymphocytic toxicity and fibrotic involution. In addition, fibrotic replacement in the axilla changes its architecture and results in a more difficult area to dissect correctly during surgery, which can also contribute to lowering the total number of lymph nodes harvested. We can also hypothesize that previous dissection from sentinel lymph node biopsy could challenge the surgical technique and eventually lower the count of lymph nodes collected because of the fibrosis caused by the cicatrization. Because no woman in the neoadjuvant chemotherapy group underwent sentinel lymph node biopsy, this strengthens the lower lymph node count found in the neoadjuvant chemotherapy group. The total number of lymph nodes retrieved from axillary dissection may be influenced by age, tumor and nodal staging, extent of axillary dissection, and histopathologic evaluation.¹¹ It is noteworthy that the mean age of the primary surgery group was higher than that of the neoadjuvant group. As described by Schaapveld and associates,¹¹ the number of total lymph nodes retrieved from axillary dissection decreases with advancing age. So, this difference in age between the two groups does not explain why we harvested fewer axillary lymph nodes in women treated by neoadjuvant chemotherapy. When looking at tumor size differences were significant; $P = 0.0002$ (Table 1).

All surgical axillary specimens were analyzed in a similar manner by pathologists by blunt dissection of the specimen without a fat dissolving technique, serial sectioning, or radiologic evaluation. This technique of gross and visual pathologic examination of specimens can explain the discrepancy in percentages of fewer than 10 lymph nodes in our study compared with that of Neuman and coworkers⁵ (45% versus 13% in the neoadjuvant group and 28% versus 3.5% in the operation-first group). In Neuman and colleagues' study, gross dissection of the specimens was

followed by serial sectioning of the adipose tissue in intervals of 2 to 3 mm. In addition, some patients underwent a level III axillary dissection, with a possible upgrade in the number of lymph nodes collected.

Our data concerning the number of lymph nodes obtained in the operation-first group is within the range reported in literature. Indeed, the median number of lymph nodes harvested from axillary dissection in operation-first patients were 11 with a range of 2-28 and in the neoadjuvant group the range was 2-23 with median 10.^{3,12,13} Fisher et al found a small, but statistically significant, difference in the median number of nodes retrieved.¹⁴

Axillary lymph node involvement is an important determinant of tumor prognosis. A greater number of positive lymph nodes is associated with a higher risk of developing systemic breast recurrence.¹⁵ Also, in neoadjuvant chemotherapy, a complete pathologic axillary response is associated with a favorable prognosis.¹⁶ As a matter of fact, in studies of neoadjuvant chemotherapy for breast cancer using the multivariate method, the extent of metastatic disease in the axilla is consistently the most significant variable related to outcomes.^{15,17,14,18} So it is important to have a high level of confidence with regard to axillary staging assessment. But studies that determined the minimum number of lymph nodes necessary for reliable assessment of axillary status were not done in the context of primary systemic therapy. So retrieving fewer than 10 lymph nodes in axillary dissections of women treated by neoadjuvant chemotherapy may not represent inadequate nodal staging.

Conclusion:

This study suggests that the administration of neoadjuvant chemotherapy in breast cancer patients results in a reduced number of lymph nodes in the surgical specimen when compared with the number in patients not receiving neoadjuvant chemotherapy. Nevertheless, it is uncertain whether this affects the staging or prognosis of women suffering from invasive breast cancer. More studies assessing the number of lymph nodes in surgical specimens after neoadjuvant chemotherapy are needed to evaluate the significance and safety concerning adequate staging of breast cancer patients. Our data demonstrate a variability in axillary lymph node retrieval, depending on the degree of lymph node disease and treatment with neoadjuvant chemotherapy. These findings support the idea that a more conservative surgical approach to the axilla should be considered in patients with a significant response to neoadjuvant chemotherapy.

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Serum Uric Acid Level in Patients with Acute ST-Elevation Myocardial Infarction and Non ST-Elevation Myocardial Infarction

Sultana K N^a, Sultana N^b

Abstract

Background: Hyperuricemia is accompanied by many cardiovascular risk factors. Few studies investigated elevated serum uric acid (SUA) levels in patients with acute myocardial infarction (AMI) is highly predictive of mortality and morbidity.

Objective: To assess the levels of SUA in patients with acute STEMI and NSTEMI.

Methods: This observational study was conducted in the *department of Cardiology & Biochemistry in Dhaka Medical College Hospital, Dhaka* from July 2012 to June 2013. A total of 125 patients with AMI were studied (94 STEMI and 31 NSTEMI). Diagnosis of AMI was confirmed by Troponin I and ECG findings. The relationship between SUA level and the severity of MI was analyzed by SPSS version 17.0 software. Independent two sample t-test was done to see the mean difference of serum uric acid in patient with STEMI and NSTEMI.

Results: Among 84 male, 22.6 % and 77.4 % and among 41 female, 29.3 % and 70.7 % were suffering from NSTEMI and STEMI respectively. Hyperuricemia was found in 34.5% of male & 51.5% of female. Mean serum uric acid level was significantly higher in STEMI than NSTEMI (6.62 ± 2.41 mg/dl vs. 5.82 ± 1.31 mg/dl, $P=0.02$).

Conclusion: Study results showed that patients with STEMI have elevated serum uric acid level than NSTEMI.

Keywords: Acute ST-elevation myocardial infarction, Non ST- elevation myocardial infarction, Serum uric acid, Hyperuricemia.

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Introduction:

Acute myocardial infarction (AMI) is a life threatening (atherosclerotic disease) and leading cause of morbidity and mortality globally and is predicted that AMI will soon become the first cause of death in developed countries as well as developing countries like Bangladesh. Among the other risk factors associated with MI, hyperuricemia is also a definite risk factor and is highly predictive of mortality in patient with coronary artery diseases. After AMI, patients with hyperuricemia were found to be more susceptible to left ventricular remodeling as well as left ventricular systolic or diastolic dysfunction. Hyperuricemia is also thought to increase oxidative stress and activate inflammatory cytokines, while inducing cardiomyocyte apoptosis, then promoting myocardial remodeling.¹

Obvious atherosclerotic risk factors include high blood lipids, smoking, hypertension, diabetes mellitus, age and sex, the new risk factors of atherosclerosis are inflammatory signs, fibrinolytic function, homocysteine and probably uric acid.² Uric acid occurs naturally in the human body as a result of metabolism of purine. Purine enters the body through diet or comes from breakdown of the body's own cell during cell turnover.

Clinical and epidemiological studies have proved that SUA is significantly correlated with cardiovascular disease. Increased SUA is significantly associated with the occurrence and mortality of coronary artery diseases.³⁻⁵ Elevated SUA is highly predictive of mortality in patients with coronary artery disease and a negative prognostic marker for mortality in subjects with pre-existing heart failure.⁶ This study was undertaken to assess the relationship of serum uric acid levels in patients with acute STEMI and NSTEMI.

Materials and Methods:

This observational study was carried out in the Department of Cardiology & Biochemistry in Dhaka Medical College Hospital, Dhaka, Bangladesh from July 2012 to June 2013. Patients admitted with a clinical diagnosis of ST segment elevation acute myocardial infarction (STEMI) or non-ST

a. Dr. Kazi Nazneen Sultana; MPhil, MBBS
Assistant Professor, Department of Biochemistry
Bangladesh Medical College, Dhanmondi, Dhaka.

b. Prof. Dr. Nasima Sultana; MPhil, MBBS
Professor and Head, Department of Biochemistry
Dhaka Medical College, Dhaka.

Correspondence to:

a. Dr. Kazi Nazneen Sultana
Assistant Professor, Dept. of Biochemistry
Bangladesh Medical College, Dhanmondi, Dhaka.
Email: nazneen_bmc@yahoo.com

Cardiology, as assessed by attending physician were recruited into the study. A total of 125 consecutive patients (84 males and 41 females with age range 30-65 years) were enrolled in this study using non-random sampling technique. segment elevation acute myocardial infarction (NSTEMI) on the basis of clinical history, examination, ECG changes, biochemical marker (troponin I) in the Department of Cardiology, as assessed by attending physician were recruited into the study. A total of 125 consecutive patients (84 males and 41 females with age range 30-65 years) were enrolled in this study using non-random sampling technique. Among them 94 were STEMI and 31 were NSTEMI. The patients who had congenital heart disease, chronic kidney diseases, gouty arthritis, patients getting urecemic drugs, pregnant & lactating women were excluded. After taking informed consent data were collected by structured questionnaire. Clearance was obtained from the institutional ethical committee. SUA was statistically compared to observe the association with AMI. Results were analyzed statistically in SPSS version 17.0 and expressed as their mean±SD. p-value <0.05, considered as significant.

Laboratory measurement:

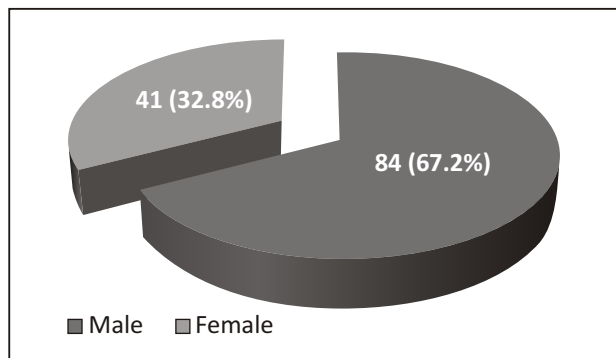
Quantitative measurement of serum uric acid was estimated by Uricase PAP method.⁷

Levels of Serum uric acid:⁸⁻⁹

Normal: (male up to 7 mg/dl and female up to 6 mg/dl)
 Hyperuricemia: male >7 mg/dl (or 420µmol) and female >6 mg/dl (or 360 µmol)

Results:

Figure 1: Distribution of study subjects according to sex



In this study, among 125 AMI patients, 84 were male and 41 were female (67.2% male and 32.8% female) with the age range 30-65 years.

Figure 2 shows among 84 male, 22.6% (n=19) were suffering from NSTEMI and 77.4% (n=65) from STEMI. Among 41 female 29.3% (n=12) and 70.7% (n=29) were suffering from NSTEMI and STEMI respectively (Figure 1 & 2).

Figure 2: Distribution of study subjects according to types of AMI and sex

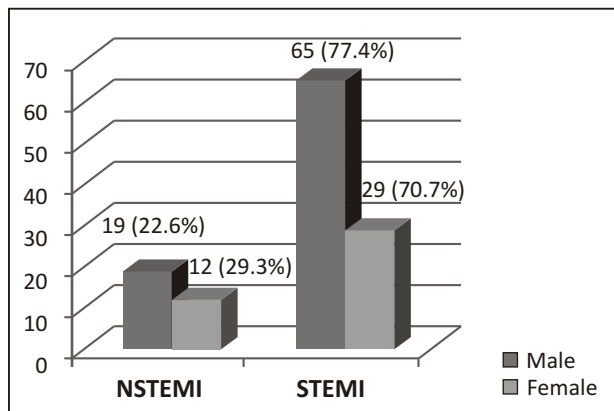


Table 1: Distribution of study subjects according to serum uric acid in different sex

Sex of patients	Study subjects		Total
	Normoureceemic	Hyperureceemic	
Male	55 (65.5%)	29 (34.5%)	84 (100%)
Female	20 (48.8%)	21 (51.2%)	41 (100%)

Table 2: Serum uric acid level according to types of AMI (n=125)

Type of MI	Frequency (No)	Uric acid in mg/dl		t value	p value
		Mean	SD		
NSTEMI	31	5.82	1.31		
STEMI	94	6.62	2.41	2.320	0.02*

Among the AMI patients 94 were STEMI and 31 were NSTEMI. The mean ±SD serum uric acid concentration in STEMI and NSTEMI were 6.62±2.41mg/dl and 5.82±1.31mg/dl respectively. Out of 125 patients 50 had hyperuricemia and 75 had no-hyperuricemia. Hyperuricemia was found in 34.5% (n=29) of male & 51.5% (n=21) of female. More than 80% of patients had high serum uric acid level. SUA was statistically compared to observe the association with AMI. Mean serum uric acid level was significantly higher in STEMI than NSTEMI (6.62±2.41mg/dl vs. 5.82±1.31mg/dl, p= 0.02) as shown in Table 1 & 2.

Discussion:

AMI is the most important form of ischemic heart disease (atherosclerotic disease) and the leading cause of death worldwide, particularly among East Asian populations. The incidence of MI increases with age; however, the actual incidence is dependent on predisposing risk factors

for atherosclerosis. Uric acid promotes the development of atherosclerosis, while causing a variety of cardiovascular events. The possible mechanisms vary. One of the possible mechanism is that hyperuricemia cause oxygenation of low density lipoprotein and promote lipid per oxidation, which in turn increases the thickness of intima to produce atherosclerosis. In addition, the high level of SUA also increases platelet aggregation and the formation of uric acid crystals, promoting coronary thrombosis.¹⁰⁻¹⁴

Hyperuricemia is accompanied by many cardiovascular risk factors and highly predictive of mortality in patients with coronary artery disease. Unfortunately, AMI and its early treatment remain limited. It is clear that preventive measures can reduce the morbidity, mortality and cost of MI. The aim of this observational study was to assess the relationship of hyperuricemia in patients with acute STEMI and NSTEMI.

Out of the 125 study subjects, 94 were suffering from STEMI, while 31 were from NSTEMI. Among 84 male, 22.6% NSTEMI and 77.4% STEMI whereas among 41 female 29.3% NSTEMI and 70.7% STEMI. This finding was consistent with study done by Kojima et al.¹⁵

The results of the present study showed that serum uric acid levels in patients with STEMI was increased. It was found significantly higher ($p=0.02$) serum uric acid concentration in STEMI (6.62 ± 2.41 mg/dl) than NSTEMI (5.82 ± 1.31 mg/dl). This finding conforms to the study done by Chen et al.¹⁶

Nadkar et al studied 100 patients more than 18 years of age and found 65 had STEMI, while 35 were NSTEMI. SUA levels were significantly higher in patients of STEMI¹⁷ which is similar to current study. Elevated serum uric acid concentration was significantly related with severity of AMI and most of the patients were suffering from STEMI and significant relationship with SUA was found. The exists association between hyperuricemia and myocardial infarction that had been found in different studies¹⁵⁻¹⁷ including current study has need to be evaluate whether this association is cause, effect or coincidence.

Although the results of this study support the hypothesis, there were some facts that the study was conducted with small sample size because of time limitation and financial constrains in a single hospital and sample was taken purposively. So, it may not be adequate to represent the total population, therefore basic studies are warranted in this point of view.

Conclusion:

Traditional modifiable risk factors are now being treated but there is a pressing need to identify additional treatable risk factors that are easily measured and highly prevalent at low cost in general population. Hyperuricemia is such type of potentially modifiable risk factor of AMI. Routine assessment of high serum uric acid levels in patients with

risk of MI along with other predisposing factors might be helpful for prevention and better management of AMI patients and more attention should be protected about the increasing burden of hyperuricemia in developing countries.

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Trace Mineral Status Related to Levels of Glycated Hemoglobin of Type 2 Diabetic Subjects

Yeasmin R^a, Muttalib M.A.^b, Sultana K N^c, Alam R^d

Abstract

Background: Diabetes mellitus (DM) is of major and increasing global public health importance. People with diabetes are at increased risk of premature disability and death associated with vascular, renal, retinal and neuropathic complications. Direct association of trace elements in both type 1 and type 2 diabetes has been observed in many research studies. An alteration in the metabolism of these minerals has been demonstrated in diabetes.

Objectives: To investigate zinc (Zn), copper (Cu), manganese (Mn) and magnesium (Mg) levels in the serum of patients with type 2 diabetes and age-matched healthy subjects and also to assess the association between these elements and glycated hemoglobin (HbA1c).

Methods: This cross sectional comparative study was done from January 2015 to July 2015. The study population consisted of 100 type 2 diabetic patients taken from OPD of BIRDEM and 100 age-matched non-diabetic healthy subjects within the age range of 30-70 years taken from the workers of BIRDEM. This study was done by the fund of BMRC. Informed consent was obtained from individuals before enrollment into the study. Clearance was obtained from the institutional ethical committee. Aged 30-70 years; known as type 2 diabetic patients for the past two to five years; and non-diabetic individuals considering the glucose tolerance test or FBS < 80 mg/dl were considered as control. Level of Zn, Cu, Cr, Mn, Mg and HbA1c were measured and compared in both groups. Statistical analysis as done by using Microsoft Excel and SPSS version 16.

Results: In this study, significantly lower Cu levels ($P < 0.001$), Zn levels ($P < 0.001$), Mn ($p < .01$) and Mg levels ($P < 0.001$) were found in patients with DM in comparison with healthy subjects. We also found significant higher levels of HbA1c ($P < 0.001$) in the DM group than in the healthy group. Patients with DM had altered metabolism of Zn, Cu, Mn, and Mg, and this may be related to increased values of glycated hemoglobin.

Conclusion: Imbalance in the levels of studied trace elements may play an important role in the pathogenesis of DM and it requires further broad spectrum study.

Keywords: Diabetes mellitus, serum, zinc, copper, chromium, manganese, magnesium, HbA1c.

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Introduction:

Type 2 DM is on track to become one of the major global public health challenges of the 21st century. It accounts for approximately 90 to 95% of all diagnosed cases of diabetes. Patients with type 2 diabetes may have complications like cardiovascular disease, nephropathy, and retinopathy and poly neuropathy. According to WHO report, the

prevalence of diabetes in adults worldwide has risen.^{1,2} The prevalence of DM in Saudi population is high and 90% of diabetic patients suffer from type 2 DM almost one Saudi in four beyond the age of 30 has DM.³ Some estimate that it will be 40-50% in 2020.⁴ There is accumulating evidence that the metabolism of several trace elements is altered in DM and that these nutrients might have specific roles in the pathogenesis and progress of this disease.^{5,6} Zinc (Zn) is an essential trace metal that is directly involved in the synthesis, storage, secretion, and conformational integrity of insulin monomers and that Zn assembles to a dimeric form for storage and secretion as crystalline insulin.^{6,7} Lower levels of Zn may affect the ability of pancreatic islet cells responsible for the production and secretion of insulin, such as in type 2 diabetes.⁶ Epidemiological studies have reported decreased plasma and intracellular Zn concentrations in conjunction with increased urinary Zn excretion in diabetic patients.

- a. Dr. Roksana Yeasmin; M.Phil, MPH
Associate Professor of Biochemistry, Ibrahim Medical College, Dhaka
- b. Dr. M. A. Muttalib; M.Phil
Professor of Biochemistry, Ibrahim Medical College, Dhaka
- c. Dr. Kazi Nazneen Sultana; M.Phil
Assistant Professor of Biochemistry, Bangladesh Medical College, Dhaka
- d. Dr. Rashedul Alam, M.Phil
Assistant Professor of Biochemistry, Army Medical College, Comilla

Correspondence to:

- a. Dr. Roksana Yeasmin,
Associate Professor of Biochemistry, Ibrahim Medical College, Dhaka

In subjects with type 2 DM with low Zn intake, the risk of coronary heart disease increases by a factor of two to four times and is a major cause of mortality among diabetic patients.^{6,7} Copper (Cu) and Zn play a pivotal role in the oxidant/antioxidant mechanism, imbalance of which leads to increased susceptibility to oxidative damage of tissues, thereby leading to the pathogenesis of DM or diabetic complications.⁸ Cu acts as a pro-oxidant and may participate in metal-catalyzed formation of free radicals. However, Cu and Zn act as structural and catalytic components of some metalloenzymes. Cu is necessary for the catalytic activity of enzymes such as Cu/Zn superoxide dismutase (SOD) that is involved in the protection of cells from superoxide radical. Zn acts as an antioxidant by protecting sulfhydryl groups of proteins and enzymes against free-radical attack in the body.⁹

The changes in the metabolism of Cu and Zn that occur during oxidation stress may be important in several processes where oxidative stress is implicated.^{10,11} Both the essentiality and toxicity of these metals in the pathogenesis of DM and diabetic complications are often reported.^{12,13} Some investigators have reported the hypothesis that glycosylated proteins bind transition metals such as Cu and iron (Fe) and that such glycocholates play an important role in the etiology of peripheral vascular dysfunction and peripheral neuropathies in DM.¹⁴ Magnesium (Mg) is the fourth most abundant cation in the body and second in the intracellular environment. It takes part in more than 300 enzymatic reactions.¹⁵⁻¹⁶ Deficiency of Mg has been associated with the variety of clinical conditions, including type 2 DM. Mg depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes,¹⁷ as well as on the evolution of complication such as retinopathy, thrombosis and hypertension. Moreover, low serum Mg is a strong independent predictor of the development of type 2 diabetes.¹⁸ Recent studies have also indicated that Mg deficiency may be associated with increased oxidative and nitrosamine stress through reduction in antioxidants and increased lipid per oxidation.¹ Reduced plasma levels of Mg have been documented in both type 1 and type 2 DM, especially in poorly controlled DM.¹⁹ The cause of hypomagnesaemia was attributed to osmotic renal losses from glycosuria, decreased intestinal absorption, and redistribution of Mg from the plasma into blood cells due to the effects of insulin.^{17,19} There are also reports of altered metabolism of other micronutrients such as Fe and manganese (Mn) in diabetes. Mn is a cofactor for a number of enzymatic systems including arginase, which has been found to be elevated in diabetic rats and mice.⁶ It was suggested that Mn is required for normal insulin synthesis and secretion.^{6,16} Diabetes is a free radical associated disease. Investigations carried out in diabetic patients revealed oxidative stress load.^{20,21} Oxidative destruction of sub-cellular membrane lipids has been implicated along with other types of intracellular oxidative damage in the normal aging process and in pathophysiology of a number of chronic illnesses. Complex antioxidant mechanism, including antioxidant vitamins and

minerals exists to limit the effects of these reactions.²⁰ DM being a degenerative disease, therefore, maybe initiated as a result of peroxidation caused by free radicals. Some trace metals such as Mn, Cu and vanadium possess antioxidant properties. Deficiency of these metals may thus increase susceptibility to the disease. The development of diabetic late complications (cataract, retinopathy, nephropathy, and neuropathy) is associated with an increased presence of free radicals and therefore elevated oxidative stress of the human body.^{19,20} Thus diabetic patients elicit a higher rate of blindness, kidney disease, gangrene, and coronary heart disease several times more than do non-diabetic subjects. The aim of the present study was to compare the status of some minerals of patients with type 2 DM with non-diabetic healthy subjects and also to assess the association between these elements and glycated HBA1C.

Material and Methods:

This cross sectional comparative study was conducted from January 2015 to July 2015 on 100 type 2 diabetic subjects (DM group) from OPD of BIRDEM and 100 age-matched non-diabetic male subjects (control group) within age range 30-70 years taken from the employees of BIRDEM. Informed consent was sought and obtained from individuals before enrollment into the study. Clearance was obtained from the institutional ethical committee. Non-diabetic individuals were selected subject to the results of glucose tolerance test or FBS < 80 mg/dl.

Patients who had diabetes other than type 2 DM, diabetic patients who had been treated with glucocorticoids, patients who had taken diuretics, subjects who had acute complications such as severe infections, major operations, trauma, GI disorders, severe cardiovascular/respiratory disease, patients who were presenting with ketoacidosis, subjects on any concomitant medication such as antioxidant vitamins, minerals, herbal treatment that may interact with glycemic status and oxidative stress parameters alcoholics were excluded from the study.

Body weight and height were measured and used to calculate the body mass index (BMI). Following enrollment, both patients and controls were instructed for the following: not to change their lifestyle or their dietary habits and not to take any dietary supplements. The diet was not monitored.

Sample collection and preparation: Fasting blood samples were collected into labeled centrifuge tubes, after an 8-12 h overnight fast, from the subjects by venipuncture. The blood samples were centrifuged at 2000 rpm for 10 min using a desktop centrifuge and the serum separated and kept in labeled sample bottles at -70°C until further analysis.

Instrumentation: The sera were analyzed for FBG and lipid profile using an auto analyzer (Roche Modular P-800, Germany). The concentration of trace elements of each sample was measured by Graphite Furnace Atomic Absorption spectrometer (VARIAN, Model Spectra AA 30P) using calibration method. The accuracy of

determination was evaluated by measuring the metal contents of certified biological reference materials (Seronorm Trace Elements Serum; Nycomed Pharma, Oslo, Norway). HbA1C was measured by HPLC method.

Statistical Analysis: Results were presented as mean \pm standard deviation. The significance of difference in the trace elements level in samples between two groups was tested using t-test analysis. Association between variables was determined using the Pearson correlation analysis on Microsoft Excel and SPSS software version 16. A two-sided p value <0.05 and <0.01 was considered statistically significant for the t-test and Pearson correlation analysis, respectively.

Results:

Table 1: Physical characteristics of diabetic patients and controls

Characteristic	Type-2 DM (cases)	Non Diabetic Controls	p Value
Age in years	48 \pm 10.44	42 \pm 9.37	<.001
Height in (C.M)	158 \pm 11.77	163 \pm 7.7	<.001
Weight (in K.g)	62 \pm 9.004	65 \pm 7.7	<.01
B.M.I (Ht/m ²)	25.04 \pm 3.29	25 \pm 2.71	<.05
Hip (C.M)	101 \pm 7.94	96 \pm 8.26	<.001
Waist (C.M)	94 \pm 8.52	86 \pm 8.22	<.001
W:H	.924 \pm .033	.881 \pm .04	<.001

The mean age of diabetic patients was 48 \pm 10.44 years versus years 42 \pm 9.37 years of non-diabetic subjects. The diabetic patients were generally heavier than the control subjects. The results of the BMI indicated that the diabetic subjects were overweight. There was significant difference in the BMI of the diabetic patient when compared with the control group (Table 1).

Table 2: Chemical characteristics of diabetic patients and controls

Biochemical characteristics	Type-2 DM Mean \pm SE	Non-Diabetic Controls mean \pm SE	p Value
TAG	226 \pm 124.16	138 \pm 89.23	<.001
Cholesterol	192 \pm 42.11	165 \pm 33.06	<.001
LDL-C	113 \pm 34.52	95 \pm 30.05	<.001
HDL-C	37 \pm 5.49	41 \pm 9.003	<.001
HBA1C	8.41 \pm 1.62	5 \pm .330	<.001
Zn	0.941 \pm .246	1.21 \pm .105	<.001
Cu	0.771 \pm .483	1.142 \pm .239	<.001
Mg	14 \pm 3.613	18 \pm 1.72	<.001
Mn	0.091 \pm .049	0.106 \pm .030	<.01

Baseline characteristics of patients with DM (DM group) and healthy subjects (control group) as well as serum concentrations of Zn, Cu, Cr, Mn, and Mg are shown in Table 2. We found significantly lower Cu levels ($p < 0.001$), lower Zn levels ($p < 0.001$), mg ($p < 0.001$), and Mn ($p < 0.05$) in patients with DM in comparison with healthy subject.

Table 3: Concentration of trace elements and HBA1C, FBS, ABF, in type-2 DM and controls

Parameters	Type-2DM Mean \pm SD	Control	T test
FBS	7.65	4.99	Significant
ABF	10.82	6.5	Significant
HBA1C	8.41	5.87	Significant

Fasting blood glucose and HbA1c were significantly higher in diabetic patients than in non-diabetic control ($p < .001$) as shown in Table-3.

Discussion:

Trace elements have been accepted as essential for optimum health. The significance of trace elements in normal growth and metabolism cannot be overemphasized. There is, however, an accumulating evidence that the metabolism of several trace elements is altered in DM.^{6, 19, 22} Some of these trace elements act as antioxidants and prevent membrane per oxidation. The beta cells of the pancreas, the cells that produce insulin, are sensitive to oxidative stress. This is due largely to the fact that their intracellular antioxidant defense mechanisms are weak compared to liver tissues.²³ Oxidative stress is thus suggested to be a potential contributor to the development of DM and the associated complications.²⁴ This may not be unconnected to the fact that the antioxidant status including antioxidant mineral elements may be inadequate in diabetic subjects. The metabolic significance of the evaluation of antioxidants in diabetic patients is therefore of paramount importance. In addition to the antioxidant roles of some of these mineral elements, they may act directly on glucose metabolism. The results of the current work indicated an imbalance in the levels of trace elements in type 2 DM. We found significantly reduced the levels of Zn, Cu, Mn and Mg in patients with DM when compared with healthy subjects (Table -2). Several reports have indicated^{6, 19, 27, 36} that the metabolism of some trace elements such as Cu and Zn is altered in DM and that these alterations might be a contributing factor in the pathogenesis of this disease. It has been also suggested^{8, 19} that hyperglycemia increases the production of free radicals and decrease the efficiency of antioxidant defense systems. It is well known that Cu and Zn play a vital role in oxidative stress.⁹ Therefore, changes in the levels of Cu and Zn may influence the equilibrium in the antioxidant defense system and enhance the toxic effect of metal

dependent free radicals. These associations may in this way initiate and potentiate the pathogenetic processes leading to diabetic complications.^{12,30,37} Cu and Zn are needed for essential activity of antioxidant enzyme Cu/Zn SOD. SOD catalyzes dismutation of superoxide radical into hydrogen peroxide. Therefore, abnormal metabolism of Cu and Zn may affect the function of SOD and result in decreased protection of cells from superoxide radical. Moreover, under conditions of hyperglycemia, glycated proteins exhibit increased affinity to Cu ions and may result in glycocholates formation. The glycocholates can be accumulated in the endothelium and participate in redox reactions. Therefore, alterations in the metabolism of Cu can be an important contributing factor for the progression of diabetic vascular complications.^{13,37} The serum Mn level of diabetic subjects in the current work was significantly ($p < 0.01$) different from the value obtained for the control subjects. Mn is a cofactor of many enzymes including mitochondrial SOD.³⁸ Mn-activated enzymes play important roles in the metabolism of carbohydrates, amino acids, and cholesterol. There are conflicting reports of Mn deficiency in DM.^{21,42} Diabetic patients with the higher blood levels of Mn were reported to be better protected from oxidation of LDL cholesterol. LDL oxidation contributes to the development of intra-arterial plaque, which can lead to heart attack and stroke. It has been established that diabetic patients have higher levels of fasting blood glucose, glycated hemoglobin and lipoproteins than non-diabetic patients^{40,39}. The higher levels of fasting blood glucose seen in diabetic patients are a result of insulin deficiency or insulin resistance associated with DM.^{42,43} In conclusion, the present results demonstrate that there is an imbalance in the levels of some trace elements such as Cu and Zn among patients with DM in comparison with healthy subjects. These changes may play an important role in the pathogenesis of this disease by the participation of these elements in the oxidative stress. We have also shown that the increased levels of Cu and Cu/Zn ratio and the decreased levels of Zn, Cr, and Mg are associated with increased values of HbA1c in diabetic patients. These findings may contribute to explaining the role of impaired metabolism of some mineral elements in the pathogenesis of diabetes. We conclude that impaired metabolism of Cu, Zn, Cr, and Mg may be suggested as a contributing factor in the progression of DM and also in the development of diabetic complications. The present study provides significant evidence showing that altered metabolism of Cu, Zn, Mn and Mg is strongly associated with the increased levels of HbA1c. These associations might represent a risk factor for the development of diabetic complications.^{36,37,41} Our findings indicate that it is necessary to take into consideration possible changes in the metabolism of these metals, mainly their associations with long-term hyperglycemia.

Conclusion:

The type-2 DM patient should receive long term micronutrients (Zn, Cu, Mg and Mn) supplementation to avoid micronutrient deficiency related complications.

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Stress among Medical Students in Selected Medical Colleges in Dhaka City

Chaklader MA^a, Jahan F^b, Rahman M^c

Abstract

Background: Medical students suffer from high stress levels compared with students in other majors. The excessive stress can lead to physical and mental health problems leading to reduce self-esteem and their academic achievement and personal or professional development.

Objectives: The objective of current study was to explore the nature of stress among medical students by determining the sources and pattern of stress and the factors affecting it.

Methods: This is a cross-sectional study conducted on the students of public and private medical college of Dhaka city. A pretested questionnaire for socio-demographic information and Medical Student Stressor Questionnaire (MSSQ) was used to evaluate stress levels and stressors among medical students. School and ethical committee clearance were obtained prior to the study. Data were analyzed using SPSS version 16.

Results: Of the medical students who were administered the questionnaire, 301 (84.08%) respondents participated in this study. Mean age of medical students was 20.99±1.43 years. Top 5 stressors was academic related stressors. 1st was “tests/examination” stressor. 37.2% students reported high stress from Academic Related Stressors; 37.7% 3rd year and 40.6% 5th year students reported severe stress from academic related stressors. About 30.8% 3rd & 27.5% 5th year students showed severe stress from intrapersonal & interpersonal related stressors. There was a significant association between private and public medical college for students' stress level related to IRS (Intrapersonal & Interpersonal Related Stressors), SRS (Social Related Stressors), DRS (Drive Related Stressors) and GARS (Group Activities Related Stressors).

Conclusion: The predominant forms of stressors which were found among medical students were academic, interpersonal and teaching and learning related stressors. All forms of stressors became more obvious in clinical years specially 3rd and 5th year. Students from private medical college reported higher stress level compare to public medical college's students.

Key words: Stress, Medical students, Medical College

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Introduction:

Stress is the body's reaction to a change that requires a physical, mental & emotional adjustment or response to a stressor.¹ An event that triggers the stress response may include: environmental stressors, daily stress events, life changes, work/study place stressors, chemical stressors and social stressor.^{2,3} It is mentioned that tertiary education is highly stressful to students.⁴ Stress is common in medical students and stress is differed from students of medical (Health Professions) to non-health professions

undergraduate students.⁵ For nearly half a century, stress in medical graduate students has been a topic of concern.⁶ Over the last three decades, numerous studies have examined, and these studies showed that medical students' sources of stress are diverse educational settings, full work-study loaded day, clinical trainings, difficult patients, sleep deprivation, financial concerns, assessments, the academic environment & lack of time for relaxation are factors that have been cited most.^{7,8,9,10,11,12,13} Stress may have a negative effect on cognitive functioning, physical wellbeing and psychological functioning.^{8,9,14} Stress can affect the vital parameters. The excessive stress can lead to physical (palpitation, insomnia, fatigue, nausea, skin disease, impaired bowel movement, hypertension, chest pain, peptic ulcer etc.) and mental health problems (anxiety, depression & even suicide thoughts) leading to reduce self-esteem, and poor academic performance, personal or professional development.^{8, 9, 11} As a result, medical students may feel inadequate and unsatisfied with their career as a medical practitioner in the future. Stressors of medical students generally were grouped into six categories; academic related stressors (ARS), intrapersonal and interpersonal

a. Dr. Mainul Alam Chaklader; MPH, MBBS
Assistant Professor, Department of Community Medicine
Bangladesh Medical College

b. Dr. Fiona Jahan; MPH, BDS
Research Assistant, International Center for Economic Policy research

c. Dr. Mahruha Rahman; MTM, MBBS
Assistant Professor (cc), Dept. of Transfusion Medicine, UAMCH

Correspondence to:

a. Dr. Mainul Alam Chaklader; MPH, MBBS
Assistant Professor, Department of Community Medicine
Bangladesh Medical College
Email: drmacmisha@gmail.com

related stressors (IRS), teaching and learning-related stressors (TLRS), social related stressors (SRS), drive and desire related stressors (DRS), and group activities related stressors (GARS).¹⁵ Most studies showed that academic related stressors were the most significant source of stress.^{13,15,16,17,18,19} Studies from developing countries like Thailand, India, Bangladesh, Malaysia, Nepal, Pakistan have reported stress among medical students and have also underscored the role of academics as a potential stressor.¹⁶ Studies from India, Malaysia, Nepal, Pakistan showed that prevalence of stress among medical students is 21%-46%.^{7,8,10,11,13,16,17,20,21} In Bangladesh we have 15 Govt. medical colleges & 48 non-govt. medical colleges and every year around 5500 students are admitted in these medical colleges. Only few studies have been conducted in Bangladesh. If the source and factors associated with the stress can be recognized early, it is possible to cope with the stress and may prevent the future harmful consequences. The objective of this study was to determine the status of stress and explore the sources of stress (stressors) among medical students.

Materials and Methods:

Current study was a cross-sectional study which was carried out among 358 students (sample size=358) from 1st to 5th year of MBBS in two medical colleges (one public and one private medical college) in Dhaka city. Sick students and students who had exams weren't included in the study. Pre-tested semi-structured self-administered questionnaire was given to each student in a face to face sessions in a lecture hall separately according to the year of study. The questionnaire collected information on socio demographic variables and also on sources & levels of stress. A newly developed instrument, the modified Medical Students Stressors Questionnaire (MSSQ), used to identify sources of stress. The items on MSSQ represent 20 events that have been reported to be possible sources of stress in medical students. Respondents were asked to rate each event in themselves by choosing from five responses: 'causing no stress at all', 'causing mild stress', 'causing moderate stress', 'causing high stress' & 'causing severe stress'. The MSSQ scored by assigning a value of "zero to four" for each of the respective responses. The process of filling in the questionnaire took about 15 minutes to complete and they were to be returned on the same day. Verbal consent was obtained from all participants. Completion of the questionnaires was voluntary and would not affect their progression on the medical courses.

Data Management and Data Analysis:

All data collection forms were given serial numbers. Data were entered, checked for data entry errors, explored and cleaned. Data were entered on Windows' Statistical Package for Social Sciences (SPSS 16.0 version) and Microsoft Excel. Data analyzed by Windows' Statistical Package for Social Sciences (SPSS 16.0 version) and Microsoft Excel. Descriptive statistics were used for the

analysis of the demographic data and the stressor items. Cross tabulation and Pearson chi-square test done to see the distribution of the medical students between their stress level and their academic year and to see relation between respondents' medical college and their stress level.

Results:

This study had 84.08% response rate (301/358). Of total 301 participants, 161 students were from private medical college and 140 students were from public medical college.

Table 1: Distribution of medical students according to sex and age (n=301)

Sex	No.	%	
Male	115	38.2	
Female	186	61.8	
Total	301	100	
Age	No.	%	Mean±SD
18-20	128	42.5	20.99±1.43
21-22	117	38.9	
23-24	56	18.5	
Total	301	100	

Table 1 shows about 61.8% were females and 38.2% were male students. The mean age of students was 21 years, most of the respondents were aged 18-20 years (42.5%).

Table 2: Distribution of medical students according to academic related background (n=301)

Medium of school	No.	%
Bengali	241	80.1
English	60	19.9
Choosing of medical profession	No.	%
Parental pressure	126	41.9
Own interest	175	58.1
Total	301	100

Most of the students (80.1%) were from Bengali medium; 175 (58.1%) students choose medical profession as career as own wish and 41.9% choose medical profession as parental wish (Table 2).

Among 301 students 150 (49.8%) took part in exercise and among 150 students who took part in exercise, 38.7% students used to do exercise regularly (Table 3). Most of the students (72%) do walking as exercise. Almost 40% students watch TV as their leisure activity; 43.5% students spent their free time with friends and 40.9% spent free time with family. About 36.2% students' sleeping duration was 6-7 hours; 30.9% students had difficulty in sleeping and among them 38 (40.9%) had delayed sleep disorder and 26 (28%) had insomnia.

Table 3: Distribution of medical students according to their life style related factors (n=301)

Taking part in physical exercise-	No	%
Yes	150	49.8
No	151	50.2
Leisure activities	No	%
Play sports	45	15
Watching TV	120	39.9
Reading	42	14
Surf the internet	71	23.6
Visit friends and family	1	0.3
Shopping	9	3
Visit outdoor spaces	7	2.3
Travel	4	1.3
Concerts	1	0.3
Arts	1	0.3
Smoking habit-	No	%
Yes	12	4
No	289	96
Cigarettes per day	No	%
10 or less	8	66.7
11 to 20	2	16.7
21 to 30	0	0
31 or more	2	16.7
Alcohol drinking habit-	No	%
Yes	14	4.7
No	287	95.3

Majority of the students (96%) students didn't have smoking habit. Among 12 (4%) students who had smoking habit, most of them (66.7%) used to take 10 or less cigarettes per day. 95.3% students didn't have alcohol drinking habit (Table 3).

About 37.2 % (112) students suffered high stress related to Academic related stressors whereas 27.2% students suffered severe stress. In Interpersonal and intrapersonal related stressors group 26.9% students (81) reported severe stress and 25.6% reported moderate stress. Moderate stress level seen in 31.6% students, related to Teaching and Learning related stressors. In Social related stressors, mild stress level was in 30.6% students; 25.2% students suffered mild stress in Drive & desire related stressor group; 31.2% & 30.2% students reported moderate and high stress level respectively in related to Group activities related stressors (Table 4).

Table 5 shows rank of each stressor based on the degree of stress perceived by the students. Here “tests/ examinations” stressor ranked top 1st stressor. Top 5 are Academic Related Stressors. Then next 2 ranked stressors are Intrapersonal & Interpersonal Related Stressors, rank 8, 9 are Teaching & Learning Related Stressors. Top 11 stressors causes moderate to high stress among students.

Table 4: Stress level among respondents (medical students)

Level of stress	Academic Related Stressors (ARS)	Intrapersonal & Interpersonal Related Stressors (IRS)	Teaching & Learning Related Stressors (TLRS)	Social Related Stressors (SRS)	Drive & Desire Related Stressors (DRS)	Group Activities Related Stressors (GARS)
No stress at all (0)	1 (0.3%)	26 (8.6%)	16 (5.3%)	31 (10.3%)	70 (23.3%)	16 (5.3%)
Mild stress (1)	33 (11%)	52 (17.3%)	60 (19.9%)	92 (30.6%)	76 (25.2%)	71 (23.6%)
Moderate stress (2)	73 (24.3%)	77 (25.6%)	95 (31.6%)	90 (29.9%)	67 (22.3%)	94 (31.2%)
High Stress (3)	112 (37.2%)	65 (21.6%)	73 (24.3%)	58 (19.3%)	54 (17.9%)	91 (30.2%)
Severe stress (4)	82 (27.2%)	81 (26.9%)	57 (18.9%)	30 (10%)	34 (11.3%)	29 (9.6%)
Total						301 (100%)

Table 5: Stressors ranked by mean degree of stress perceived by medical students

Rank	Items	Stressors	*Degree of stress Mean (SD)
Causing moderate to high stress			
1	Tests/examinations	ARS	2.68 (1.22)
2	Large amount of content to be learnt	ARS	2.55 (1.1)
3	Heavy workload	ARS	2.55 (1.25)
4	Falling behind in reading schedule	ARS	2.38 (1.21)
5	Lack of time to review what have been learnt	ARS	2.35 (1.24)
6	Conflict with teacher (s)	IRS	2.29 (1.53)
7	Verbal or physical abuse by teacher (s)	IRS	2.25 (1.46)
8	Uncertainty of what is expected of me	TLRS	2.25 (1.32)
9	Lack of recognition for work done	TLRS	2.12 (1.3)
10	Verbal or physical abuse by personnel(s)	IRS	2.1 (1.47)
11	Not enough feedback from teacher(s)	TLRS	2.05 (1.23)
Causing mild to moderate stress			
12	Verbal or physical abuse by other students (s)	IRS	1.99 (1.51)
13	Feeling of incompetence	GARS	1.98 (1.34)
14	Need to do well (imposed by others)	GARS	1.9 (1.3)
15	Facing illness or death of the patients	SRS	1.77 (1.44)
16	Participation in class presentation	GARS	1.72 (1.35)
17	Unable to answer questions from patients	SRS	1.72 (1.27)
18	Unwillingness to study medicine	DRS	1.62 (1.41)
19	Parental wish for you to study medicine	DRS	1.42 (1.44)
20	Talking to patients about personal problems	SRS	1.14 (1.29)

* Degree of stress classification: 0 - 1.00 is 'causing nil to mild stress', 1.01 - 2.00 is 'causing mild to moderate stress', 2.01 - 3.00 is 'causing moderate to high stress' and 3.01 - 4.00 is 'causing high to severe stress'

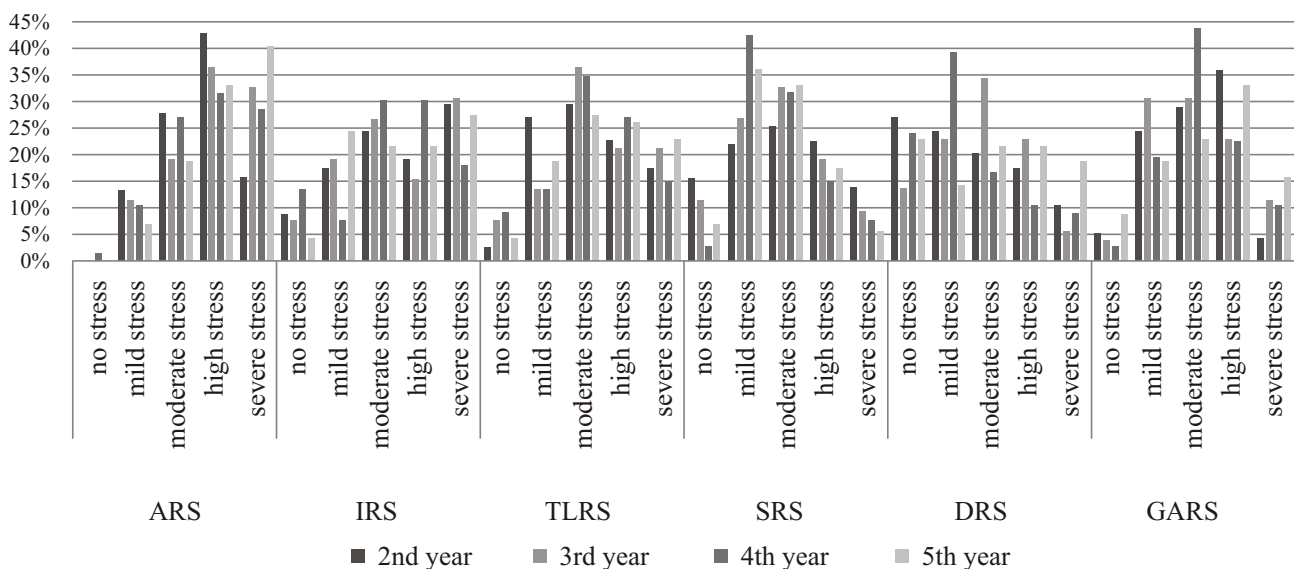


Figure 1: Distribution of respondents according to their stress level and their academic year

In related to Academic Related Stressors, in 2nd year students' percentage (43%) of high stress level was higher

Table 6: Distribution of respondents according to their medical college and stress level.

	Stress level	Private Medical	Public Medical	*P-value
ARS	No stress	0%	0.70%	0.709
	Mild Stress	9.90%	12.10%	
	Moderate Stress	24.80%	23.60%	
	High Stress	36%	38.60%	
	Severe Stress	29.20%	25%	
	Total	100%	100%	
IRS	No stress	7.50%	10%	0.006
	Mild Stress	13.70%	21.40%	
	Moderate Stress	25.50%	25.70%	
	High Stress	18%	25.70%	
	Severe Stress	35.40%	17.10%	
	Total	100%	100%	
TLRS	No stress	5.60%	5%	0.078
	Mild Stress	14.30%	26.40%	
	Moderate Stress	31.70%	31.40%	
	High Stress	28.60%	19.30%	
	Severe Stress	19.90%	17.90%	
	Total	100%	100%	
SRS	No stress	11.80%	8.60%	0.000
	Mild Stress	22.40%	40%	
	Moderate Stress	26.70%	33.60%	
	High Stress	24.20%	13.60%	
	Severe Stress	14.90%	4.30%	
	Total	100%	100%	
DRS	No stress	14.90%	32.90%	0.000
	Mild Stress	21.70%	29.30%	
	Moderate Stress	24.20%	20%	
	High Stress	23.60%	11.40%	
	Severe Stress	15.50%	6.40%	
	Total	100%	100%	
GARS	No stress	2.50%	8.60%	0.004
	Mild Stress	18.60%	29.30%	
	Moderate Stress	30.40%	32.10%	
	High Stress	37.30%	22.10%	
	Severe Stress	11.20%	7.90%	
	Total	100%	100%	

p-value is significant at level <0.05

compared to other academic years. But severe stress level is comparatively higher in 5th year (40.6%) as shown to Figure 1. In 3rd (30.8%) & 5th year (27.5%) students suffered severe stress level more than 2nd & 4th year from Intrapersonal & Interpersonal Stressors. Related to Teaching & Learning Related Stressors percentages of moderate stress level among 3rd (36.5%) & 4th (34.8%) year students are more than 2nd & 5th year. In 3rd (32.7%), 4th (31.8%), and 5th (33.3%) year moderate stress level more than 2nd year from Social Related Stressors was reported. Drive & Desire Related Stressors caused moderate (34.6%) to high stress (23.1%) among 3rd year students more than other academic years. High stress among 2nd year (36%) & 5th year (33.3%) is more than 3rd, 4th year students related to Group Activities Related Stressors (Figure 1).

Table 6 shows that from private medical college 29.20% students and 25% students of public medical college reported severe stress level related to ARS. Total 35.40% students from private medical college showed severe stress level related to IRS which was higher than students (17.10%) from public medical college. Table-6 results showed that high stress level is higher among students (28.60%) of private medical college than public medical college (19.30%) in TLRS. About 14.90% private medical college's students reported severe stress level related to SRS whereas from public medical college only 4.30% students reported severe stress (Table-6). About 15.50% Students of private medical college reported severe stress level related to DRS which is higher than students (6.40%) of public medical college. From private medical college 37.30% students showed high stress level related to GARS whereas 22.10% students of public medical college showed high stress. There was significant associations between private and public medical college for four domain stressor group which are IRS (Intrapersonal & Interpersonal Related Stressors), SRS (Social Related Stressors), DRS (Drive Related Stressors) and GARS (Group Activities Related Stressors).

Discussion:

Stress is the body's reaction to a change that requires a physical, mental & emotional adjustment or response to a stressor¹ and an event that triggers the stress response may include: environmental stressors, daily stress events, life changes, work/study place stressors, chemical stressors and social stressor.^{3,4} Stress is common in medical students and stress is differed from students of medical (Health Professions) to non-health professions undergraduate students.⁷

Academic related stressors refer to any scholastic, university, college, educational or student events that cause stress on students.¹⁵ Current study shows that prevalence of stress is higher in Academic related stressors group (ARS) compared to other stressors group; 37.2% students suffered high stress related to Academic related stressors whereas

27.2% and 24.3% suffered severe stress and moderate stress respectively in this stressors group (Table 4). A high score in this domain indicates that academic matters are the main sources of stress. Many studies have reported that the major stressors of medical students were academic related.^{4,16,17,19,22,23}

Interpersonal stressors generally relate to relationships between individuals including as verbal, physical and emotional abuse caused by other persons, and conflict with personnel, teachers, colleagues, and staff. In Interpersonal and intrapersonal related stressors group 26.9% reported severe stress, which were higher than Indian study conducted in a rural medical college, Ahmednagar which showed 0% severe stress level related IRS¹⁶ and also higher than Saudi Arabian study which conducted in Taibai University which reported 4.9% severe stress level related IRS⁴. And moderate stress was reported in about 25.6% (Table 4).

Teaching and learning related stressors refer to any events related to teaching or learning that causes stress.¹² In this current study most of the students showed moderate (31.6%) to high stress level (24.3%) in TLRS (Teaching & Learning Related Stressors) group, high scores in this domain indicates that TLRS group is one of the main sources of stress (Table 4). From an Indian medical college 59% students reported moderate stress level related TLRS¹⁶ and a Saudi Arabian study showed that 32.5% students reported high stress level in this stressors group.⁴ Consequently, it indicates that teaching and learning activities in these institutions are unfriendly to students. This requires looking at components of teaching and learning process to determine the causes of stress on the students.

Majority of the students suffered moderate stress level in SRS (Social Related Stressors) group, moderate and mild stress level was in 29.9%, 30.6% students respectively (Table 4) and moderate stress level here is lower than Indian study which showed 54% students reported moderate stress level¹⁶ and also lower than Saudi Arabian study which showed 59.7% students in this stress level related to SRS⁴. Social related stressors refer to any form of community and societal relationships that cause stress.¹² It generally relates to leisure time with family and friend, working with the public, private time for own self, working interruption by others, and facing patients' problems.¹²

Drive and desire related stressors generally relates to unwillingness to study medicine due to various reasons such as not being one's choice to study it, wrongly choosing the course, being demotivated after knowing the reality of medicine, parental wish to study medicine, and following friends to study medicine.¹² This domain showed low prevalence of stress, 25.2% mild stress and 22.3% moderate stress level reported (Table 4) and here

moderate stress level percentage is also lower than Indian study (35% moderate stress reported) which conducted in Ahmednagar¹⁶ and Saudi Arabian study (40.7% moderate stress level reported).⁴

Group activities related stressors (GARS) relates to participation in group discussions, group presentations and others expectations to do well.¹² About 31.2% (94) & 30.2% (91) students reported moderate and high stress level respectively in related to Group activities related stressors (Table 4) which is higher than Indian study (14% high stress level), conducted in Ahmednagar¹⁶ and bit higher than Saudi Arabian study which showed 25.2% high stress level among students related GRS.⁴

Some recent studies showed that there was relation present between students' daily activities like exercise, entertainment with stress level.^{17,21,24,25} In this study half of the students (50.2%) didn't have habit take part in exercise, and among who takes part in exercises 61.3% students didn't have habit to do exercise daily (Table 3). Students mostly spent their leisure time by watching TV (39.9%), internet surfing (23.6%) etc, but few students visited outdoor spaces (2.3%) or travel (1.3%) during their free time (Table 3). Current study shows that most of the students (60.8%) live in student's hostel (Table 2), previous studies showed that stress level was high among who lives in hostel, away from family, they reported home sickness.^{17,26,27}

In current study, top 5 stressors were related to academic matters, top five stressors were "tests/examinations", "large amount of content to be learnt", "heavy workload", "falling behind in reading schedule", "lack of time to review what have been learnt" as shown in Table 5. Previous studies showed also that academic related stressors were the most responsible to causing high stress level among medical students.^{16,17,19,21,27,22,23} Eleven stressors were rated as causing moderate to high stress among medical students (Table 5), study done by Yusoff et al showed that 7 stressors caused moderate to high stressors, and all top 10 stressors were related to academic matters.¹⁹ This studies showed score of 20 stressors was high compare to previous recent studies,^{17,21} score of intrapersonal & interpersonal related stressors was high compare to other past studies.^{17,21} Here 7th, 10th, 12th ranked stressors in IRS group (Table 5). "Uncertainty of what is expected of me", "lack of recognition for work done" showed high mean score (Table 5) than previous studies, these two stressors were in TLRS group. However, the severity level of stress caused by some stressors may be significantly different from studies done elsewhere.^{17,21,27}

In current study showed prevalence of high to severe stress level was higher among 3rd & 5th year's medical students than 2nd, 4th year's students as shown in figure 1. Social Related stressors caused high stress level among 2nd year

students more than other medical year's students (Figure 1). Previous most of the studies shows that clinical year's (3rd-5th) students reported high stress level than academic years (1st, 2nd).^{4,19,27,28}

Current study carried out in a private and public medical college to see the difference of stress level between these two medical colleges (table 6). This study showed that students from private medical college reported more stress level than public medical college and it showed there was significant association between public and private medical college for four domain stressor group which are IRS (Intrapersonal & Interpersonal Related Stressors), SRS (Social Related Stressors), DRS (Drive Related Stressors) and GARS (Group Activities Related Stressors) and there was an insignificant association between public and private medical college for two domain stressors group (ARS & TLRs) shown in Table 6. A comparative study which conducted in Bangladesh among 8 medical colleges also showed that there was significant differences between public and private medical colleges for stress scores of study population.²⁹

Conclusion:

This current study found that most of the medical students experienced moderate to high level of stress, and stress level comparatively was higher among the students of 3rd & 5th year. The top ten stressors were related to academic, intrapersonal & interpersonal and teaching and learning. Most of the stressors were contributed by the academic matters. There was significant associations between private and public medical college for four domain stressor group which are IRS (Intrapersonal & Interpersonal Related Stressors), SRS (Social Related Stressors), DRS (Drive Related Stressors) and GARS (Group Activities Related Stressors).

Recommendation:

More emphasize should be put on designing assessment that are friendly to psychological health of the students as well as developing effective intervention to improve the student psychological wellbeing. This will ensure that our curriculum and activities set for our medical students are in the range of their coping limit. Continuous supervision of students by the university' academic supervisor is needed. More detailed study design, including randomization and control (comparison) groups need to be done into future research to explore more information about academic related matters/ stressors.

Study limitation:

Timing of distribution of the questionnaire should have been during the middle of their clinical rounds but that was not feasible as reaching students in their clinical rounds in the hospitals was difficult.

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Feto-Maternal Perspective of Maternal ABO Incompatibility and Neonatal Hyperbilirubinemia

Habib A^a

Abstract

Neonatal jaundice/hyperbilirubinemia is considered pathological when jaundice appears within 24 hours of birth and is associated with serum bilirubin of more than 12 mg /dl persisting beyond 7-10 days of presentation. Prematurity, neonatal/ congenital sepsis, hypothyroidism are known confounding factors in this setting. Blood group incompatibility (ABO / Rh type or both) are responsible for Haemolytic disease of the new born (HDN) presenting with haemolytic jaundice. The aim of this review article is to summarize the implications of maternal ABO incompatibility on neonatal outcome and management of such pregnancies.

Severe hyperbilirubinemia, if not recognized may give rise to kernicterus and neonatal convulsions. Rh-isoimmunization arising in a Rh-incompatible couple is the commonest immune-mediated cause of neonatal anaemia/jaundice/ hydrops (in the presence of high Rh titres). Its occurrence can be prevented through pre-conceptional precautions, antenatal screening and Anti-Rh D vaccination at appropriate time and dose. However in Rh compatible couple, ABO incompatibility/ anti-A iso-immunization may rarely be considered as a cause of hydrops in a mother of O blood phenotype bearing a foetus of AO or BO blood group. ABO HDN may present as severe hyperbilirubinemia at the time of birth or as hydrops foetalis (gross foetal ascitis, pleural effusion from resultant anaemic heart failure). Early detection by antenatal screening, preventive intervention and availability of appropriate treatment at all levels of health care system are the essential tools for its elimination.

Keywords: Neonatal hyperbilirubinemia, ABO incompatibility.

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Introduction:

HDN is by far the most dangerous form of jaundice in the new born as the bilirubin level can rise rapidly into the toxic range. Feto-maternal transfusions in Rh-incompatible pregnancies result in production of Rh anti-D IgM and IgG. Rh Anti-D IgG is responsible for a positive Coomb's test and haemolysis in the foetus. Depending upon the level of haemolysis proportional to the Anti-D titre, the newborn may present with neonatal anaemia, jaundice or overt hydrops. Historically the most common cause of immune hydrops was rhesus haemolytic disease. With current obstetric management through prenatal and post-natal vaccination with Rhimmunoglobulin of Rhnegative mothers in a Rh-incompatible relation, Rh iso-immunisation is now rare in resource rich countries. ABO incompatibility and resultant ABO HDN has emerged as an important cause of early hyperbilirubinemia and /or hydrops fetalis. The aim of this review article is to provide a clinical overview about the different aspects of ABO HDN with their feto-maternal implications.

a. Dr. Asma Habib; FCPS
Assistant Professor, Department of Obstetrics and Gynaecology
Bangladesh Medical College and Hospital, Dhanmondi, Dhaka

Correspondence to:

a. Dr. Asma Habib; FCPS
Email: asma.imam2003@ yahoo.com

Materials and Methods:

This review article has used published literature from recent journals and relevant text books of paediatrics, haematology, genetics and internet search. This compilation has been inspired by a patient in a Rh-compatible relationship with mother bearing O + ve blood group and father bearing A+ve blood group whose first child suffered from severe hyperbilirubinemia (43 mg/dl or 709.5µmol/ml) and neonatal convulsion from kernicterus treated by exchange transfusion subsequently leading to severe mental retardation and choreoathetosis. In the next pregnancy 4 years later she developed hydrops foetalis at 26 weeks of gestation with gross polyhydramnios and had a spontaneous preterm vaginal delivery. Detailed sonographic anomaly screen revealed no obvious structural malformation.

She was screened negative for diabetes, Anti-phospholipid syndrome, thyroid dysfunction and TORCH panel. Post delivery normal parental karyotype along with exclusion of the common aneuploidies (chromosome 16, 18, XY) in the aborted foetus indirectly helped to exclude other aetiologies of hyrops foetalis in a rhesus compatible couple. Maternal serum titre of IgG anti-A or anti-B was advised after delivery.

Discussion:

Antenatal sonographic diagnosis of hydrops foetalis usually mandates termination of pregnancy. Looking retrospectively at the cause of hydrops, Rh- Iso-immunization should be excluded. In a Rh-compatible couple an anomaly screen with or without foetal echocardiography (if feasible) along with invasive testing for foetal karyotype should be offered as a cause of non-immune hydrops.¹ In the context of neonatal HDN maternal blood testing include maternal blood group and Rh type, Kleihauer stain for detection of feto-maternal transfusion, an indirect Coomb's antibody screen, complete blood count with differentials and erythrocyte indices, haemoglobin electrophoresis after exclusion of certain haemoglobinopathies (HbA disease/ Hb Bart), and glucose-6-phosphate dehydrogenase (G-6-PD) deficiency screen are indicated. Additional maternal serology includes TORCH titres, syphilis screen, and parvovirus B19 IgG and IgM titers.^{1,2}

Diagnosis of neonatal anaemia/jaundice:

Recognition of neonatal anaemia due to haemolysis is clinically important even if the anaemia is mild and apparently trivial. Transient or mild haemolysis in the neonatal period may be the first sign of an underlying problem with impact on subsequent growth and development. In the setting of neonatal anaemia/jaundice the following abnormalities may be observed on Complete Blood Count and haematological indices of the neonate:

- Low haemoglobin concentration
- Increased nucleated RBCs giving a false impression of elevated leukocyte count, reticulocytosis as high as 40% reflecting a state of erythropoiesis, polychromasia, anisocytosis, spherocytes and cell fragmentation. However a low reticulocyte count is observed in fetuses on in utero intravascular transfusion and with Kell alloimmunization.
- Hypoglycemia is common and is due to islet cell hyperplasia and hyperinsulinism secondary to release of metabolic by products such as glutathione from lysed RBCs. It has been observed that normalization of glucose level does not correct the auto-hemolysis in ABO incompatibility unlike in hereditary spherocytosis.
- In PBF, spherocytes (< 40%) are more commonly observed in cases of ABO incompatibility in comparison to Rh-incompatibility. In severe hemolytic disease, schistocytes and burr cells may be observed, reflecting ongoing disseminated intravascular coagulation.

Serologic tests to find out the cause of anaemia/jaundice include the following:

- Coomb's test: direct and indirect: In contrast to Rh alloimmunization, in ABO incompatibility only 20-

40% of infants exhibit a positive direct Coomb's antibody test. In a recent study, positive direct antibody test results were found to have a positive predictive value of only 23% and a sensitivity of only 86% in predicting significant hemolysis and need for phototherapy, unless the findings are strongly positive (4+). This is because fetal RBCs have less surface expression of type-specific antigen compared with adult cells. A prospective study has shown that the titres of maternal immunoglobulin G (IgG) anti-A or anti-B may be more helpful in predicting severe hemolysis and Hyperbilirubinemia in this context. The sensitivity and specificity of maternal IgG titres of 512 or higher in predicting need for intra-uterine transfusion was 90% and 73%, respectively.⁴

Although the indirect Coombs test result (neonate's serum with adult A or B RBCs) is more commonly positive in neonates with ABO incompatibility, it has poor predictive value for hemolysis. This is because of the differences in binding of IgG subtypes to the Fc receptor of phagocytic cells and, in turn, in their ability to cause hemolysis.⁵

Therefore the escalation of haemolysis and consequent neonatal hyperbilirubinemia needs to be monitored intensively through both clinical and biochemical parameters.

- In case of ABO incompatibility high maternal titres of IgG Anti-A or Anti-B may be detected on three forms: IgG1, IgG2 and IgG3. IgG2 is more commonly found in maternal serum but has weak lytic activity, which leads to the observation of little or no hemolysis with a positive direct antibody test result. On the other hand, significant hemolysis is associated with a negative direct antibody test result when IgG1 and IgG3 are predominant antibodies, which are in low concentration but have strong lytic activity, crossing to neonatal circulation. This is the fallacy of direct Coomb's test.⁶

Incidence of ABO HDN:

World-wide Anti-D still remains the most frequent allo-antibody to cause significant haemolytic anaemia due to poor recognition and /or prevention of Rh-incompatibility by Anti- D vaccination. In UK it affects 1 in 1200 pregnancies and still results in 50 deaths per year. However ABO incompatibility is now the most common cause of HDN in the UK occurring in 15 % of pregnancies. It is particularly common in those of African origin. Although ABO incompatibility between mother and foetus (mother bearing blood group O, infant blood group A or B) is present in approximately 25% of pregnancies, haemolysis is relatively uncommon because of several moderating factors. ABO HDN occurs around 1 in 150 of such births. It is confined to 1% of O group mothers with high titres of IgG antibodies. Majority of naturally occurring Anti-A and

Anti-B antibodies are of the IgM subclasses that do not cross the placenta due to their large molecular configuration, but some mothers "naturally" have IgG anti-A or IgG anti-B antibodies due to widespread exposure of naturally occurring A-antigens and B-antigens. These small molecular weight proteins can traverse the placental barrier with ease.^{3,4}

Whereas some mothers of genotype OO (blood group O) may be sensitized by fetal-maternal transfusion of ABO incompatible red blood from a husband having either blood group A, with genotype AA or AO, or more rarely, blood group AB, with genotype AB and produce immune IgG antibodies. Moreover, it would be very rare for ABO sensitization to be caused by therapeutic blood transfusion. In addition, neonatal red cell A and B antigens are not fully glycosylated and are therefore weakly antigenic at birth; there is also widespread expression of A and B antigens on other cells throughout the body thereby blocking/mopping up of any antibody that crosses the placenta. However, haemolysis due to Anti-A is more common than Anti-B IgG.⁵

Clinical features of ABO HDN:

An infant born to an alloimmunized mother shows clinical signs based on the severity of haemolysis. The cardinal features are jaundice, anaemia, hepato-splenomegaly and fetal hydrops in severe cases. Jaundice typically manifests at birth or in the first 24 hours after birth with rapidly rising unconjugated bilirubin level. Occasionally, conjugated hyperbilirubinemia is present because of associated placental or hepatic dysfunction in infants with severe hemolytic disease. Clinically significant jaundice occurs in as many as 20% of ABO-incompatible infants.^{5,6} Anaemia is most often due to destruction of antibody-coated RBCs by the reticuloendothelial system. The suppression of erythropoiesis by intravascular transfusion (IVT) of adult Hb to an anemic fetus can also cause anaemia.

Anemia is not the only cause of hydrops in ABO HDN. Hydrops results from hypoxia, anemia, congestive cardiac failure and hypoproteinemia secondary to hepatic dysfunction. Excessive hepatic hematopoiesis causes portal and umbilical venous obstruction and diminished placental perfusion. Increased placental weight and oedema of chorionic villi also interferes with placental transport. Commonly, hydrops is not observed until the haemoglobin level drops below approximately 4 gm/dl (Hct < 15%).^{6,7}

HDN is a rare cause of 'blueberry muffin' baby. These children have generalized hemorrhagic purpuric eruptions that on histopathology showed dermal erythropoiesis. Although the exact cause of diffuse dermal erythropoiesis is unknown, during normal embryologic development extramedullary hematopoiesis occurs in a number of organs, including the dermis; this activity persists until the

fifth month of gestation. Normally, leukocytes phagocytize the erythroblastic elements by 34-38 weeks gestation.⁸ The presence of blueberry muffin lesions at birth represents postnatal expression of this normal fetal extramedullary hematopoiesis. Hemolytic disease of the newborn (ABO or Rh incompatibility) are known causes for 'blueberry muffin' appearance. The presence of generalized edema of varying degrees, Coomb's positive hemolytic anemia, and laboratory documentation of unconjugated hyperbilirubinemia distinguish the aetiology from congenital infections and malignancies producing similar cutaneous manifestations.^{9,10}



Figure 1: Blue berry muffins showing the blue berry bits peeping through the surface of the baked cakes\



Figure 2: Cutaneous purpuric eruptions resembling the blue berry appearance in HDN.

Comparison of Rh and ABO Incompatibility:

Table 1: Comparison of Rh and ABO Incompatibility^{3,4}			
Characteristics		Rh	ABO
Clinical aspects	First born	5%	50%
	Later pregnancies	More severe	No increased severity
	Stillborn/hydrops	Frequent	Rare
	Severe anemia	Frequent	Rare
	Jaundice	Moderate to severe, frequent	Mild
	Late anemia	Frequent	Rare
Laboratory findings	Direct antibody test	Positive	Weakly positive
	Indirect Coombs test	Positive	Usually positive
	Spherocytosis	Rare	Frequent

Diagnostic tool (Antenatal and post-natal):

Routine antenatal antibody screening blood tests (indirect Coomb's test) do not screen for ABO HDN. If IgG anti-A or IgG anti-B antibodies are found in the pregnant woman's blood, they are not reported with the test results, because they do not correlate well with ABO HDN. Diagnosis is usually made by investigation of a newborn that has developed hyperbilirubinemia within 24 hours of birth. The Technical Manual continues to cite the direct agglutination test with immediate spin as the gold standard serologic test to detect ABO incompatibility in new born sample.¹¹ As mentioned by various authors, serologic failures result from a combination of weak antibody and poor expression of the corresponding antigen, e.g., the anti-A produced by group B individuals and the weak A antigen of apparent A₂B RBCs. However, ABO-HDN tends to occur in newborns whose mothers have high levels of IgG Anti-A or Anti-B antibody. The methods used to detect the culprit antibody in maternal blood in susceptible /high-risk mothers are: Antibody activity after neutralization with A or B blood group substance present in saliva, denaturation of IgN using 2-mercaptoethanol and indirect antiglobulin technique.^{6,11}

Prevention of ABO HDN:

Rh iso- immunization can usually be prevented by administration of anti-D gamma globulin at adequate dose within 72 hours up to 10 days after delivery to Rh- negative women following Rh- positive delivery, abortion, amniocentesis or tubal pregnancy or by antenatal immunoprophylaxis. However, the prevention of recurrence of ABO HDN in subsequent pregnancy particularly imparts on mothers with high titres of IgG anti-A/ B. The provision of plasmapheresis in mothers with previous hydrops babies has been debated. Paternal heterozygous A /B (that is AO or AB) inheritance may by

chance result in OO foetus, rendering that pregnancy free from the consequences of the effect of ABO HDN. It has been found that foetuses of O negative (Rh negative) mothers with a AB Rhesus positive partner is protected against the consequences of ABO HDN due to the lysis of immunised RBCs in the foetal circulation.^{12,13}

Management of ABO HDN:

Treatment of moderate or severe HDN caused by ABO antibodies is similar to that for Rh disease; with phototherapy, exchange transfusion (ET) depending upon the severity of haemolysis. Phototherapy should be given if the serum bilirubin reaches 12 mg/dl within 18 hours or 14 mg/dl within 24 hours. Severe hyperbilirubinaemia is the main indication for exchange transfusion using O group blood.^{13,14}

Prognosis of ABO HDN:

Overall survival is 85-90% but reduced to 15% for hydropic foetuses. Most survivors of alloimmunized gestation are intact neurologically. Fetal hydrops does not seem to affect long-term outcome in ABO HDN. However, neurologic abnormality has been reported to be closely associated with severity of anemia and perinatal asphyxia.¹²

Conclusion:

Though actual incidence of ABO HDN is not known in our country but it is for sure that due to ignorance and delayed reporting there happens improper and inadequate management of cases leading to neonatal mortality and morbidity as well.. Registration of Rh-negative mothers for receiving timely screening, preventive intervention and appropriate treatment with availability of medical needs and facilities are to be ensured at all levels with special attention to primary level of health system.

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Pelvic Mass: An Atypical Presentation of Pelvic Tuberculosis

Akter A^a, Uddin M N^b, Imtiaz K S^c

Abstract

Female genital tuberculosis is not uncommon in countries where pulmonary tuberculosis is wide spread. A 40 years old married woman, mother of four children presented with history of lower abdominal pain, irregular per vaginal bleeding & swelling of the abdomen for 3 months. She was malnourished, weighted 37kg with moderate anemia. Per speculum examination showed that cervix was broad & hypertrophied and in bimanual examination uterus was bulky in size, ill-defined mass felt through the both lateral fornices which was adherent to the uterus. USG of lower abdomen revealed bilateral adnexal mass. She was treated with laparotomy followed by adhesiolysis & total abdominal hysterectomy with bilateral salpingo-oophorectomy. After histopathological examination, patient was diagnosed as a case of tuberculosis of fallopian tube. She was underwent with anti-tubercular drugs & general condition of patient was improving.

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Introduction:

Female genital tuberculosis is not uncommon in countries where pulmonary tuberculosis is wide spread. In 92% of cases, genital tuberculosis is secondary to focus in the lungs, lymph nodes, intestine, urinary tract, bones and joints. The most common site of pelvic tuberculosis is fallopian tubes.¹ Genital organs most frequently affected include fallopian tubes (95-100%), endometrium (50-60%), ovaries (0-30%), cervix (5-24%) & vulva and vagina (1-2%).¹⁻⁸ Mostly genital tuberculosis is diagnosed during evaluation for infertility. Major presenting symptoms of genital tuberculosis are infertility (45-55%), pelvic pain (50%), poor general health (25%) and menstrual disturbance (20%). So genital tuberculosis should be considered in patients presenting with adnexal mass and a history of infertility.² There may be hormone dependence of infection given that 80% of cases occur in the reproductive age.^{2,5}

Female genital tuberculosis is treated with the same combined anti tuberculosis drugs therapy used in pulmonary & extra pulmonary tuberculosis but the diagnosis is critical. This paper briefly describes the pelvic tuberculosis which present as clinical features suggestive of malignant ovarian tumour.

Case Summary:

A 40 years old lady, married for 24 years, P4+0, ALC: 18 years, housewife presented with history of lower abdominal pain, irregular per vaginal bleeding & swelling of the lower abdomen for 3 months. She gave no personal or family history of pulmonary or extra pulmonary tuberculosis. On examination, she was malnourished, pulse was 88 beats/min, normotensive, weight was 37kg, moderately anaemic; jaundice & oedema was absent, no accessible lymph node was palpable. Per abdominal examination showed that lower abdomen was swollen and a tender ill-defined mass was present which about (14x10 cm) with no ascitis. In per speculum examination, cervix was broad & hypertrophied, no growth, erosion or ulcer was present. In bimanual examination, uterus was bulky in size, ill-defined mass felt through the both lateral fornices which was adherent to the uterus. Per rectal examination-rectal mucosa was free. Her Hb was 7gm/dl, ESR: 90 mm in 1st hour, CA-125: 50IU. USG of lower abdomen revealed bilateral adnexal mass measures about (8.9x 7.3 cm & 6.5 x 5.5 cm). Per operative findings revealed bilateral tubo-ovarian mass, gut & urinary bladder was densely adherent to the uterus. After adhesiolysis total abdominal hysterectomy with bilateral salpingo-oophorectomy was done. By keeping a drain tube in situ, abdomen was closed in layers. Histopathological examination revealed granulomatous lesion suggestive of tuberculosis of fallopian tube. Now patient is treated with anti-tubercular drugs & general condition of patient is improving.

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- a. Dr. Afroza Akter; FCPS, MCPS
Assistant Professor, Department of Gynecology & Obstetrics,
International Medical College & Hospital, Gazipur
- b. Dr. Mohammad Nizam Uddin; DA, MBBS
Assistant Professor, Department of Anesthesiology,
International Medical College & Hospital, Gazipur
- c. Dr. Khondker Saif Imtiaz; MPH, DPS, PGDDM, MBBS
Assistant Professor, Department of Community Medicine
International Medical College, Gazipur

Correspondence to:

- a. Dr. Afroza Akter
Assistant Professor, Department of Gynaecology & Obstetrics
International Medical College & Hospital, Gazipur
E-mail: dr.afrozaakterdoly@gmail.com



Figure 1: Uterus with bilateral tubo-ovarian mass

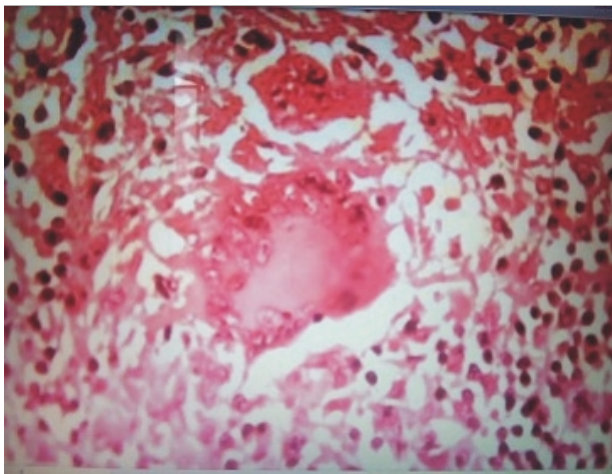


Figure 2: Histopathological findings of tuberculosis

Discussion:

Tuberculosis is one of the most important communicable diseases in the world. The most common site of pelvic tuberculosis is fallopian tubes.¹ Although it may involve the genital tract and frequently results in infertility, the presentation of the disease as a pelvic mass is uncommon.² While the incidence of tuberculosis has declined in the United States, genital tuberculosis should be considered in patients presenting with adnexal mass and a history of infertility.² There may be hormone dependence of infection

given that 80% of cases occur in the reproductive age.^{2,5} In the index case, though standard anti-tubercular regimen was initiated, the major determinant of the outcome of treatment is the patient adherence to the drug regimen.

Pelvic organs are infected from a primary focus, usually the chest, by haematogenous spread. The primary lesion is often healed by the time of presentation. Female genital TB is a rare disease in some developed countries but it is a frequent cause of chronic pelvic inflammatory disease (PID) and infertility in other parts of the world. Major presenting symptoms of genital tuberculosis are infertility (45-55%), pelvic pain (50%), poor general health (25%) and menstrual disturbance (20%).⁸⁻¹⁶ The presence of extra genital foci of TB, as a rule, is rare when genital lesion is discovered. The extent of genital lesion may be minimal or advanced. Minimal genital TB is usually asymptomatic except for sterility. Examination of pelvis may reveal no abnormality.

Microscopically, there are granulomatous lesion. Once the diagnosis of genital tuberculosis is confirmed, it is important to rule out tuberculosis in other parts of the body. A chest radiograph and three early morning sputum, early morning urine samples for AFB stain and culture are recommended

Before the advent of effective chemotherapy, surgery was the mainstay of treatment of genital tract TB and post-operative complication such as bowel fistula (14%) and mortality from primary disease (2.2%) were high. Experts suggest that extra-pulmonary tuberculosis may be even easier to treat than pulmonary tuberculosis owing to the decreased concentration of organisms in these lesions and increased accessibility of the sites. If surgical intervention is needed, chemotherapy makes it safer, easier and more effective if the regimen contain multiple drugs and taken regularly for a sufficient period of time.

While the incidence of tuberculosis has declined in the United States, genital tuberculosis should be considered in patients presenting with adnexal mass and a history of infertility.² One such case is presented here, and diagnosis and treatment are described.

Conclusion:

Female genital tuberculosis is not uncommon in countries where pulmonary tuberculosis is wide spread. Although it may involve the genital tract and frequently results in infertility, the presentation of the disease as a pelvic mass is uncommon. So in our country any patient who present with pelvic mass, possibility of tuberculosis should be keep in mind.

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Pregnancy and Tuberculosis: Report on Three Cases and a Brief Review of Literature

Habib A^a, Rahman A F M S^b

Abstract

Management of pregnancy with Tuberculosis requires special attention with regard to institution of drug therapy, compliance, dose modification and monitoring for side-effects. The standard combined drug therapy is started after confirmation of diagnosis, which poses diagnostic challenge as in a non-pregnant population. Strict coherence to the antenatal scheme facilitates surveillance which should be done in combination with pulmonologist / medicine specialist and obstetrician. Non-compliance with drug regimen is a major problem during and beyond pregnancy. Supervision, strict compliance to drug with alleviation of common fears of consumption of drugs in pregnancy through dissemination of information and incentive scheme may be necessary to encourage proper use of prescribed medication. Here we describe three cases of tuberculosis (two cases of extra-pulmonary and one case of pulmonary TB with dissemination) along with pregnancy and puerperium. Proper institution of drug therapy has resulted in good maternal and perinatal outcome.

Key words: Pregnancy, Tuberculosis, Extra-pulmonary tuberculosis, port-site tuberculosis.

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Introduction:

There is no good evidence to suggest that pregnancy is an independent risk factor for infection with *Mycobacterium tuberculosis* and that the course and outcome of TB are altered by pregnancy. Clinical suspicion and confirmation of the diagnosis of TB in pregnancy is often challenging, due to the non-specific sign /symptoms, masking of the classical features by pregnancy itself and hesitation of institution of multi-drug therapy during pregnancy. However, prompt treatment with standard Anti-Tuberculosis regimens has been found to be associated with good obstetrical outcome. Treatment with standard drug and weight-specific dose therapy is safe and effective in pregnancy irrespective of site of Tuberculosis. Isoniazide (INH), Rifampicin and Ethambutol are used initially. Ethambutol can be stopped when sensitivities show that the other two drugs are adequate.¹ Here we present three cases of pregnancy complicated by tuberculosis and their management with follow up.

Case Summary:

Case 1:

A 29 year old hypertensive female Para4 (3 normal vaginal delivery and 1 cesarean section) had undergone

laparoscopic Cholecystectomy 2 years back for chronic cholecystitis. She complained of recurrent discharge from the umbilical port with evidence of non-healing point. Wide and deep local excision of that area was done and histopathology revealed necrotizing granulomatous inflammation forming a tubercular sinus tract. She was started on anti-tuberculosis treatment with standard regimen with 5 tablets Rimstar 4 Fixed Dose Combination (FDC) according to her weight. The patient underwent the local excision procedure at 5 weeks 2 days amenorrhoea with a negative pregnancy test report. The wound healed naturally with time. The patient presented 4 months later with the complaints of heaviness in the lower abdomen and persistent amenorrhoea. Ultrasonogram of the lower abdomen revealed 18 weeks of pregnancy. She was advised to continue the Anti-Tuberculosis medication along with Tablet Pyridoxine and Folic Acid supplementation. The patient started her pregnancy with a body weight of 84 kg and she gained 14 kg throughout her pregnancy. She developed gross oedema of both limbs at 22 weeks and elevation of blood pressure without proteinuria. Anti-hypertensive medication Tablet Methyl-Dopa was instituted with titration of dose with the progression of gestation. The patient was advised to wear pneumatic compression TED stocking for the prevention of DVT. She was non-diabetic and non-asthmatic. At 36^w weeks, she complained of persistent less foetal movement for 2 days and after completion of steroid prophylaxis with foetal monitoring, she underwent LUCS with bilateral tubal ligation and delivered a healthy male child of 3.3 kg with good APGAR score. The child was free of any obvious anomaly. The patient had a normal post-operative convalescence with her operative area also healed nicely.

a. Dr. Asma Habib; FCPS
Assistant Professor, Department of Obstetrics and Gynecology,
Bangladesh Medical College and Hospital, Dhaka

b. Dr. A F M Saidur Rahman; FCPS
Resident Assistant Professor, Department of Medicine,
Bangladesh Medical College and Hospital, Dhaka

Correspondence to:

a. Dr. Asma Habib; FCPS
Assistant Professor, Department of Obstetrics and Gynecology,
Bangladesh Medical College and Hospital, Dhaka
Email: asma.imam2003@yahoo.com

The operative findings at LUCS: extremely dense adhesion between all the layers of the parietal wall upto the uterus. The patient was therefore advised to continue the Anti- TB medication for a total of 9 months. The child received BCG vaccination at birth. As the mother was Anti-TB therapy throughout the pregnancy and suffered from Extra-Pulmonary TB (umbilical port site and pelvic TB), INH prophylaxis for the baby was considered unnecessary.

Case 2:

A 28 year old Primigravida patient was detected to have repeated (2) episodes of urinary tract Infection with negative culture/sensitivity report at 14 weeks and 18 weeks. She did not respond to the empirical antibiotic therapy. With the high clinical suspicion of renal tuberculosis on the basis of repeated sterile pyuria, she was advised to have ALS (Antibody against Lymphocyte secretion) for TB by cell culture and ELISA performed at International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Mohakhali, Dhaka. The antibody titre was highly suggestive of TB. She was started on anti-TB therapy at 20 weeks and she responded within 2 weeks with negative urine R/M/E and C/S report. She completed the standard 9 months anti-TB regimen. The drug therapy was supplemented with Tab. Pyridoxine, folic acid and later with Vitamin K. The patient had a normal antenatal period and delivered a healthy female of 2.8 kg at term by LUCS for the indication of foetal distress. The child subsequently developed a hemangioma on the left sided chest wall which was treated conservatively.

Case 3:

A grossly emaciated 20 year old female was referred from the Out Patient Department of Medicine of Bangladesh Medical College Hospital with a history of vaginal delivery 21 days back. She was suffering from high grade fever, anorexia and chronic cough. She weighed 31 kg, Para 2 (normal vaginal delivery). Considering the degree of extreme emaciation, she was screened for Diabetes Mellitus, Tuberculosis, Hyperthyroidism and AIDS. All screened negative except for ALS for TB, which was highly suggested of TB with positive chest radiographic findings. She was started on Anti-tubercular medication with a diagnosis of disseminated Tuberculosis with primary Pulmonary Foci. After follow-up after 7 months, she had gained 10 kg weight. Her child was also healthy with normal growth parameters. She was advised to complete 9 months therapy with strict compliance.

Discussion:

Presentation and Prevalence:

It is generally believed that pregnancy does not influence the course of pulmonary or extra-pulmonary TB. But there are some reports of aggravation of the condition during pregnancy. In advanced countries when TB is diagnosed

early and treated, TB rarely influences the outcome of pregnancy. However, the same inference cannot be extrapolated for a vast majority of the population in developing countries where the burden of TB occurs and pregnant woman with TB often presents late for management. Moreover, in some countries, Multi drug resistant (MDR)/Extensively Drug resistant (XDR)-TB has been found to increasingly involve pregnant woman and this disease with or without concomitant HIV infection immensely complicates the management of cases. In developing and under-developed countries, prevalence of TB in pregnancy parallels its prevalence in the general population and kills more women of reproductive age than all the combined causes of maternal mortality.² Incidence of TB with pregnancy in certain ethnic groups in London has approached 1%.³ As regard to site, in two UK studies, 53% and 77% of pregnant women were reported to have extra-pulmonary TB similar to that reported in a Mexican study, though case control studies from India and USA both reported lower (9% and 13%, respectively) rates of extra-pulmonary disease.⁴

Early diagnosis of TB may be difficult when associated with pregnancy as it may mimic some of the physiological changes that occur during pregnancy, i.e. increased respiratory rate, fatigue, cough (74%), weight loss (41%), fever (30%).² Malaise and fatigue (80%) was found to be a common presenting manifestation of TB with pregnancy. Except for weight loss (which to some extent can be compensated by weight gain during pregnancy), none of the other symptoms can warn the caregiver that they may be dealing with associated TB.

Renal tuberculosis may manifest as pyrexia of unknown origin/ prolonged fever and perinephric abscess. Urinalysis and intravenous pyelography are suggested investigations for diagnosis. Intravenous pyelography is however contraindicated in pregnancy. Sterile pyuria is also a classic manifestation of renal tuberculosis with or without haematuria. Presence of extensive intra-abdominal adhesions presenting as sub-acute intestinal obstruction may result from intestinal tuberculosis. Active TB of spine can cause deformed pelvis, paraplegia and may be associated with delayed progression of labor due to loss of Ferguson reflex.⁵

Maternal complication rates with both pulmonary and extra pulmonary untreated TB are increased and include pregnancy- induced hypertension (8.6%), respiratory failure (5.8%) and oligohydramnios (2.9%). Relative risk of overall maternal complication was 3.1 and preterm labor was increased eightfold. Fetal growth retardation was noted in several studies. In the North Indian study, for cases with pulmonary TB, 20.2% of neonates were small for gestational age whereas among patients with non-lymph node extra pulmonary TB, 33% babies were of low birth weight. Overall incidence of perinatal mortality is high where TB has affected pregnancy. The rates were 10% in the North Indian study and 8.6% in the Mexican study.⁶

No maternal mortality was reported from different case studies, except one report from Papua New Guinea in which maternal deaths was attributed to pulmonary, meningeal and miliary TB. 45% of the children born were growth retarded and a perinatal mortality rate has been recorded at 137/1000 births. This study shows how the neglected TB with pregnancy can play havoc with both the mother and the newborn baby, whereas studies in developed and developing countries have shown that if the diagnosis is made early and adequate treatment given, there should not be much difference in the outcome of pregnancy with and without TB.⁷

Diagnostic Tools and Its Fallacy:

Early diagnosis of TB is crucial to prevent the spread of the disease in the community; as for management of Tuberculosis in a pregnant woman imparts graver significance with regard to maternal well-being and foetal outcome. However, the clinical and laboratory diagnosis, follow-up of the infection activity, and response to therapy are not always easy to evaluate. Although culture of bacteria is the reference standard in diagnosis and follow-up of disease, it can take up to 68 weeks to isolate *M. tuberculosis*. Moreover it is estimated that a false-negative culture result may be obtained for 10%–20% of TB cases.⁸

A rapid serological test for diagnosis, follow-up of disease activity, and response to therapy would be useful to clinicians. The purified protein derivative (PPD) skin test (Mantoux test) is an important tool for diagnosis of latent TB infection and disease in the developed world where BCG vaccination is not part of the routine immunization schedule, but it has low predictive value in bacilli Calmette-Guérin (BCG) vaccinated individuals, as well as in individuals living in areas where TB is endemic where tuberculin test more often confuses than contributes to the diagnosis. Early studies of Mantoux Test (MT test) during pregnancy have showed high false-negative skin tests, whereas later, more tightly controlled studies with adequate controls suggested that pregnancy may not measurably affect the response to TB skin test. The low predictive value is a result of cross-reactivity with BCG and atypical mycobacteria. Another important diagnostic tool is chest X-ray which is usually avoided during pregnancy.

The ALS (Antibodies from lymphocyte secretion) assay for TB method is an immunological assay in which TB-specific antibodies are secreted by peripheral blood mononuclear cells (PBMCs); B-lymphocytes or plasma cells in particular, and the antibody levels are measured by ELISA. It better reflects active disease than antibodies in serum. The sensitivity and specificity of the test was 93%, indicating that ALS that used BCG vaccine as an antigen would enable rapid detection of *M. tuberculosis* infection (within 45 days) in patients with active TB. Previous vaccination with BCG does not hamper the test for identification of TB; it could successfully differentiate between BCG-vaccinated and *M. tuberculosis* infected patients.

The positive predictive value of the test was 97%. However, it may be noted that the performance characteristic (positive predictive value) of the assay may vary on the basis of the prevalence of TB in the tested population. The basis of ALS test is that active TB would provide continuous antigen stimulation resulting in antibody-producing cells in circulation. In contrast, inactive TB might result in high antibody titers in serum, but would be less likely to stimulate antibody-producing cells in circulation. Because this method does not require a specimen taken from the site of disease, it also may be useful in diagnosis of extra-pulmonary/childhood TB.⁸

Port-site tuberculosis:

Port-site tuberculosis following laparoscopic surgery, as in our first case is rare with only isolated cases reported in literature.^{9,10} Laparoscopic instruments are the source of infections in most cases. All patients developed chronic discharging sinuses, similar to our first case. Proper sterilization of laparoscopic instruments is of utmost importance in prevention. Most widely used method to sterilize laparoscopic instruments is to immerse the instruments in 2% glutaraldehyde (GTA) for 20 minutes. Ten per cent glutaraldehyde solutions range in concentration from 2.4% to 2.6% and have variable maximum use lives. According to guidelines of ESGE (European Society of Gastrointestinal Endoscopy) and European Society of Gastrointestinal Endoscopy Nurses and Associates, Glutaraldehyde failed to eliminate all atypical mycobacterium using standard contact times. This is further complicated by the emergence of Glutaraldehyde resistant Mycobacterium; certain strains are resistant to even high GTA concentration (up to 7%) which proves that GTA is non-effective against specific rapidly growing mycobacteria and should be substituted by orthophthaldehyde (OPA) and peracetic acid (PA) based solutions for high level disinfection (HLD). But the efficacy and the properties of these new disinfectants need to be evaluated further. Instruments need to be pre-cleaned properly before immersing in GTA for disinfection. Instruments should be dismantled and all blood clots, tissues etc., should be removed under running water before sterilization. As, after washing, some amount of water goes into GTA solution, its concentration decreases, making it less efficient. It is imperative that solution should be regularly changed and instruments should be dried before immersion in GTA solution; although autoclave is the best method of sterilization.^{11,12}

Drugs and their side-effects:

The most significant toxic side effect of isoniazide in animal and human studies is demyelination (causing peripheral neuropathy). This can be prevented by supplementation with pyridoxine (vitamin B6). Hepatotoxicity may be more common in pregnancy and liver function test should be performed monthly during pregnancy. Most studies do not show a significant

elevation in the congenital anomaly rate above the background 2-3 per cent in uses of rifampicin in pregnancy.¹ Liver enzyme induction, with theoretical vitamin K deficiency, should prompt maternal oral Vitamin K supplementation in the third trimester to prevent haemorrhagic disease of the newborn (HDN). The theoretical risks of fetal ocular toxicity/ retrobulbar neuritis with ethambutol have not been borne out in practice. Although pyrazinamide is usually avoided in pregnancy, there are no data to suggest a harmful effect and it should be used if needed as a second line agent. Streptomycin has well-recognized fetal ototoxicity with safer alternatives now being available.

Compliance with antituberculosis drugs poses special problems during pregnancy because of concerns about potential teratogenic effects. Studies have confirmed the safety of isoniazide, rifampicin and ethambutol. Little is known about the fetal effects of pyrazinamide. In case of tuberculous meningitis, the administration of pyrazinamide because of its bactericidal effects and penetration of cerebrospinal fluid has found to have no adverse effects on the fetus in the published literatures. All the Anti-tuberculous drugs are compatible with breast-feeding.¹³

Presently, one of the greater concerns is the evolution and increased prevalence of drug-resistant TB across the globe. Resistance to two first-line drugs like Isoniazid (INH) and Rifampicin is called MDR-TB, and when in addition to these drugs, the disease is also resistant to Fluro-quinolone and second-line injectable drugs, the disease is called extended drug resistant TB (EDR-TB). Worldwide, 9.9% of the cultured bacteria are resistant to first-line drugs and 1.4% are MDR-TB. MDR-TB is now prevalent in Russia, South Africa and China. Smear-positive and culture-positive pulmonary TB in India is observed in 100-160/10⁵ population and 100-250/10⁵ population, respectively, and the proportion of new MDR-TB is also not insignificant at 0.5-5.3% in previously treated case. The problem of extensively drug-resistant TB (XDR-TB) is emerging very fast and is spreading all over the world including India.⁶ This is important with respect to TB with pregnancy where many of the second-line drugs are teratogenic and need to be prescribed with great caution and the outcome of the treatment with best of the regimens is suboptimal. Ethionamide, Proethionamide, and Cycloserine should not be used for pregnancy either because of lack of information or possible teratogenic effect.¹⁴

Provided the prescribed drugs have been taken properly, an active TB sufferer will become non-infectious within 2 weeks of commencing treatment. If the mother is still sputum positive, specialist infection control nursing will be necessary. The new born should be immunized with BCG and also given prophylactic antibiotics (usually isoniazide). Separation of the infant from its mother is not necessary unless she is non-compliant or another care

provider /family member is highly infectious. It would seem prudent to send the placenta for microbiological investigation. Evidence of Acid-fast bacilli should increase surveillance of the newborn.¹⁵

Conclusion:

Anti-tubercular drugs are hepatic enzyme-inducers and significantly reduce the contraceptive efficacy of oral contraceptive pills, making the client predisposed to conception. Following conception, due to ignorance or misconception that anti-TB drugs are teratogenic, early pregnancies are frequently being terminated. The first message that should be circulated is that standard anti-TB drug regimens have been found to produce no added risk of congenital anomaly than that of the general population. Secondly, the maternal and foetal outcome after institution of anti-TB drugs in diagnosed cases is found to be satisfactory.

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College News

Obituary:

- Chowdhury Sajjadul Karim Ph.D, former Hony. Secretary of BMSRI and former Advisor of Care Taker Govt. of Bangladesh, died on 20th November, 2015 from severe pneumonia.
- Meherun Nessa Khanam, Deputy Librarian, Library of BMC died on 24th November 2015 from thalassemia.

College Events:

The commencement ceremony of 1st year MBBS students (BM-30), session 2015-2016, was held on 9th January 2016 in the college premises of BMC. The occasion was graced by Mr. Mohammed Nasim MP, Hon'ble Minister, Ministry of Health & Family Welfare, Government of the People's Republic of Bangladesh as Chief Guest.

Seminar in BMC:

- Seminar on "Personality disorders and its various aspects" was held on 10th September 2015. Speaker was Prof. Mahmood Hasan, Head, Dept. of Psychiatry, BMC.
- Seminar on "Lung Cancer" was held on 26th November 2015 in BMC. Speaker was Dr. Zafor Md. Masud, Associate Professor and Head of the Dept. of Oncology, BMC.
- Celebration of "Breast Cancer Awareness Month" was held on 30th October 2015, organized by Oncology department of BMC.
- Celebration of "World Hospice Day" was held on 10th October, 2015 organized by Oncology department of BMC. A cycle rally was arranged in the campus of BMC on that occasion.

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

- Dr. Zafor Md. Masud, Associate Professor and Head of the Dept. of Oncology, BMC attended the ESMO Asia 2015 Congress held in Singapore from 18-21 December, 2015.
- Dr. Md. Tarek Alam, Associate Professor, Dept. of Medicine, BMC attended the 20th Congress of the Asian Pacific Society of Respiriology 2015 held at Kuala Lumpur, Malaysian from 3-6 December, 2015.
- Prof. Dr. Md. Fazlul Kadir, Professor, Dept. of Medicine, BMC, attended the World Diabetes Congress 2015 held from 30th November to 4th December, 2015 at Vancouver, Canada.
- Prof. Dr. Mahmood Hasan, Professor and Head of the

Dept. of Psychiatry, BMC attended the 40th Annual Conference of Indian Psychiatric Society North Zone held on 3-4 October, 2015 at Srinagar, Jammu and Kashmir, India.

- Dr. Akhil Chandra Biswas, Associate Professor, Dept. of ENT, BMC, attended the 17th Annual Conference of Skull Base Surgery Society of India from 8-11 October, 2015 at Bangalore, India.
- Prof. Dr. M. Touhidul Haque, Professor and Head of the Dept. of Cardiology, BMC, attended the 81st Asian Medical Center Interventional Cardiology Training Program (ACT Program) held at Seoul, Korea from 5-8 October, 2015.
- Prof. Md. Zahid Hassan Bhuiyan, Professor, Dept. of Urology, BMC, attended the 35th Congress of the Société Internationale D'Urologie held at Melbourne, Australia from 15-18 October, 2015.
- Prof. Dr. A.H.M. Shamsul Alam, Professor and Head of the Dept. of Surgery, BMC, attended the Conference of Hernia Society held at India from 10-12 September, 2015.
- Prof. Afreen Munim, Professor and Head of the Dept. of Physiology, BMC, attended the 13th Inter Medical School Physiology Quiz at Kuala Lumpur, Malaysia from 12-13 August, 2015.
- Dr. Kazi Salma Binte Faruky, Assistant Professor, Dept. of Physiology, BMC, attended the 13th Inter Medical School Physiology Quiz at Kuala Lumpur, Malaysia from 12-13 August 2015.
- Dr. Zafor Md. Masud, Associate Professor and Head of the Dept. of Oncology, BMC attended the 23rd Asia Pacific Cancer Conference 2015 held at Bali, Indonesia from 20-22 August, 2015.
- Prof. Md. Ashraful Islam, Professor and Head of the Dept. of ENT, BMC, attended the 68th AOICON 2016 held at Gurgaon, India from 28-31 January, 2016 as an esteemed faculty from Bangladesh.
- Prof. Dr. Mohammad Nurul Huq, Professor and Head of the Dept. of Paediatrics, BMC, attended the 15th Asia Pacific Congress of Pediatrics (APCP), 53rd Annual Conference of Indian Academy of Pediatrics (PEDICON) and 5th Asia Pacific Congress of Pediatrics Nursing (APCPN) held at Hyderabad, India from 21-24 January, 2016.

New promotion in BMC

Dr. Kazi Nazneen Sultana, Assistant Professor of Biochemistry, BMC