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## From the Desk of Editor-in-Chief

We are delighted to inform that the Volume 9, Number 1 of the Dhaka Central International Medical College Journal (DCIMCJ) is going to be published very soon. In this issue we have added a new section, Medical Quiz: Images. We are grateful to Almighty Allah. We are sending the complimentary copies of the journal to the libraries of most of the medical college and other medical institutions in Bangladesh. Already our journal has been approved by Bangladesh Medical & Dental Council (BMDC). We invite the doctors of medical colleges and institutes to submit their research articles to the journal committee for publication. We accept both hard & soft copies of the articles. We go through the papers and if necessary, communicate the authors. We also thank all the authors for giving us opportunity to publish their research papers in this journal. We have tried our best to avoid erroneous information. We like to add here that DCIMC Journal and its editorial board accept no liability for any inaccurate and misleading information, opinion and statements. It is the responsibility of the individual author (s). We have mentioned the instruction for the authors in this issue. We request the contributing authors to follow the instructions for their manuscripts. We appreciate our chairman, editors, members and advisors for their encouragement and also appreciate the contributors and reviewers for their participation. Last of all we welcome valuable suggestion, opinion, advice and constructive criticisms for improvement of the quality of the journal.



**Prof. Bidhu Bhushan Das**

Editor-in- Chief

## INFORMATION FOR AUTHORS

### Manuscript preparation and submission:

#### Guidelines for the Authors:

The Dhaka Central International Medical College Journal provides publication (six monthly) of articles in all areas of the subject. The Journal welcomes the submission of manuscript that meets the general criteria of significance and scientific excellence.

Papers must be submitted with the understanding that they have not been published elsewhere (except in the form of an abstract or as part of a published lecture, review, or thesis) and are not currently under consideration by another journal published by **INTERNATIONAL RESEARCH JOURNALS** or any other publisher.

The submitting (corresponding) author is responsible for ensuring that article's publication has been signed and approved by all the other co-authors. It is also the author's responsibility to ensure that the articles emanating from a particular institution are submitted with the approval of the necessary institutional requirement. Only an acknowledgment from the editorial office officially establishes the date of receipt. Further correspondence and proofs will be sent to the corresponding author(s) before publication unless otherwise indicated. It is a condition for submission of a paper that the authors permit editing of the paper for readability. All enquiries concerning the publication of accepted papers should be addressed to –

Editor-in-Chief,  
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**Electronic submission** of manuscripts is strongly encouraged, provided that the text, tables, and figures are included in a single Microsoft Word file (preferably in Arial font).

**Submit Manuscripts** as e-mail attachment to the editorial office at: [jdcimc@yahoo.com](mailto:jdcimc@yahoo.com)

A manuscript number will be mailed to the corresponding author within two working days. The cover letter should include the corresponding author's full address and telephone / fax numbers and should be in an e-mail message sent to the editor, with the file, whose name should begin with the first author's surname attachments or triplicate Hard copy with a soft copy.

#### Article types:

Five types of manuscripts may be submitted:

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It will be preferably written invited only and usually covers a single topic of contemporary interest.

#### Original articles:

These should describe new and carefully confirmed findings, and experimental procedures should be given in sufficient detail for others to verify the work. The length of a full paper should be the minimum required to describe and interpret the work clearly.

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Submissions of reviews and perspectives covering topics of current interest are welcome and encouraged. Reviews should be up to date. Reviews are also peer-reviewed.

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This should cover uncommon and /or interesting cases with appropriate confirmation process.

## Review process:

All manuscripts are initially screened by editor and sent to selective reviewer. Decisions will be made as rapidly as possible, and the journal strives to return reviewers comments to authors within 3 week. The editorial board will re-review manuscripts that are accepted pending revision. The DCIMCJ editorial board will try to publish the manuscript as early as possible fulfilling all the rigorous journal needs.

## I. A. Preparing manuscript for submission to DCIMCJ

Editors and reviewers spend many hours reading manuscripts that are easy to read and edit. Much of the information in this journal's Instructions to Authors is designed to accomplish that goal in ways that meet each journal's particular editorial needs. The following information provides guidance in preparing manuscripts for this journal.

### Condition for submission of manuscripts:

- All manuscripts are subject to peer-review.
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Information provided in the manuscript is important and likely to be of interest to an international readership.

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1. Manuscript should be written in English and typed on one side of A4 (29 x 21cm) size white paper.
2. Margin should be 5 cm for the header and 2.5 cm for the remainder.
3. Style should be that of modified Vancouver.
4. Each of the following section should begin separate page:
  - Title page
  - Summary/abstract
  - Text
  - Acknowledgement
  - References
  - Tables and legends

Page should be numbered consecutively at the upper right hand corner of each page beginning from the title page

### I. A. 1.a. General Principles:

- The text of observational and experimental articles is usually (but not necessarily) divided into the following section: Introduction, Methods, Results, and Discussion. This so-called "IMRAD" structure is a direct reflection of the process of scientific discovery.

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- Authors need to work closely with editors in developing or using such new publication formats and should submit supplementary electronic material for peer review.
- Double-spacing all portions of the manuscript-including the title page, abstract, text, acknowledgments, references, individual tables, and legends- and generous margins make it possible for editors and reviewers to edit the textline by line and add comments and queries directly on the paper copy.
- If manuscripts are submitted electronically, the files should be double-spaced to facilitate reviewing and editing.
- Authors should number on right upper corner of all of the pages of the manuscript consecutively, beginning with the title page, to facilitate the editorial process.

#### **I. A.1.b. Reporting guidelines for specific study designs:**

Research reports frequently omit important information. Reporting guidelines have been developed for a number of study designs that DCIMC journals ask authors to follow. Authors should consult the information for Authors of this journal. The general requirements listed in the next section relate to reporting essential elements for all study designs. Authors are encouraged also to consult reporting guidelines relevant to their specific research design. A good source of reporting guidelines in the EQUATOR network (<http://www.equator-network.org/home/>) or CONSORT network (<http://www.consort-statement.org>).

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1. Article title. Concise title is easier to read than long, convoluted ones. Titles that are too short may, however, lack important information, such as study design (which is particularly important in identifying type of trials). Authors should include all information in the title that will make electronic retrieval of the article both sensitive and specific.
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- Structured abstracts are essential for original research and systematic reviews. Structured abstract means introduction, methods, results and conclusion in abstract
- Should be limited to 250 words
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- Both the main and secondary objectives should be clear.
- Provide only directly pertinent primary references, and do not include data or conclusions from the work being reported.

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- References should be numbered consecutively in the order in which they are first mentioned in the text.
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- If a paper version of the manuscript is submitted, it should contain print copies of tables and figures; they are all needed for peer review and editing, and the editorial office staff cannot be expected to make the required copies.
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As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

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2. Authorship and conflicts of interest form
3. Manuscript
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**General outline for article presentation and format:**

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- ▲ Font size should be 12 in arial
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- ▲ Title page contains all the desired information (vide supra)
- ▲ Running title provided (not more than 40 characters)
- ▲ Headings in title case (not ALL CAPITALS, not underline)
- ▲ References cited in superscript in the text without brackets after with/without comma (,) or full stop (.)
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**Tables and figures:**

- ▲ No repetition of data in tables/graphs and in text
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  - ▲ Mention conflict or interest if any
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  - ▲ Do not use subheadings in the abstract
  - ▲ Give full title of the manuscript in the Abstract page
  - ▲ Not more than 200 words for case reports and 250 words for original articles
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  - ▲ Key words provided – arrange them in alphabetical order (three – five)
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  - ▲ Word limit 150-200 words
  - ▲ Pertinent information only

- **Material and methods:**
    - ^ Study Design
    - ^ Duration and place of study
    - ^ Ethical consent
    - ^ Patient consent
    - ^ Statistical analysis and software used.
  - **Result:**
    - ^ Clearly present the data
    - ^ Avoid data redundancy
    - ^ Use table information at the end of the sentence before full stop between the small bracket
  - **Discussion:**
    - ^ Avoid unnecessary explanation of someone else work unless it is very relevant to the study
    - ^ Provide and discuss with literatures to support the study
    - ^ Mention about limitation of your study
  - **Conclusion:**
    - ^ Give your conclusion
    - ^ Any recommendation
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    - ^ Acknowledge any person or institute who have helped for the study
  - **Reference:**
    - ^ Abide by the Vancouver style
    - ^ Use reference at the end of the sentence after the full stop with superscript
  - **Legends:**
    - ^ Table
    - ^ Figures
- The editor reserves the right to style and if necessary, shorten the material accepted for publication and to determine the priority and time of publication
-

## Dengue Fever and Social Awareness

Begum R<sup>1</sup>, Karim S<sup>2</sup>

### Introduction:

Dengue fever is an infectious disease that is transmitted through an intermediate vector of mosquitoes, namely the female *Aedes* mosquito. This mosquito also transmits Chikungunya, Zika and Yellow fever viruses. It has become a seasonal disease in many tropical countries, one of which is Bangladesh and continues to attract the attention of policymakers every year. Dengue which is mostly found shortly after rainy season. This disease has shown the increasing tendency to some part of Southeast Asia. An enormous outbreak of dengue took place in Bangladesh in 2000 and the situation was quite alarming.

Dengue virus is a single stranded positive polarity RNA virus, belongs to the family Flaviviridae. It is transmitted through the bite of an infected female mosquito of *Aedes* species - mainly the species *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*. There are 4 distinct, but closely related, serotypes of the virus (DEN-1, DEN-2, DEN-3 and DEN-4). Recovery from infection by one serotype provides heterotypic or cross-immunity to the other serotypes. This is only partial and temporary, lasts only a few months, but homo type immunity is lifelong. For this reason, a person can be infected with a dengue virus as many as four times in his or her lifetime. Subsequent infections (secondary infection) by other serotypes increase the risk of developing severe dengue. The fifth variant DENV-5 has been isolated in October 2013. DENV-5 has been detected during screening of viral samples taken from a 37 year old farmer admitted in a hospital in Sarawak state of Malaysia in the year 2007.

### Situation in Bangladesh:

Dengue is the most common mosquito-based viral disease in developing countries like Bangladesh. Each year the rate of infection and mortality rate is increasing. Dengue infection was first reported in Bangladesh in 1964, but it was not considered a public health concern at that time. After 2000, dengue started to spread out rapidly and become an epidemic. Among the Southeast Asian states, Bangladesh had a lower dengue prevalence, but in recent years the scenario has changed. In 2000, dengue attacked 5,551 individuals and the number of deaths was 93. Since 2003, the death rate has declined gradually, with zero fatalities in subsequent couple of years, but a devastating turn with 10,148 cases and 26 deaths in 2018. In 2019, during January to July, number total cases were 18,484, with 57 deaths.

In 2017, the number of infectious cases was 2769 and it jumped to 10148 cases in 2018. In 2019, the Directorate General of Health Services (DGHS) (9) recorded 87953 cases with 81 deaths, a 9- fold expansion in the occurrence rate of dengue from the previous year (6, 8, 20, 21). After analyzing previous studies, it can be stated that the number of dengue cases and deaths are highest in the warmer months from July to November. Bangladesh has been experiencing episodes of dengue fever in every year since 2000. All four serotypes have been detected, with DENV-3 predominance until 2002. After that, no DENV-3 or DENV-4 was reported from Bangladesh. During 2013-2016, DEN2 was predominant followed by DEN-1 in circulation. Institute of Epidemiology, Disease Control Research (IEDCR) predicted that as the serotypes DENV-3 and DENV-4 are in circulation in the neighbouring countries, they may create epidemics of secondary & dengue in the near future in Bangladesh.

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In 2017, reemergence of DENV-3 was identified; subsequently there was a sharp rise in dengue cases from the beginning of the monsoon season in 2018.

### **Fact about dengue vaccine:**

The first licensed dengue vaccine, CYD-TDV (Dengvaxia®), has received regulatory approval in a number of countries. However, this vaccine has some limitations. Its efficacy against DENV2 was consistently lower than other serotypes. Protective efficacy also depended on prior dengue sero-status of the vaccinees. Lower efficacy was observed in children with < 9 years old and dengue-naïve individuals. More importantly, risk of hospitalization and severe dengue was increased in the youngest vaccine recipients (2-5 years) compared to controls. Thus, the quest of a better vaccine candidate continues. There are two live-attenuated vaccine candidates currently testing in phase III trial including DENVax, developed by US CDC and Inviragen (now licensed to Takeda) and TV003/TV005, constructed by US NIAID. In addition, there are several Phase I–II as well as preclinical phase studies evaluating vaccines for safety and immunogenicity, this include other live-attenuated platform/strategy, purified-inactivated viruses formulated with adjuvants, DNA vaccine, subunit vaccine, viral vector and also heterologous prime/boost strategies. The major difficulties of dengue vaccine development are included the lack of the best animal model, various immune status of individual especially in endemic areas and clear cut off of protective immunity.

### **Prevention:**

The incidence and transmission of dengue is influenced by a variety of factors such as uncontrolled population growth, urbanization, deterioration in waste management systems and lack of effective vector control. Due to inadequate water supply, water storage practice is also regarded as a major contributor to dengue epidemics. Moreover, illiteracy, poverty and social inequalities have been associated with poor dengue management. Prevention and control of dengue in Bangladesh, is not a sole responsibility for any single ministry and or its agencies.

It needs effective and timely coordination, collaboration and partnership, among all the concerned ministries and their agencies, led by the Ministry of Health and Family Welfare. Furthermore, strengthening of the existing efforts including capacity building and resource mobilization, and integrated surveillance, sustainable vector control, **optimum and active community participation**, and adequate monitoring and periodic evaluation throughout the year across the country, considering it an endemic disease, are strongly recommended.

Bangladesh is experiencing an increase in dengue outbreaks, especially in the urban areas. Over the past few decades, the prevalence of dengue is increasing globally due to urbanization, population growth, climate change, and other surrounding factors. Thus, it is very much essential for urban people to have sound knowledge regarding the treatment and prevention of dengue fever. Since no effective vaccine is currently available to prevent dengue, the only possible mode of prevention is vector control. Perception of dengue disease risk was much lower, while knowledge of dengue disease among community members has generally been high. Community participation is essential at the ground level. The successful participation largely depends on peoples' knowledge, awareness and attitude towards this disease. Effective dengue prevention and control is an important concern today in Bangladesh. At present, the main method to control or prevent the transmission of dengue virus is to combat the mosquito vectors. This is achieved through:

#### ➤ **Prevention of mosquito breeding:**

- Preventing mosquitoes from accessing egg-laying habitats by environmental management and modification.
- Disposing of solid waste properly and removing artificial man-made habitats that can hold water.
- Covering, emptying and cleaning of domestic water storage containers on a weekly basis.
- Applying appropriate insecticides to water storage outdoor containers;



- **Personal protection from mosquito bites:**
  - Using of personal household protection measures, such as window screens, repellents, coils and vaporizers. These measures must be observed during the day both inside and outside of the home (e.g.: at work/school) because the primary mosquito vectors bites throughout the day;
  - Wearing clothing that minimises skin exposure to mosquitoes is advised;
- **Community engagement:**
  - Educating the community on the risks of mosquito-borne diseases;
  - Engaging with the community to improve participation and mobilization for sustained vector control;
- **Active mosquito and virus surveillance:**
  - Active monitoring and surveillance of vector abundance and species composition should be carried out to determine effectiveness of control interventions;
  - Prospectively monitor prevalence of virus in the mosquito population, with active screening of sentinel mosquito collections;
  - Vector surveillance can be combined with clinical and environment surveillance.

### Conclusion:

It is recommended that public health education on dengue should be emphasized for successful dengue control program [47]. Effective education programs, public health campaigns by local NGOs and the Ministry of health should be performed especially in rural and densely populated area specifically about dengue transmission, *Aedes* mosquitoes breeding sites, early dengue diagnosis and treatment procedure. Adequate health personnel should be provided by the Ministry of health and trained them to give appropriate counselling in an effort to bring about behavioural changes among the population for promoting prevention practice of dengue.

Practical, family-oriented and community-based health education movement should be tailored to discourage negative community practices like indiscriminate refuse disposal and deficiency of drain maintenance and inspire healthy family practices that mitigate the risk of spreading of dengue. Government should take proper steps to minimize the ratio of *Aedes aegypti* mosquitoes so that the transmission of dengue viral infections can be reduced. Moreover, continuous education and monitoring should be done to ensure long-term behavioral changes towards successful dengue prevention.

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## Seroprevalence of Hepatitis B among Patients Admitted in Medicine Ward of Shaheed Monsur Ali Medical College Hospital – A Cross Sectional Observational Study

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### Abstract:

**Objective:** To determine the HBsAg status among the hospitalized patients in the department of medicine of Shaheed Monsur Ali Medical College Hospital (SMAMCH), Uttara, Dhaka. **Materials and Methods:** A cross sectional observational study was done in the department of medicine of SMAMCH, Uttara, Dhaka, from August 2012 to February 2013. One-hundred and seventy-five patients were selected from the medicine inpatient department of this hospital by systematic random sampling. HBs Ag test was performed by ELISA method. **Results:** Out of 175 patients, 77 were female and 98 were male. It was found that 14(8%) patients were HBsAg positive. Of the HBsAg positive patients, 9(9.18%) were male and 5 (6.49%) were female. Among the positive cases, 3 patients had liver disease, 2 patients had CKD & haematological disorder, 9 patients had other diseases. The positive cases had risk factors such as history of blood transfusion, I.V drug abuse, unprotected sex and unprotected shaving. There were greater percentages of HBsAg positive cases among the advanced age group, male sex, illiterate and married persons. **Conclusions:** High prevalence (8%) of HBsAg suggest that health personnel should use protective measure before any major or minor invasive procedure.

**Keywords:** Hepatitis B virus, prevalence, risk factors, hospitalized patients.

### Background:

Hepatotropic viruses cause most cases of hepatitis worldwide. Hepatitis B virus (HBV), a member of Hepadnaviridae family, is one of these viruses which causes severe liver disease, such as hepatocellular carcinoma (HCC) and life-threatening liver disease<sup>1</sup>. Hepatitis remains one of the most dominant public health problems these days. Hepatitis B virus infection is the critical cause of diseases and death worldwide<sup>2,3</sup>.

Hepatitis B virus infection is limited to the liver cells of humans and causes cirrhosis and HCC. This infection is still accounting for a significant proportion of morbidity and mortality. Globally, 2

billion people are infected with HBV, 350 million people are estimated to be chronically infected, and 50 million people are newly infected with hepatitis B every year<sup>4,5,6</sup>. The prevalence of chronic HBV infection is variable throughout the world, ranging from <1% in areas of low endemicity to over 30% in highly endemic areas. Africa has the second largest number of chronic carriers of HBsAg (>8%) next to Asia, which is considered a region of high endemicity<sup>5,7,8</sup>. Ethiopia, being part of this region, is ranked as an area with medium to high endemicity for HBV infection<sup>9,10</sup>. Worldwide, HBV infection is estimated to be the cause of 50% of reported cases of cirrhosis and 30% of liver cancer, and over 500,000 people die from them each year.<sup>11</sup> Cirrhosis, liver failure, and hepatocellular carcinoma develop in 15–40% of chronically HBV infected individuals<sup>2,12</sup>.

Africa has the second largest number of chronic carriers of HBsAg (>8%) next to Asia, which is considered a region of high endemicity<sup>5,7,8</sup>.

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Ethiopia, being part of this region, is ranked as an area with medium to high endemicity for HBV infection<sup>9,10</sup>. Worldwide, HBV infection is estimated to be the cause of 50% of reported cases of cirrhosis and 30% of liver cancer, and over 500,000 people die from them each year<sup>11</sup>. Cirrhosis, liver failure, and hepatocellular carcinoma develop in 15–40% of chronically HBV infected individuals<sup>2,12</sup>.

In highly endemic settings, perinatal, and horizontal (exposure to chronically infected household members) routes are responsible for most disease transmission<sup>13</sup>. But in low prevalence countries, the Hepatitis B virus is transmitted parenterally<sup>14</sup>. Adults infected with HBV usually develop acute hepatitis and recover. Infected children rarely develop the acute disease, but 25 to 90% become chronic carriers<sup>15</sup>. Infection with HBV is highest among developing countries. Ethiopia is among the high burden countries for HBV infection, 7.4% in the general population<sup>16</sup>. Therefore, this study aimed to determine the seroprevalence of HBV in the hospitalized patients in a tertiary level hospital to fill the existing epidemiologic gap in the area.

### Methodology:

This was a cross sectional observational study, carried out in the inpatient department of Shaheed Monsur Ali Medical College Hospital (SMAMCH) from August 2012 to February 2013 for a total of 6 months. Total 175 patients were selected by systematic random sampling method from the Medicine inpatient department of SMAMCH. After obtaining informed written consent from patient and/or attendant, data was obtained by taking history, performing relevant physical examination and checking the medical documents. Two cc blood was obtained from the patient and sent to the laboratory for checking HBsAg status. ELISA (Enzyme linked immunosorbent assay) method was used for detection of HBsAg. Data was collected using a preformed data collection sheet. Ethical clearance was taken from the institutional review board of the hospital.

All data were checked and put into the computer and were analyzed with the help of software programme SPSS v 12.0.

### Results:

A total of 175 admitted patients in the medicine department of SMAMCH were interviewed and examined clinically and subsequently their blood were sent to the laboratory with a view to assess the HbsAg status. Out of 175 patients, 77 were female and 98 were male. It was found that 14(8%) patients were HBsAg positive. Of the HBsAg positive patients, 9(9.18%) were male and 5(6.49%) were female. Among the positive cases, 3 patients had liver disease, 2 patients had CKD & haematological disorder, 9 patients had other diseases. The positive cases had risk factors such as history of blood transfusion, I.V drug abuse, unprotected sex and unprotected shaving. There were greater percentages of HBsAg positive cases among the advanced age group, male sex, illiterate and married persons.

**Table 1: Distribution of the patients by HbsAg status (N=175)**

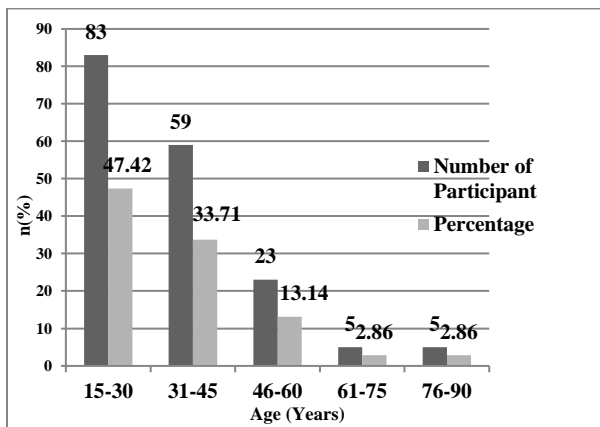
HBsAg test	No. of the patients	Percentage (%)
Positive	14	8%
Negative	161	92%
Total	175	100%

Table 1 shows that out of 175 patients 14(8%) were found HBsAg positive and 161(92%) were negative. The HBsAg status among the patients was the only dependable variable of this dissertation. In the following pages table of independent variable had been shown. Each table was followed by a cross tabulation of the same independent and dependent variables. Necessary statistical test had also been shown to find out the strength of association.

**Table 2: Distribution of the patients by their disease type and HBsAg status (N=175)**

Disease type	HBsAg status		n(%)
	Positive n(%)	Negative n(%)	
Liver disease	3(75%)	1(25%)	4(100%)
Blood disease, CRF, Malignancy	2(20%)	8(80%)	10(100%)
Others disease	9(5.59%)	152(94.4%)	161(100%)

For the analytical purpose the distribution of the disease type among the patients did not followed any standard disease classification. It was done according to the chance of exposure to hepatitis B virus during the course of the disease or during their treatment. Table-2 shows that higher percentage (75%) of the patients who were HbsAg positive had liver disease, while lower percentage (5.59%) were found as HbsAg positive who had others disease.



**Figure-1: Distribution of the study participants by age (N=175)**

Figure-1 shows that the highest percentage (47.42%) of the participants were in age group between (15-30) years followed by 33.714% in (31-45) years.

**Table 3: Distribution of the participants by age and HbsAg status (N=175)**

Age in years (Age group)	HbsAg status		n (%)
	Positive n%	Negative n%	
<45	7(4.92%)	135(95.07%)	142(100%)
>45	7(21.21%)	26(78.78%)	33(100%)
Total	14	161	175

Table 3 shows that the higher percentage (21.21%) of the participants who were HbsAg positive and they were above 45 years of age. While the lower percentage (4.92%) were found as HbsAg positive who were below 45 years of age.

**Table 4: Distribution of the patients by sex and HBsAg status (N=175)**

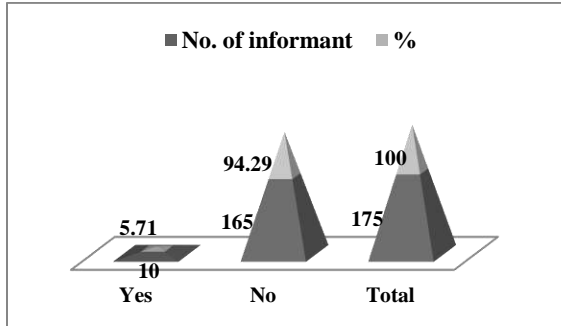
Age in years (Age group)	HBsAg status		n(%)
	Positive no (%)	Negative no(%)	
Male	9(9.18%)	89(90.81%)	98(100)
Female	5(6.49%)	72(93.5%)	77(100)
total	14	161	175

Table 4 shows that higher percentage (9.18%) of the patients were HBsAg positive in male , while lower percentage(6.49%) were found HBsAg positive in female.

**Table 5: Distribution of the patients by literacy and HBsAg status (N=175)**

Literacy of the patients	HBsAg status		n(%)
	Positive no (%)	Negative no(%)	
Literate	11(6.43%)	160(93.57%)	171(100)
Illiterate	3(75%)	1(25%)	4(100)
Total	14	161	175

Table 5: Shows that higher percentage (75%) of the patients were HBsAg positive in illiterate. While lower percentage (6.43%) of the patients were HBsAg positive in literate.



**Figure 2: Distribution of the patients by history of blood or blood product transfusion (N=175)**

Figure 2 shows that among the patients, minority (5.71%) had history of blood or blood product transfusion whereas the majority (94.29%) had no history of transfusion.

**Table 6: Distribution of the patients by history of blood or blood product transfusion and HBsAg status (N=175)**

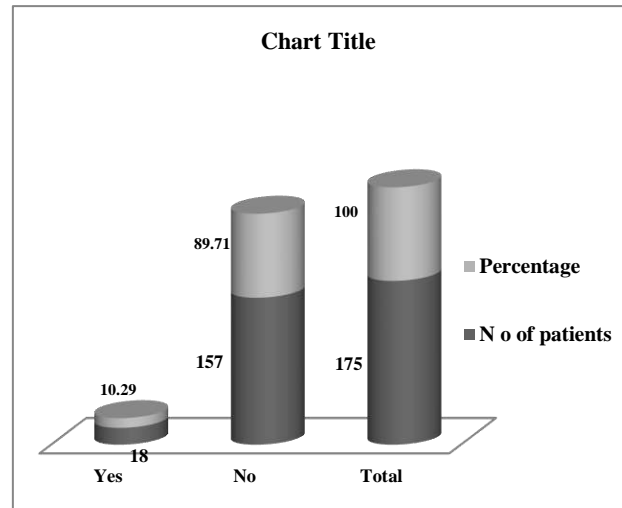
History of blood or blood product transfusion	HBsAg status		n (%)
	Positive no (%)	Negative no (%)	
Yes	3(30%)	7(70%)	10(100)
No	11(6.67%)	154(93.33%)	165(100)
Total	14	161	175

Table 6 shows that majority (30%) of the patients were HbsAg positive who had history of blood or blood product transfusion. while the minority (6.67%) of the patients were found HbsAg positive, had no history of blood or blood product transfusion in past.

**Table 7: Distribution of the patients by I,V/I,M drug abuse and HbsAg status (N=175).**

History of I.V/I.M drug abuse	HBsAg status		n(%)
	Positive no(%)	Negative no(%)	
Yes	1(50%)	1(50%)	2(100)
No	13(7.51%)	160(92.49%)	173(100)
Total	14	161	175

Table 7 shows that majority (50%) of the patients were HBsAg positive, who had history of parenteral drug abuse while minority (7.51%) of the patients were HBsAg positive, who had no history of drug abuse.



**Figure 3: Distribution of the patients by history of sexual exposure (N=175)**

Figure 3 shows that majority (89.71%) of the patients had no history of sexual exposure, while minority (10.29%) of the patients had history of sexual exposure.

**Table 8: Distribution of the patients by sexual exposure and HBsAg status (N=175)**

History of sexual exposure	HBsAg status		n(%)
	Positive no (%)	Negative no(%)	
Yes	5(27.78%)	13(72.22%)	18(100%)
No	9(5.73%)	148(94.27%)	157(100%)
Total	14	161	175

Table 8 shows that majority (27.78%) of the patients were HBsAg positive, who had history of sexual exposure.

**Table 9: Distribution of the patients by HBsAg status and unprotected shaving (N=175)**

Unprotected shaving	HBsAg status		n(%)
	Positive no(%)	Negative no(%)	
Yes	2(28.57%)	5(71.23%)	7(100)
No	12(7.14%)	156(92.86%)	168(100)
Total	14	161	175

Table 9 shows that majority (28.57%) of HBsAg positive patients had history of unprotected shaving.

### Discussion:

The major objective of the study was to determine the HBsAg status among the admitted patients in the medicine ward of SMAMCH. All this findings are discussed below. This findings were also compared to findings of other researchers.

In this study it was seen that among 175 admitted patients in the Medicine Department of SMAMCH, 14 (8%) were HBsAg positive which was almost similar to the study carried out by Ahmed et al, who found the frequency of HBsAg positive case among the hospitalized patient to be 9-12%<sup>17</sup>.

The SMAMCH is a payable hospital for the economically solvent group of people. So the present figure represent the HBsAg status of economically solvent group of people. This group of people definitely had higher education and awareness and purchasing capacity regarding health care than the other people of the country and hence there is a chance of higher rate of HBsAg positive cases in the government hospitals where both middle class and poorer people receive their health services. This can be confirmed by further study.

The 8% of HBsAg positive cases do not indicate the true figure of hepatitis B virus infection. It is known that 90% cases of hepatitis B virus infection are self limiting. So we can assume hepatitis B virus infection in Bangladesh is much higher than the present figure. But this should be confirmed by further prospective studies. Among the patients of liver disease, the HBsAg positive cases were highest (75%). The number of patients of liver disease were already known as a case of chronic HBV infection or suffering from its complication included in this group. There was another group of patients classed as high-risk group because they had chance of acquiring hepatitis B virus infection during their risky procedure of investigation or treatment which may infect them by HBV, as for example CRF, malignancies, ITP& leukaemia. In rest of the patients only 5.59% were HBsAg positive. This last group of patients had no significant history that might be contributed to HBV infection. It is evident that the age group less than 45 years had lower percentage (4.92%) of HBsAg positive and age group above 45 years had higher percentage (21.21%) of HBsAg positive cases. The male patients were 9.18% and female were 6.49% of HBsAg positive. It was found that HBsAg positive cases were higher (75%) among the illerate people than the literate who were 6.43% of HBsAg positive. This finding indicates that literacy might have positive impact on awareness of hepatitis B infection prevention. Those who had received blood or blood product were more HBsAg positive (30%) than those who had not received and HBsAg positive in 6.67% of cases, which was statistically highly significant.

The HBsAg positive cases were 50% among those who were parenteral drug abusers and 7.51% in non-abusers. This increased rate may be due to the shared needle or use of infected needle. The HBsAg positive case were more 28.51% among the patients who had history of unprotected shaving and was less (7.14%) who had not.

### Conclusion:

The study concluded that the prevalence of HBV was 8% among the hospitalized patients in the department of medicine of Shaheed Monsur Ali Medical College Hospital. The major risk factors were unprotected shaving, unlawful sex and had a history of blood or blood product transfusion. The prevalence of this study may not represent the prevalence of other government hospitals, because Shaheed Monsur Ali Medical College Hospital is a payable hospital and situated in a area of Dhaka where economically solvent group of people are living. The study had some limitation such as, only a few poor illiterate patients were included in this study which can be done by future study in government hospital. High prevalence (8%) of HBV suggest that health personel should use protective measure before any major or minor invasive procedure.

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## Comparative Study of Outcome of Labour in Vaginal Delivery Versus Lower Segment Caesarean Section in Eclampsia

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### Abstract:

Eclampsia is uniquely a disease of pregnancy. It is recognized that termination of pregnancy is the only definitive treatment of eclampsia. This study was done to compare the outcome of labour in vaginal delivery with lower segment caesarean section in eclampsia. This prospective cross-sectional comparative study was carried out in eclampsia department of Obstetrics and Gynaecology in Dhaka Medical College Hospital from January 2019 to June 2019. It was carried out on the antepartum and intrapartum eclamptic patients in eclampsia ward in DMCH with fulfillment of inclusion criteria and excluding the exclusion criteria during the study period (n=106). All the relevant data was recorded from admission upto discharge. Total 47 (44.33%) eclamptic patients out of 106 cases were delivered vaginally and the number of caesarean section was 59 (55.666%). Maternal mortality rate was 3.77% (4 cases), same number of patients died in each group. Perinatal mortality was 19.81%, no significant differences were found regarding perinatal outcome between these two groups. There was no significant difference between maternal and foetal outcome whatever may be the mode of delivery if the cases were judiciously selected.

**Keywords:** Eclampsia, Vaginal delivery, Lower segment caesarean section

### Introduction:

Over 300,000 women die in each year due to pregnancy related causes and most of those deaths occur in developing countries<sup>1</sup>. Eclampsia is a multisystem disorder of unknown aetiology and one of the leading causes of high maternal and perinatal morbidity and mortality during pregnancy<sup>2</sup>. Worldwide approximately 63000 maternal deaths occur annually due to eclampsia and preeclampsia<sup>3</sup>. In developed countries, the maternal death rate is reportedly 0-1.8%<sup>4</sup>.

The rate is higher in developing countries<sup>5</sup>. Poor socioeconomic condition, illiteracy, neglected antenatal care and lack of proper management of preeclampsia in time probably the causes of increase incidence of eclampsia in developing countries<sup>6</sup>. In Bangladesh current MMR is 172/100,000 live births<sup>7</sup>. Eclampsia accounts for 24% of maternal death in Bangladesh<sup>8</sup>.

Among the referral hospitals in Bangladesh, Dhaka Medical College Hospital is dealing with the highest number of eclampsia patients<sup>9</sup>. The definite treatment of eclampsia is termination of pregnancy<sup>10</sup>. In recent years, there has been a great tendency to use caesarean section more freely. But after the introduction of MgSO<sub>4</sub> as an anticonvulsant agent most of the patients remain convulsion free for several hours<sup>12</sup>. In this situation if there is no other obstetric indications for caesarean section, if the pelvis is adequate and

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foetal lie, presentation are favourable, foetus not in distress, labour may be induced or augmented. If the labour progresses well then vaginal delivery can be allowed. If the delivery can be done vaginally operative complications can be avoided. This study will be designed to find out whether outcome of labour (maternal and foetal) varies with routes of delivery.

### Materials and methods:

It is a prospective comparative study. This study was conducted in the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital from January 2019 to June 2019 on the antepartum and intrapartum eclamptic patients in eclampsia ward with fulfilment of inclusion criteria and having no exclusion criteria (n=106). Inclusion Criteria: 1. Eclampsia with gestational age more than 36 weeks. 2. Singleton pregnancy. 3. Cephalic presentation. 4. Foetal heart sound present. Exclusion Criteria: 1. Eclampsia with gestational age less than 36 weeks. 2. Eclampsia with renal failure, coagulation failure, liver diseases, HELLP Syndrome and acute pulmonary oedema. Detail history was taken, physical examination was performed and necessary, available investigations were done. Patients were treated by injection Magnesium Sulphate for controlling convulsion, injection Hydralazine for controlling hypertension. Vital functions, fluid intake-output and reflexes were checked every 30 minutes intervals. For obstetric management, antepartum and intrapartum patients were separated. In intrapartum patients, when there was no foetal distress, pelvis was adequate, foetal lie, presentation was favourable and no other obstetric indications for caesarean section were present, artificial rupture of membrane was done if it was intact and intravenous oxytocin was used for augmentation when it was necessary. But when there was foetal distress or any other obstetric indication for caesarean section (e.g. cephalopelvic disproportion, obstructed labour, unsatisfactory progress of labour, failed induction of labour etc) was present caesarean section was done.

In case of antepartum patients, if cervical score was favourable, pelvis was adequate and no other obstetric indications for caesarean section was present, induction of labour was done. But if cervix was not favourable or any obstetric indications for caesarean section, patient was selected for caesarean section. Patient who was induced or augmented was monitored strictly by partograph. If the progress of labour was satisfactory, vaginal delivery was allowed, but second stage was cut short by forceps/ventouse. If the progress of labour was not satisfactory or any foeto-maternal complications arise, delivered immediately by caesarean section. Patients who underwent caesarean section were taken as control. Foeto maternal outcome of all patients who were delivered by caesarean section and vaginally were compared separately in both ante and intrapartum eclamptic patients.

### Results:

In Dhaka Medical College Hospital, during study period eclamptic patients were 447(6.11%) and study population were 106(1.44%). The mean ( $\pm$ SD) age of the patients was  $21.35\pm 4.05$  years in vaginal delivery group and  $21.85\pm 3.08$  years in caesarean section group. Statistically the difference in mean age between the two groups is not significant. In this study, in both groups, gravidity (median) was 1. Mean ( $\pm$ SD) gestational age of our study population was  $37.26\pm 5.06$  weeks in vaginal delivery group and  $37.25\pm 0.71$  weeks in caesarean section group. Statistically the difference is not significant. Mean ( $\pm$ SD) Diastolic blood pressure was  $108.24\pm 21.48$  mm of Hg in vaginal delivery group and  $111.34\pm 8.83$  mm of Hg in caesarean section group and mean ( $\pm$ SD) proteinuria was  $2.53\pm 5.09$  in vaginal delivery group and  $2.52\pm 4.93$  was in caesarean section group. No significant statistical difference was present between the groups.

Among the 106 subjects, 79 (74.52%) came from poor socioeconomic condition (monthly income taka <3000), 24 (22.64%) came from lower middle (monthly income taka 3000 to 5000) and only 3 (2.83%) came from upper middle (monthly income taka >5000) socioeconomic condition. Among the 106 subjects, 93(87.73%) were housewives, 12(11.32%) were garments workers and 1(0.94%) was service holder. Number of illiterate patients of the study subjects was 53 (50%), 42 (39.62%) had primary education, 9 (8.49%) had secondary and 2 (1.88%) had higher secondary education. Among the study subjects, 81 (76.41%) were nullipara, 14 (13.20%) had one previous child, 5 (4.71%) had two previous children. 2 (1.88%) and 4 (3.77%) had three and four children respectively.

Out of 106 study subjects, 47 (44.33%) were delivered vaginally and 59 (55.66%) were delivered by caesarean section. Out of 59 eclamptic patients who underwent caesarean section, 22 (37.29%) were due to unfavourable cervix, 17 (28.81%) were due to cephalo-pelvic disproportion and 9 (15.25%) were due to foetal distress. Unsatisfactory progress of labour was the indication in 6 (10.17%) cases, obstructed labour and abruptio Placenta were the indications in 4 (6.78%) and 1 (1.69%) respectively.

**Table I: Outcome of labour of the antepartum patients induced for vaginal delivery (n=23)**

Mode of delivery	No. of patient	Percentage
Vaginal delivery	19	82.61
Caesarean section	4	17.39
Total	23	100.00

The number of the patients delivered vaginally were significantly high.  $P < 0.001$ , obtained by Z test ( $Z=3.12$ ).

**Table II: Outcome of labour of the intrapartum patients allowed for vaginal delivery (n=30)**

Mode of delivery	No. of patient	Percentage	P-value
Vaginal delivery	28	93.33	
Caesarean section	2	6.67	$P < 0.001$ , $Z=4.74$
Total	30	100.00	

The number of the patients delivered vaginally were significantly high.  $P < 0.001$ , obtained by Z test ( $Z=4.74$ ).

**Table III: Comparison between mode of delivery and maternal complications**

Complications	Vaginal delivery (n=47)	Caesarean Section (n=59)	P -value <sup>a</sup>
Postpartum haemorrhage	7 (14.89%)	6 (10.17%)	0.725 ( $P > 0.05$ )
Pulmonary oedema	6 (12.76%)	11 (18.64%)	0.836 ( $P > 0.05$ )
Infections	2 (4.25%)	6 (10.17%)	1.206 ( $P > 0.05$ )
Death	2 (4.25%)	2 (3.39%)	0.228 ( $P > 0.05$ )

<sup>a</sup> **Z test:** Statistically there was no significant difference between two groups. P value was obtained by Z test and was not significant ( $P > 0.05$ ).

**Table IV: Distribution of foetal outcome of the patients delivered vaginally.**

Outcome	Number	Percentage
Healthy baby	25	53.19
Mildly asphyxiated and alive after resuscitation	13	27.67
Highly asphyxiated and died after resuscitation	6	12.76
Still born	3	6.38
<b>Total</b>	<b>47</b>	<b>100</b>

**Table V: Distribution of foetal outcome of the patients delivered by caesarean section.**

Outcome	Number	Percentage
Healthy baby	32	54.24
Mildly asphyxiated and alive after resuscitation	15	25.42
Highly asphyxiated and died after resuscitation	11	18.64
Still born	1	1.69
<b>Total</b>	<b>59</b>	<b>100</b>

**Table VI: Foetal outcome of vaginal delivery and caesarean section group.**

Mode of delivery	Perinatal death	Healthy baby	Total	P value
Vaginal Delivery (n=47)	9	38	47	X <sup>2</sup> = 0.083 P > 0.05
Cesarean Section (n=59)	12	47	59	
<b>Total</b>	<b>21</b>	<b>85</b>	<b>106</b>	

P value was >0.05, obtained by chi square test (X<sup>2</sup> = 0.83) and test was not significant.

**Discussion:**

Eclampsia is a serious obstetric complication. Termination of pregnancy is the definitive treatment of eclampsia. The purpose of this study was to find out whether routes of delivery has any influence on fetomaternal outcome and to find out suitable route of delivery in eclamptic patients. Hospital incidence, age group, parity, clinical parameters (blood pressure, proteinuria) and socioeconomic condition of the study subjects were compared with studies by Liza<sup>14</sup>, Ramin<sup>15</sup>, Taner<sup>16</sup> and Munro<sup>17</sup>. All characteristics showed similarity between our study and these studies<sup>14-17</sup>. Occupation, education and income have a significant influence on the quality of patient's nutrition and antenatal care.

In our study, 76.41% patients were young nulliparous, 74.52% belonged to poor socioeconomic group, 50% patients were illiterate and only 39.62% had primary education. These results are comparable with other results<sup>13-16</sup>. In our study, intrapartum and antepartum eclamptic patients having good cervical score with favourable lie and presentation of foetus and absence of any obstetric indications that needed immediate caesarean section, were induced or augmented for vaginal delivery and patients having any obstetric indications for immediate caesarean section were only selected for caesarean section. Mean age, gravida, gestational age, diastolic BP and proteinuria were compared between these two study groups and they were well matched. In present study, total 47 (44.33%) eclamptic patients out of 106 cases were delivered vaginally and the number of caesarean section was 59 (55.66%), none of them were underwent due to eclampsia alone. 30 Intrapartum patients were allowed for vaginal delivery, 28 (93.33%) were delivered successfully and only 2 (6.67%) needed caesarean section and 23 antepartum patients were induced, 19 (82.61%) were delivered and 4 (17.39%) needed caesarean section. So significant number of patients who aimed at vaginal delivery were delivered successfully without any significant maternal or foetal complications.

In another study done at DMCH during January to July 1998 by Liza<sup>14</sup>, it was found that 36% of eclamptic patients were delivered vaginally. The result was not similar to the present study. In that study the eclamptic patients who needed immediate caesarean section and whose delivery were imminent were excluded and patients were not selected on the basis of cervical score, they were selected randomly. So induction failure rate was high and incidence of vaginal delivery was relatively lower than our study. On the other hand caesarean section was 64% in that study done by Liza which was relatively high. In a study by Taner et al showed that, incidence of caesarean section was 50.12% and all of them underwent due to definite obstetric indications<sup>14,16</sup>.

Another study by Ramin<sup>15</sup> in Minnesota, USA showed that vaginal delivery in eclamptic patients was 52.45% and gestational age near term were the good candidates for induction and were delivered successfully and well recovered. The concept and findings of these studies were consistent with our study. Regarding maternal complications, in our study, we did not find any better outcome in caesarean section group.

Moreover, pulmonary oedema and wound infection rate were apparently higher in caesarean section group than the patient delivered vaginally. Though postpartum hemorrhage rate was slightly higher in vaginal delivery group, but not statistically significant. In a study by Menro<sup>17</sup> it was found that, acute pulmonary oedema developed more in post operative period than in post natal period due to transient reflex hypertension in eclamptic patients during intubation. This may be so extreme as to cause acute pulmonary oedema. Excessive fluid administration in post operative periods may also be responsible and the findings are comparable with our results. In a randomized study by Liza<sup>14</sup>, she also did not find any significant difference regarding maternal complication between two

study groups and study findings were consistent with our findings. Maternal deaths in caesarean section group and vaginal delivery group were 4 (3.77%) in our study. Among 2 deaths in post caesarean cases, one was due to anaesthetic hazard on operation table and other due to pulmonary oedema. In vaginal delivery group, one was due to postpartum hemorrhage and other was due to DIC. In a study by Taner et al<sup>16</sup>, it was found that maternal death in eclamptic patients who underwent caesarean section were relatively higher (14.9%) than eclamptic patients delivered vaginally (13.03%). In a randomized study by Liza<sup>14</sup>, showed that maternal death did not reduce in eclamptic patients who underwent caesarean section. In that study maternal death in both group was same. Perinatal death in our study was 21 (19.81%). Perinatal mortality in patient delivered vaginally was 9 (19.14%) and caesarean section group was 12 (20.33%). Statistically there was no significant difference in perinatal death between the two groups.

In a study by Ramin KD<sup>15</sup> showed that perinatal mortality was 2.48% and perinatal death was same in both vaginal delivery and caesarean section groups. The previously mentioned study by Liza<sup>14</sup> showed that, perinatal mortality was higher in vaginal delivery group than caesarean section group. These findings are inconsistent with the findings of the present study. The reason was that probably there was no gestational age limit of that study as prematurity is one of the main cause of perinatal mortality. In the present study, the eclamptic patients who had proteinuria greater than 3gm/24 hours, diastolic BP greater than 110 mm Hg and convulsion-admission interval greater than 12 hours, were associated with poor foetal outcome. The findings of the present study was found consistent with the findings of Repke et al<sup>18</sup>, they showed that foetal wastage was markedly higher in those who had higher and uncontrolled BP, severe proteinuria, high uric acid level and altered liver functions.

In our study, perinatal outcome of the patients selected for caesarean section were compared with the patients allowed vaginal delivery but later needed caesarean section. It was found that statistically there was no significant difference between these two groups.

Like our study several other studies<sup>13-16</sup> have shown that mode of delivery did not have any significant influence on the maternal and foetal outcome in eclamptic patients if the cases were judiciously selected. So, after proper control of convulsion and blood pressure, patients who are suitable for vaginal delivery can be allowed for vaginal delivery.

Progress of labour should be monitored strictly and frequently and if the labour progress well it can be continued and if any obstetrical indication for caesarean section arises, pregnancy should be terminated by immediate caesarean section. So all eclamptic patients may not need caesarean section, except those who have definite obstetric indications.

### Conclusion:

Eclampsia is one of the grave diseases in pregnancy which is still one of the major causes of maternal mortality in Bangladesh. Termination of pregnancy is the final management of eclampsia and caesarean section is frequently undertaken as a method of termination now a days. But from this study it can be concluded that there is no significant difference between maternal and foetal outcome whatever may be the mode of delivery if the cases are judiciously selected.

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## Association of Insulin Resistance with Pregnancy Induced Hypertension

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### Abstract:

**Background:** Pregnancy induced hypertension (PIH) is a major complication of pregnancy affecting adversely both mother and fetus. It is a component of metabolic syndrome characterized by central adiposity, hypertension, glucose intolerance, dyslipidemia and insulin resistance (IR). **Objective:** To assess the association of IR with PIH. **Material and methods:** In this cross sectional study 77 PIH subjects were studied along with age matched pregnant control after 20 weeks of pregnancy. Blood glucose, serum lipid and plasma C peptide were measured and HOMA%B and HOMA%S were calculated by Homeostasis Model Assessment. **Results:** There was no significant difference present in age, gestational weeks, fasting plasma glucose, plasma cholesterol, HDL, LDL levels between control and PIH groups. But SBP, DBP, MBP, plasma triglyceride, C peptide, HOMA%B levels were significantly increased and HOMA%S level was significantly decreased in PIH group than those of control group. For control group, age, gestational weeks and SBP were negatively correlated but DBP, MBP, fasting glucose, serum triglyceride, cholesterol and LDL were positively correlated and not significant with C peptide. In PIH group, age, gestational weeks, fasting glucose, HDL, serum triglyceride, cholesterol and LDL were positively correlated and not significant. SBP, DBP and MBP were positively correlated and significant with C peptide. In control, HOMA%S has negative and non-significant correlation with SBP, DBP and MBP but has negative and significant correlation with fasting glucose. In PIH HOMA%S has negative and significant correlation with SBP, DBP, MBP and fasting glucose. **Conclusion:** From the results, the study concluded that there is association between insulin resistance and pregnancy induced hypertension.

**Keywords:** Insulin resistance, PIH, C peptide, HOMA%B, HOMA%S

### Introduction:

Hypertension, a common disorder in pregnancy, constitutes a major risk factor for morbidity and mortality both for mother and child all over the world<sup>1</sup>. The worldwide incidence of the disorder is still high in spite of the significant improvement of mother and child care over the last decades. Hypertension complicates 5-10% of pregnancies which includes preeclampsia, gestational hypertension, pregnancy induced hypertension, eclampsia and chronic hypertension<sup>2</sup>.

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Pregnancy may induce hypertension in women who are normotensive before pregnancy and may aggravate hypertension in those that are hypertensive before pregnancy. Pregnancy induced hypertension (PIH) includes Preeclampsia (PE) and Gestational hypertension (GH). Hypertension developing after 20 weeks of gestation accompanied by significant proteinuria is known as PE. On the other hand, in GH blood pressure elevation detected for the first time after mid pregnancy and distinguished from PE by the absence of proteinuria<sup>2</sup>.

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Preeclampsia is responsible for approximately 50,000 maternal deaths yearly worldwide, 25% of all cases of fetal growth restriction and 15% of preterm births in developed countries<sup>3,4,5</sup>. It is the main cause of maternal mortality in these countries and is associated with a 5-fold increase in perinatal mortality<sup>6</sup>. The incidence of preeclampsia (PE, the proteinuric version of pregnancy induced hypertension or PIH) in developing countries is particularly high due to lack of proper care of the mother during pregnancy. Geographic, social, economic and racial differences are responsible for an incidence that is up to three times higher in some populations. In developing countries, preeclampsia complicates 4.4% of all deliveries and may be as high as 18% in some setting in Africa<sup>7</sup>.

Although a fairly good degree of knowledge has now been accumulated on the etiopathogenesis of PE, the exact biochemical events leading to the biochemical events leading to the disorder remain still unclear. It is now well acknowledged that the causes of PIH include immune, genetic, environmental, nutritional basis and placental abnormalities<sup>6,8</sup>. All may contribute to endothelial dysfunction which may underlie several critical features of PE, including vasoconstriction, hypertension and loss of usual pregnancy associated refractoriness to pressor effect of angiotensin II, increased platelet aggregation and proteinuria<sup>9</sup>.

Hypertension develops during pregnancy and remits after delivery, implicating the placenta as a central culprit in the disease. An initiating event in PIH has been postulated to be reduced placental perfusion that leads to widespread dysfunction of maternal vascular endothelium<sup>10</sup>. Vascular endothelium has many important functions including control of smooth muscle tone through vasoconstrictor and vasodilator substance and regulation of anticoagulant, antiplatelet and fibrinolysis functions via release of different soluble factors. It has been suggested that release of these factors from the placenta in response to ischemia results in endothelial dysfunction of the maternal circulation.

The widespread endothelial dysfunction may manifests as dysfunction of multiple organ system including central nervous system, hepatic, pulmonary, renal and hematological system<sup>11</sup>. PE can affect the fetus via decreased uteroplacental blood flow. This decreased perfusion manifest clinically as non-reassuring fetal heart rate testing, low score on biophysical profile, oligohydramnios and fetal growth restriction in severe cases<sup>12</sup>.

PIH is associated with well documented risk for the mother and fetus. It is not only dangerous for both mother and baby but also unpredictable in onset and progression and incurable except by termination of pregnancy<sup>13</sup>. Early detection of PIH is important, as women are usually asymptomatic and seldom notice the sign of incipient PIH. A large number of clinical and biochemical tests have been employed to predict women at risk of PIH<sup>11</sup>.

Insulin resistance syndrome provides a possible link between hypertensive pregnancy and many of its risk factors and sequels in both pregnancy and later life. Increased incidence of cardiovascular diseases in diabetic patients is well known phenomenon, but sufficient data has now been accumulated to claim that insulin resistance is associated with a higher risk of cardiovascular problems even in the absence of diabetes. In women whose pregnancies are complicated by hypertension, there appears to be an exaggeration of insulin resistance and associated metabolic changes. Exaggerated hyperinsulinemia relative to normal pregnancy is well described in women with established preeclampsia or gestational hypertension<sup>14,15</sup>.

Normal pregnancy is associated with hyperinsulinemia and insulin resistance. Insulin sensitivity decreases during pregnancy with peaks in the third trimester<sup>16-19</sup> and after delivery it returns to prepregnancy level rapidly<sup>20</sup>. The basis of insulin resistance in normal pregnancy is not well understood. It is postulated that various hormonal changes in pregnancy, particularly human placental lactogen, cortisol, progesterone and estrogen are responsible for the loss of insulin sensitivity in this condition<sup>21</sup>.

Substantial evidence has now been accumulated to suggest that PIH is associated with greater degree of insulin resistance than characteristics of normal pregnancy. Although a few studies claim that only GH and not PE is associated with insulin resistance<sup>22,23</sup>. The overwhelming data supports the idea that both GH PE are insulin resistant conditions<sup>8</sup>. The usual period of onset of PIH (late pregnancy)<sup>16</sup> corresponds with the maximal degree of insulin resistance and it supports a possible association. Collectively, this data suggest that insulin resistance may contribute to the pathogenesis of preeclampsia<sup>24</sup>.

Postulated mechanism through which IR might increase blood pressure includes sympathetic nervous activation, renal sodium retention, increased cation transport, increases vascular smooth muscle growth and associated endothelial dysfunction<sup>25-28</sup>. Amplified mid pregnancy  $\beta$ -cell secretory activity (as reflected in fasting and postprandial C-peptide concentration) is associated with subsequent development of PIH and this association is independent of obesity and mid pregnancy blood pressure<sup>29</sup>.

### Methods:

This case-control cross sectional study was conducted at the department of Gynecology and Obstetrics and Biomedical research group, Bangladesh Institute of Research and Rehabilitation in diabetes, Endocrine and Metabolic Disorders (BIRDEM) during the period of January 2006 to January 2007. A total of 77 [PE (52) + GH (25)] pregnant women with PIH as diagnosed by American College of Obstetrics and Gynecology (ACOG) criteria were selected as case, 52 age-matched healthy pregnant women were selected as controls after 20 weeks of pregnancy. After taking informed written consent clinical examination was done by standard methods. After 8-12 h fasting overnight blood and urine samples were collected. Blood glucose was measured by Glucose Oxidase method, serum lipid by enzymatic colorimetric method and plasma C peptide was measured by chemiluminescence based ELISA, HOMA%B and HOMA%S were calculated

by Homeostasis Model Assessment and were used as a markers of insulin secretory capacity and insulin sensitivity respectively. Urine protein was estimated by a specific reagent strip.

Data were expressed as mean  $\pm$ SD for and median (range) for non-parametric values. Comparison between groups were done using independent t-test to compare means and Mann-Whitney U test for skewed data. Data were processed by computer using SPSS program and then analyzed. *p* value of <0.05 was considered as significant.

### Results:

The median (range) age in (years) of the study groups were control 25 (18-37) and PIH 25 (18-37). There was no significant difference of gestational weeks but SBP, DBP and MBP were significantly higher in PIH groups than those of control group (Table 1).

There was no significant difference in the fasting plasma glucose levels between control and PIH groups. C peptide, HOMA%B levels were significantly increased but HOMA%S level was significantly decreased in PIH group than those of control group (Table 2).

Plasma triglyceride level was significantly increased in PIH group but there were no significant difference present in the plasma cholesterol, HDL, LDL levels between control and PIH groups (Table 3).

For control group, age, gestational weeks and SBP were negatively correlated and not significant with C peptide. But DBP, MBP, fasting glucose, serum triglyceride, cholesterol and LDL were positively correlated and not significant with C peptide. In PIH group, age, gestational weeks, fasting glucose, HDL, serum triglyceride, cholesterol and LDL were positively correlated and not significant. SBP, DBP and MBP were positively correlated and significant with C peptide. (Table 4).

In control, HOMA%S has negative and non significant correlation with SBP, DBP and MBP but has negative and significant correlation with fasting glucose.

In PIH HOMA%S has negative and significant correlation with SBP, DBP, MBP and fasting glucose (Table 5).

**Table 1: Clinical characteristics of the study subjects**

Variables	Control (n=52)	PIH (n=77)	p value
Age (Years)	25 (18-37)	25 (18-37)	0.212
Gestational wks.	33 (27-40)	33 (22-39)	0.193
Parity	2 (1-6)	2 (1-6)	0.708
SBP (mm of Hg)	108.06 ± 6.26	156.95 ± 14.59	<0.001
DBP (mm of Hg)	65.38 ± 5.53	105.3 ± 10.49	<0.001
MBP (mm of Hg)	78.91 ± 5.78	122.54 ± 10.98	<0.001

Data are presented as mean± SD for parametric value and median (range) for non-parametric value. n= Number of subject. SBP= Systolic blood pressure. DBP= Diastolic blood pressure. MBP= Mean blood pressure.

**Table 2: Glycemic and insulinemic status of the study subjects**

Variables	Control (n=52)	PIH (n=77)	p value
F Glucose (mmol/l)	4.05 ± 0.54	4.17±0.50	0.303
C-peptide (ngm/ml)	1.59 ± 0.60	3.58±0.84	<0.001
HOMA %B	152.6 (73.7-321.6)	248.6 (84.9-383.1)	<0.001
HOMA %S	99.3 (11.9-205.8)	39.5 (18.8-185.5)	<0.001

Data are presented as mean± SD for parametric value and median (range) for non-parametric value. n= Number of subject. F Glucose= Fasting plasma glucose. HOMA %B= Insulin secretory capacity by Homeostasis Model Assessment; HOMA %S= Insulin sensitivity by Homeostasis Model Assessment.

**Table 3: Lipidemic status of the study subjects**

Variables	Control (n=52)	PIH (n=77)	p value
TG (mg/dl)	215.5 (46-368)	240.0 (67 - 906)	0.013
Cholesterol (mg/dl)	210.5 (132-290)	215.0 (134 - 443)	0.685
HDL (mg/dl)	38.8 (21.0-63.3)	37.1 (12.7-60.1)	0.438
LDL (mg/dl)	125.6 (63.1-219.2)	39.5 (18.8 - 185.5)	0.891

Results are expressed as median (range). n= Number of subject. Mann Whitney U test was done as a test of significance. TG= Triglyceride; Chol = Cholesterol; HDL= High Density Lipoprotein; LDL= Low Density Lipoprotein.

**Table 4: Relation of C peptide with various parameters of the study subjects**

Variables	Control (n=52)		PIH (n=77)	
	r	p	r	p
Age (years)	-0.100	0.483	0.037	0.748
Gestational weeks	-0.193	0.171	0.115	0.321
SBP (mmHg)	-0.019	0.892	0.274	0.016
DBP (mmHg)	0.108	0.447	0.259	0.023
MBP (mmHg)	0.134	0.343	0.304	0.007
F Glucose	0.248	0.096	0.078	0.503
Triglyceride (mg/dl)	0.135	0.339	0.029	0.806
Cholesterol (mg/dl)	0.026	0.856	0.089	0.443
HDL (mg/dl)	-0.043	0.760	0.007	0.951
LDL (mg/dl)	0.009	0.943	0.078	0.500

Pearson’s correlation coefficient are performed for the analysis; p<0.05 are considered as statistically significant; n= number of subjects.

**Table 5: Relation of HOMA%S with various parameters of the study subjects**

Variables	Control (n=52)		PIH (n=77)	
	r	p	r	p
Age (years)	0.132	0.350	0.094	0.418
Gestational weeks	0.221	0.115	0.251	0.280
SBP (mmHg)	-0.051	0.721	-0.194	0.061
DBP (mmHg)	-0.201	0.152	-0.244	0.033
MBP (mmHg)	-0.137	0.333	-0.253	0.026
F Glucose	-0.404	0.003	-0.150	0.193
Triglyceride (mg/dl)	-0.012	0.934	0.009	0.937
Cholesterol (mg/dl)	0.039	0.782	-0.500	0.666
HDL (mg/dl)	0.070	0.621	-0.289	0.808
LDL (mg/dl)	0.031	0.829	-0.055	0.635

Pearson's correlation coefficient are performed for the analysis;  $p < 0.05$  are considered as statistically significant; n= number of subjects.

### Discussion:

PIH becomes an important public health problem particularly in developing countries. It is grouped as a member of the bigger family of "metabolic syndrome" which is characterized by central adiposity, hypertension, glucose intolerance, dyslipidemia, hyperinsulinemia and insulin resistance. It is difficult to control adiposity in pregnancy due to limited usability of simple anthropometric parameters (like BMI) in pregnancy. Studies with measurement of prepregnancy BMI have shown that higher BMI is related to increased risk of PIH. Dyslipidemia has been known as a constant feature of PE<sup>8</sup> and it has been demonstrated in Bangladeshi subjects.

Triglyceride, fatty acids and LDL cholesterol have been reported to be higher and HDL cholesterol levels were lower in PIH than those in women with normotensive pregnancy<sup>14,30</sup>.

Study done by Lorentzen<sup>15</sup> showed that elevated triglyceride and fatty acid precedes the development of this condition. Pronounced hyperlipidemia, mainly hypertriglyceridemia has been reported in women with PE and has been related to insulin resistance<sup>14</sup>.

The PIH group in the present study also exhibits dyslipidemia with significantly higher triglyceride levels as compared to control. Elevated serum lipid has been reported antedating the development of PIH. Oxidized lipid may impair endothelial function directly or indirectly by effects on prostaglandin, including increase synthesis of thromboxane and inhibiting synthesis of prostacyclin<sup>31</sup>.

Hyperinsulinemia, resulting from a feedback loop created by insulin resistance, is considered as the converging point of various pathologies in metabolic syndrome. A study done by Bartha et al<sup>30</sup> by minimal model technique, found that insulin sensitivity in women with PE was 37% lower than control concluding PE is a state of insulin resistance.

In a small study using the euglycemic clamp technique, insulin resistance was greatest in women with GH whereas result were similar in women with normotensive pregnancy and women with PE<sup>30,32</sup>. In a recent study using minimal model technique women with PE were more insulin resistant than normotensive control<sup>14</sup>.

Although cross sectional studies cannot distinguish whether insulin resistance antedates or results from PIH, other data have demonstrated that insulin resistance precedes the development of this condition<sup>8</sup>.

In the present study a typical picture of hyperinsulinemia (as represented by elevated level of C peptide) and insulin resistance has been found in PIH subjects (Table 2). The insulin secretory capacity of PIH subjects (as represented by HOMA%B) was also increased. The mean percent decrease of insulin sensitivity, as compared to control, was more than 50%, which is higher than that seen by Barth et al<sup>30</sup>.

**Conclusions:**

The study concluded that insulin resistance, as expressed by increased serum C peptide, increased HOMA%B, decreased HOMAS% and increased serum lipid profile is associated with PIH.

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## Ultrasound Features of Malignancy in Partially Cystic Thyroid Nodules.

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### Abstract:

**Objective:** To seek for the ultrasound (US) findings of partially cystic thyroid nodules that are associated with malignancy. **Materials and Methods:** We reviewed the US characteristics of 22 surgically confirmed partially cystic papillary carcinomas, and compared them with those of 80 benign partially cystic nodules. The review cases were selected in a random order from a total of 100 partially cystic nodules that were diagnosed with an US-guided fine needle aspiration biopsy over a period of 5 years (January 2017 to January 2022) at different institutions. **Results:** In partially cystic thyroid nodules, a taller-than-wide shape (100%,  $p < 0.001$ ) and spiculated or microlobulated margin (58.3%,  $p = 0.003$ ) were significantly associated with malignancy. In terms of internal solid portion of the nodule, eccentric configuration (68.0%,  $p < 0.001$ ), non-smooth margin (81.3%,  $p < 0.001$ ), hypoechogenicity (30.0%,  $p < 0.042$ ), and microcalcification (89.5%,  $p < 0.001$ ) were more frequently demonstrated in malignant nodules than benign ones. **Conclusion:** In partially cystic thyroid nodules, understanding the characteristics of US findings is important to make a precise diagnosis of malignant nodules.

**Keywords:** Partially cystic nodule, partially cystic papillary carcinoma, cystic papillary carcinoma

### Introduction:

Partially cystic nodules are nodules that have both solid and cystic components, and comprise of 18% to 35% of surgical specimens<sup>1,2</sup>. Since most partially cystic thyroid nodules are the result of a degenerative process, arising from underlying benign lesions, such as nodular hyperplasia, the management of partially cystic thyroid nodules is often undervalued. However, thyroid carcinomas can also show a cystic change (10-28% of papillary thyroid carcinomas), often related to size<sup>3,4</sup>. The rate of malignancy for partially cystic thyroid nodules was 5.2% in a recent study<sup>5</sup>. Thus far, there is little information regarding the ultrasound (US) findings of partially cystic nodules, associated with malignancy. Lee et al.<sup>6</sup> reported that more than 50% of solid portions, eccentric solid portions, and microcalcifications are associated with an increased risk of malignancy.

Kim et al. reported that an eccentric solid portion with an acute angle, microcalcifications, and macrolobulation or irregular free margin can significantly increase the risk of malignancy<sup>5</sup>.

Current guidelines in Korea<sup>7</sup> only consider the size (>1 cm) as a criterion for fine needle aspiration (FNA), regardless of the cystic portion. Similar revised guidelines from the American Thyroid Association<sup>8</sup> consider 1.5-2.0 cm (in nodules with any suspicious US features) or 2.0 cm (in nodules without any suspicious US features) as the threshold size for FNA of partially cystic nodules. On the other hand, the guidelines of the American Association of Clinical Endocrinologists/ European Thyroid Association recommend FNA for nodules larger than 1.0 cm that are solid and hypoechoic nodules<sup>9</sup>. There were no comments concerning the US features, which suggest malignancy in partially cystic nodules. We compared the US findings of partially cystic papillary carcinomas to those of benign nodules.

### Materials and methods:

**Patient Selection:** We reviewed the surgical excision data of the hospitals from January 2017 to January 2022, and enrolled 22 patients (15 women and 7 men ranging in ages from 17 to 70 years, mean 50.8 years)

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diagnosed with papillary thyroid carcinomas with partially cystic feature in the US images. Next, we randomly selected 80 of 1000 patients for the control group, using the random sampling function of a software package {PASW Statistics 18 (Statistical Package for the Social Sciences [SPSS] Inc., Chicago, IL, USA)}. These patients were diagnosed with benign partially cystic thyroid nodules, at both initial and repeat FNA, during the same period. The control group consisted of 64 women and 16 men, ranging in ages from 33 to 73 years (mean 52.3 years), and the cytological diagnosis of nodules were as follows: nodular hyperplasia (n = 69), colloid with benign follicular cells (n = 7), and benign follicular lesion (n = 4).

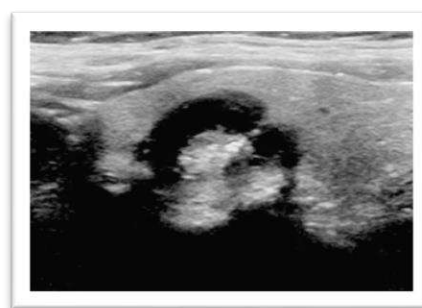
The US and US-guided FNA were performed by board-certified radiologists with 8-10 years of experience in thyroid imaging. VOLUSON E10, VOLUSON E8 (GE medical systems) high-frequency 13-MHz linear transducers were used. The cytology was interpreted by cytopathologists and a specimen was "adequate" if there was a minimum of six groupings of well-preserved thyroid cells, each consisting of at least 10 cells per group.

### Image analysis:

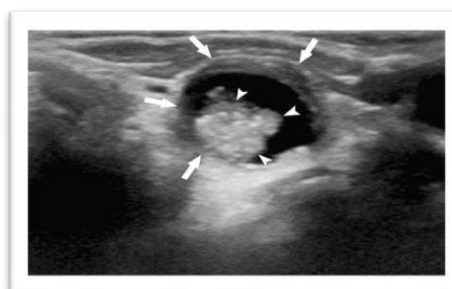
Partially cystic nodules were defined by the presence of any anechoic components in US, except completely anechoic nodules. All US images of partially cystic nodules were retrospectively evaluated by board-certified radiologists in consensus, having 8-10 years of experience in thyroid imaging.

Each nodule was evaluated for the following US findings of entire nodule: size (the longest diameter), internal content (predominantly solid vs. predominantly cystic vs. spongiform), shape (ovoid to round vs. taller-than-wide vs. irregular), and margin (smooth vs. spiculated or microlobulated vs. ill-defined). US examination of internal solid portion included configuration (eccentric vs. non eccentric) (Figs. 1 a, b and 2), margin (smooth vs. non-smooth),

echogenicity (markedly hypoechoic vs. hypoechoic vs. isoechoic vs. hyperechoic), and calcification (microcalcifications vs. macrocalcifications vs. rim calcifications vs. none). We described the margin (of entire nodule), shape, echogenicity, and calcification. A spongiform internal content also followed that group's definition (7) as the aggregation of multiple microcystic components in more than 50% of the volume of the nodule, resulting in a honeycomb or "puff pastry" appearance.



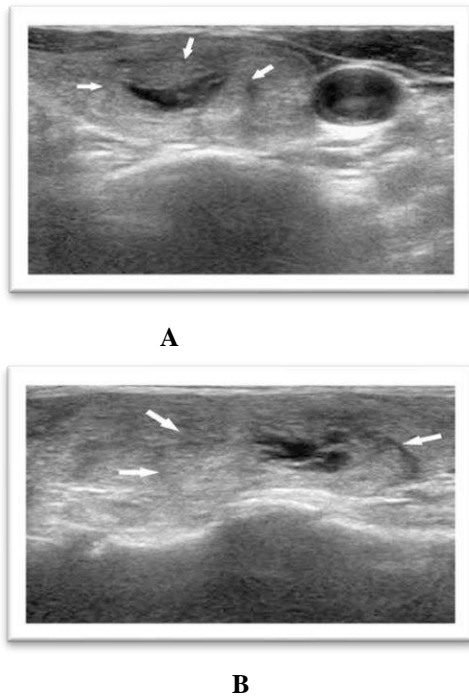
**a**



**b**

**Fig 1:** (a) Longitudinal ultrasound image of papillary thyroid carcinoma in 53-year-old woman shows predominantly cystic nodule. Entire nodule has smooth margin. Internal protruding eccentric solid position contains multiple punctate round echogenic foci suggesting microcalcifications.

(b) Transverse ultrasound image of predominantly cystic nodule in 69-year-old woman. Eccentric solid portion protruded internally and contained multiple microcalcifications. Note difference between smooth margin of entire nodule (arrows) and non-smooth margin of internal solid portion (arrowheads). Papillary thyroid carcinoma was diagnosed by fine needle aspiration and surgery.



**Fig 2:** Example of non-eccentric configuration of internal solid portion. Transverse (**A**) and longitudinal (**B**) US images show partially cystic nodule with isoechoic internal solid portion in 57-year-old woman. Entire nodule has ill-defined margin (arrows). Nodular hyperplasia was diagnosed by US-guided fine needle aspiration.

An eccentric configuration had an internal solid portion, which was not located in the center, and was abutted on only one side of the cyst wall. A non-eccentric configuration was defined as all partially cystic thyroid nodules other than the eccentric configuration, including spongiform nodules. In the aforementioned standardized terminology<sup>7</sup>, an ill-defined margin of the entire nodule is defined by the inability to differentiate the tumor from that of the normal parenchyma. We classified the margin of internal solid portion, as smooth or non-smooth.

### Data analysis:

The  $\chi^2$  test or Fisher's exact test was used to compare the quantitative variables, while the Student's t test and Mann-Whitney U test were used to evaluate the size, as well as the longest diameter.

A two-tailed p value of  $< 0.05$  indicated a significant statistical difference. Statistical analysis was performed by using PASW Statistics 18 (SPSS Inc., Chicago, IL, USA).

### Results:

Malignancy in partially cystic nodule can be characterized by a taller-than-wide shape (100%,  $p < 0.001$ ) and spiculated or microlobulated margin (58.3%,  $p = 0.003$ ) of the entire nodule.

Further findings of internal solid portion included an eccentric configuration (68.0%,  $p < 0.001$ ), non-smooth margin (81.3%,  $p < 0.001$ ), hypoechogenicity (30.0%,  $p = 0.042$ ) and microcalcifications (89.5%,  $p < 0.001$ ). Predominantly, solid nodules were not significantly associated with malignancy.

The characteristics of a benign nodule included spongiform internal content (100%,  $p = 0.036$ ), ovoid to round shape (83%,  $p = 0.001$ ), and smooth margin (84.3%,  $p < 0.001$ ) in the entire nodule, while the internal solid portion included a non eccentric configuration (93.5%,  $p < 0.001$ ), smooth margin (89.5%,  $p < 0.001$ ), isoechogenicity (89.6%,  $p = 0.010$ ), and lacking calcifications (96.1%,  $p < 0.001$ ). The US features of all 102 cases, including those without significant differences, are summarized in Table 1.

**Table 1: US Features of Benign and Malignant Partially Cystic Thyroid Nodules**

US features	Malignant nodules (n= 22)	Benign nodules (n= 80)	$\rho$
<b>Entire nodule</b>			
Longest diameter (cm)*	1.9	1.5	0.314
<b>Internal content</b>			
a) Predominantly solid	12 (23.1)	40 (76.9)	0.706
b) Predominantly cystic	10(27.8)	26(72.2)	0.260
c) Spongiform	0(0)	14(100)	0.036
<b>Shape</b>			
a) Ovoid to round	16(17.0)	70 (83.0)	0.001
b) Taller than wide	5 (100)	0(0)	<0.001
c) Irregular	1 (33.3)	2 (66.7)	0.521
<b>Margin</b>			
a) Smooth	14 (15.7)	75 (84.4)	0.001
b) Spiculated or microlobulated	7 (58.3)	5 (41.7)	0.003
c) Ill defined	1 (100)	0 (0)	0.216
<b>Internal solid portion Configuration</b>			
a) Eccentric	17 (68.0)	8 (32.0)	<0.001
b) Non eccentric	5 (6.5)	72 (93.5)	<0.001
<b>Margin</b>			
a) Smooth	9 (10.5)	77 (89.5)	<0.001
b) Non smooth	13 (81.3)	3 (18.8)	<0.001
<b>Echogenicity</b>			
a) Marked hypoechoic	1 (50)	1 (50)	0.387
b) Hypoechoic	15 (30.0)	35 (70.0)	0.042
c) Isoechoic	5 (10.4)	43 (89.6)	0.010
d) Hyperechoic	1 (50)	1 (50)	0.387
<b>Calcification</b>			
a) Microcalcifications	17 (89.5)	2 (10.5)	<0.001
b) Macrocalcifications	2 (33.3)	4 (66.7)	0.607
c) Rim calcifications	0 (0)	1 (100)	1.000
d) None	3 (3.9)	73 (96.1)	<0.001

Note – Data are number of nodules with percentages in parenthesis.

\*Indicates mean value. US= Ultrasound.

### Discussion:

There are few reports, which compares the US findings between malignant and benign partially cystic nodules. Our study is notable for analyzing the US findings of both the entire nodule and its internal solid portion, following the standardized terminology. However, we did need to re-categorize the internal content. The statistically significant US findings of the entire nodule for the depiction of malignancy were a taller-than-wide shape and spiculated or microlobulated margin. The statistically significant US findings of the internal solid portion were an eccentric configuration, non-smooth margin, hypoechogenicity, and microcalcifications. These findings do not differ greatly from the previously suggested US criteria<sup>7</sup>, indicating those criteria that are applicable to partially cystic nodules. However, we discovered that the marked hypoechogenicity of a nodule did not differ significantly, unlike the previous research<sup>8, 10</sup>. This may be due to the easier sonic transmission through the cystic component of a partially cystic nodule, compared to a solid one as suggested by Kim et al<sup>5</sup>.

Compared with two recent studies<sup>5,6</sup> regarding partially cystic nodules, we confirmed that the eccentric configuration and microcalcifications of internal solid portion, in partially cystic nodules, were significantly more frequent in malignant partially cystic nodules. This result is supported by a previous report, describing the malignant cells as more likely to be located in the intracystic pedunculated mass and/or the pericystic region than in the cyst wall (Figs.3). In other words, malignant partially cystic nodules are more likely to be an intracystic mass, protruding from the wall than the diffuse lesion, which is circumferentially located within the cystic wall that would result in a concentric configuration. A recent study<sup>5</sup> that subdivided the eccentric configuration into either an acute angle or a blunt angle to the adjacent cyst wall found that only the cases with an acute angle were associated with malignancy.

In our study, if the margin of internal solid portion was smooth, the partially cystic nodule was more likely to be benign, in accordance with a previous study<sup>5</sup>. However, we subdivided the margin of the internal solid portion based upon whether it was smooth or not. That characteristic, the lack of smoothness of the margin of the partially cystic nodule, was indicative with statistical significance of malignancy. Our finding can be explained by the histologic tendency of malignancy to grow unevenly and infiltratively without pseudocapsule formation. Most notably, the proportion of solid components of partially cystic thyroid nodules cannot predict a malignancy. Thus, radiologists should not overlook predominantly cystic nodules (Figs. 3 a, b).



a



b

**Fig 3** (a) Longitudinal ultrasound image of predominantly cystic nodule in 66-year-old woman shows eccentric configuration. Note difference between smooth margin of entire nodule (arrows) and non-smooth margin of internal solid portion (arrowheads).

This lesion was surgically confirmed as papillary thyroid carcinoma despite substantial cystic portion. (b) Transverse ultrasound image of predominantly cystic nodule in 63-year-old woman shows eccentric configuration of internal solid portion with multiple microcalcifications. Note non-smooth margin of internal solid portion (arrows). This lesion was surgically confirmed as papillary thyroid carcinoma despite substantial cystic portion.

### Conclusion:

The US findings of internal cystic portion are important in partially cystic thyroid nodules. A non-smooth margin, eccentric configuration, hypoechoogenicity, and microcalcifications are the US findings of the internal solid portion, which can suggest malignancy. These findings are useful for accurate differential diagnosis of malignant partially cystic thyroid nodules.

### Limitations:

The number of malignant cases included in this study (n = 22) was relatively small. The diagnoses of benign nodules were based on cytologic, rather than pathologic findings, because their diagnoses from FNA were not considered indications for surgery. Since this study was not a prospective study that included all partially cystic nodules as candidates of FNA, a selection bias was inevitable. We assumed an echogenic spot as either microcalcification or macrocalcification, depending on its visualized size. However, each of these echogenic spots was not confirmed pathologically. Finally, we tried to consider all tiny echogenic spots, except for comet-tail artifacts, as microcalcifications, because after surgery, they were mostly confirmed pathologically.

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## Relation of Serum Lipid profile in Patients with Psoriasis

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### Abstract:

**Background:** Psoriasis is a chronic inflammatory hyper-proliferative disease of the skin, scalp, nails and joints. It is a common chronic recurrent inflammatory skin disease with unknown etiology. Genetic, metabolic and immunologic factors play an important role in the pathogenesis of psoriasis. Beyond the skin psoriasis is often associated with comorbidities such as metabolic syndrome. Psoriasis is also an autoimmune disorder associated with alteration of different lipid metabolism. Dyslipidemia could be one of co morbidities in psoriatic patients and are likely to play an important role in the increased risk of atherosclerosis in these patients. **Objective:** The aim of the study was to find out the relation of serum lipid profile in patients with psoriasis. **Methods:** This cross sectional study was carried out in the Department of Biochemistry, Dhaka Medical College. A total number of 110 cases with 55 diagnosed case of psoriasis (group A) and 55 healthy individuals (group B) of both sexes age ranging from 18 to 60 years were selected according to selection criteria from Outpatient Department of Dermatology and Venereology, Dhaka Medical College Hospital. Serum lipid profiles except low density lipoprotein cholesterol were measured by enzymatic method and low density lipoprotein cholesterol was calculated by using Friedewald formula. **Results:** Mean  $\pm$  SD of serum total cholesterol, triglycerides and low density lipoprotein-cholesterol were significantly higher ( $p < 0.001$ ) and high density lipoprotein-cholesterol was significantly lower ( $p < 0.001$ ) in psoriatic patients than healthy individuals. Serum TC, TG and LDL-C showed significant positive correlation ( $r = + 0.696, + 0.857, + 0.783$  and  $+ 0.841$  respectively) and HDL-C showed significant negative correlation ( $r = - 0.838$ ) with psoriasis. **Conclusion:** From the present study it can be concluded that psoriasis is related with dyslipidemia. Dyslipidemia was more common in psoriatic patients, compared with non-psoriatic controls. So estimation of these parameters may helpful to prevent the complication due to alteration of these parameters.

**Keywords:** Psoriasis, lipid profile, dyslipidemia

### Introduction:

Psoriasis is a chronic, noncommunicable, painful, disfiguring and disabling disease for which there is no cure and with great negative impact on patient's quality of life. It can occur at any age, and most common in the age group 50-69<sup>1</sup>. The reported

prevalence of psoriasis in countries ranges between 0.09% to 11.4% making psoriasis a serious global problem<sup>2,3</sup>. The etiology of psoriasis remains unclear, although there is evidence for genetic predisposition<sup>4</sup>. Psoriasis can also be provoked by external and internal triggers, including mild trauma, sunburn, infections, systemic drugs and stress<sup>5</sup>. Psoriasis involves the skin and nails, and is associated with a number of co morbidities. Skin lesions are localized or generalized, mostly symmetrical sharply demarcated, red papules and plaques, and usually covered with white or silver scales. Lesions cause itching, stinging and pain. About 34.7% of individuals with psoriasis develop chronic, inflammatory arthritis (psoriatic arthritis) that leads to joint deformations and disability<sup>6</sup>. Individuals with psoriasis are reported to be at increased risk of developing other serious clinical conditions such as cardiovascular and other noncommunicable diseases<sup>7</sup>.

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Study has found psoriasis to be associated with dyslipidemia, cardiovascular disease including atherosclerosis, thrombosis and myocardial infarction<sup>8</sup>. Persons with psoriasis have a pro atherogenic lipoprotein profile, including hyper triglyceridemia, raised plasma concentrations of low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) and a lowered high density lipoprotein cholesterol (HDL-C) concentration. The chronic inflammations, a main feature of psoriasis are associated with dyslipidemia<sup>9</sup>. The up-regulation of T helper-1 mediated cytokine cascades interferon- $\gamma$ , tumor necrosis factor- $\alpha$ , interleukin-1, interleukin-6<sup>10</sup>. In psoriasis there is an increase in production of oxygen metabolites due to the presence of inflammatory cells (polymorph nuclear leukocyte) in the superficial dermis and epidermis that lead to damage of the surrounding tissue by releasing reactive oxygen species. When the oxidative stress develops, it leads to the oxidative damage of lipids and protein<sup>11</sup>. Oxidation of the low-density lipoproteins (LDL) results in the production of modified LDL. Which increased incidence of atherosclerosis in psoriatic patient<sup>12</sup>. Since dyslipidaemia is one of the criteria for diagnosing metabolic syndrome, psoriasis is also found to be associated with metabolic syndrome. Insulin resistance can lead to type 2 diabetes mellitus in psoriatic patients. Other co-morbid factors increasing the risk of dyslipidaemia in psoriatic patients include higher body mass index (BMI)  $\geq 30\text{kg/m}^2$ , family history of dyslipidaemia, sedentary life style, high fat diet and patients taking retinoids or cyclosporine for the disease<sup>13</sup>. The chronic inflammatory nature of psoriasis and dyslipidemia have been suggested to be contributing risk factors for the development of co-morbidities like atherosclerosis, coronary artery disease and myocardial infarction resulting in increased cardiovascular mortality<sup>14</sup>. There are multiple reasons for dyslipidemia associated with psoriasis. The structural and functional changes in digestive system, immune mechanism involving IL-6, tumor necrosis factor, C-reactive protein and cellular oxidative stress may be responsible for altered lipid metabolism<sup>15</sup>. Auto antibodies against oxidized LDL have been found in psoriatic patients<sup>9</sup>.

Furthermore, chronic inflammation in psoriasis leads to increased insulin-like growth factor-II (IGF-II) in the skin and blood of psoriatic patients. Insulin-like growth factor- II (IGF-II) promotes epidermal proliferation and is also linked to hyperlipidemia and in promoting atherosclerosis<sup>16</sup>. Lipid profile or lipid panel is a panel of blood test that serve as an initial broad medical screening tool for abnormalities in lipids such as cholesterol and triacylglycerol. The results of this test can identify certain genetic diseases and can determine approximate risk for cardiovascular disease, cerebrovascular disease, certain forms of pancreatitis and other disease. Lipid panels are commonly ordered as a part of physical examination, along with others panels such as the complete blood count (CBC) and basic metabolic panels (BMP)<sup>17</sup>.

#### **The lipid profile typically includes:**

S. Triglycerides

S. Total cholesterol

S. Low density lipoprotein-cholesterol (LDL-C)

S. High density lipoprotein-cholesterol (HDL-C)

Lipid metabolism playing a role in pathogenesis of psoriasis<sup>18</sup>. Lipid profile determines approximate risk for cardiovascular diseases. Dyslipidemia is one of the important risk factor for cardiovascular disease and many studies have been carried out to find the lipid profile in patients with psoriasis<sup>19</sup>. The higher prevalence of classic cardiovascular risk factors, like smoking, hypertension and obesity contribute to atherogenesis in psoriasis patients, but psoriasis itself and its systemic treatment may also stimulate premature atherogenesis increasing the cardiovascular risk<sup>20</sup>. Other co-morbid factors increasing the risk of dyslipidemia in psoriatic patients, include higher body mass index (BMI)  $\geq 30\text{kg/m}^2$ , family history of dyslipidemia, sedentary life style, high fat diet,  $\geq$  and patients taking retinoid or cyclosporine for the disease. The chronic inflammatory nature of psoriasis and dyslipidemia have been suggested to be contributing risk factors for the development of co morbidities like atherosclerosis, coronary artery disease and myocardial infarction resulting in increased cardiovascular mortality<sup>13,14,21</sup>.

This cross sectional study was conducted from July 2016 to June 2017. According to diagnostic criteria a total 55 diagnosed patients of psoriasis attending in the outpatient department of Dermatology and Venereology, Dhaka Medical College Hospital were selected as Group A. Counseling of the psoriasis patients were done and requested to attend the hospital with at least 8 hours fasting till collection of blood sample. Then same number of age and sex matched 55 apparently healthy individuals for comparing group as group B were selected from hospital premises by personal contacts among doctors, nurses, patients attendants and visitors. Counseling of the healthy individuals was also done and requested them to come with at least 8 hours fasting. After selection of the subjects, the objectives, natures, purpose and potential risk of all procedures used for the study were explained again in details and informed written consent were taken from both the patients and normal healthy individuals. Data were collected in a predesigned data collection sheet including particulars of the patients, history, physical and clinical examinations from all the subjects. All data were recorded in a predesigned data collection sheet. Continuous variables were expressed as mean  $\pm$  SD and were compared between groups by unpaired Student's t tests. Categorical variables were compared using chi-square tests and were presented as absolute frequencies with percentages. Spearman's rank correlation coefficient (r) test was used to compare relationship between parameters and psoriasis. All p values were two-tailed with significance defined as  $p < 0.05$  at the level of 95% confidence interval. All analysis was done using the SPSS version 21 package for windows.

### Results:

This cross sectional study was aimed to evaluate the relation of serum lipid profile in patients with psoriasis. For this purpose the baseline parameters were measured and biochemical parameters were estimated and statistical analysis was done according to data to prove the hypothesis. All data were processed to compute mean and standard deviation.

Difference of mean between two groups were compared by unpaired Student's 't' test, chi-square test and determination of correlation between variables was done by Spearman's ranks correlation coefficient (r) test. For all statistical analysis  $p < 0.05$  was considered as significant. Result were presented by tables and figures in the following few pages.

**Table 1: Serum lipid profile status of study subjects in both groups (N=110)**

Parameters	Groups		p value
	Group A (n=55) (mean $\pm$ SD)	Group B (n=55) (mean $\pm$ SD)	
Serum total cholesterol (mg/dl)	218.65 $\pm$ 26.90	140.73 $\pm$ 19.89	< 0.001
Serum HDL-C (mg/dl)	38.27 $\pm$ 2.61	46.56 $\pm$ 2.82	< 0.001
Serum LDL-C (mg/dl)	146.05 $\pm$ 19.18	98.42 $\pm$ 10.48	< 0.001
Serum triglyceride (mg/dl)	163.09 $\pm$ 30.40	106.71 $\pm$ 9.88	< 0.001

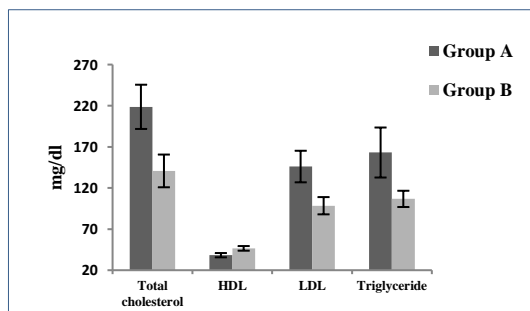
Unpaired Student's t test was done to measure the level of significance.

Group A: Psoriasis patients.

Group B: Healthy individuals.

Level of significance at p value < 0.05

**Table 1:** Shows comparison of serum lipid profile status between psoriasis patients and healthy persons. Where Serum total cholesterol, LDL and triglyceride were significantly high and HDL was significantly low in psoriasis patients than healthy persons.



**Fig-1:** multiple Bar diagram showing serum Lipid profile status of study subjects in both groups



**Table 2: Correlation of serum lipid profile with psoriasis**

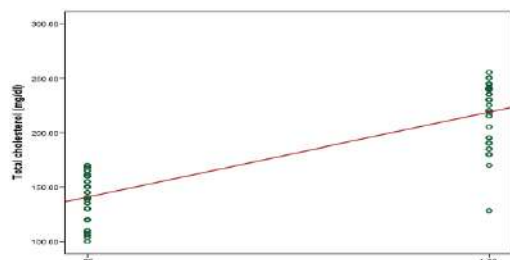
	Group A	
	r value	p value
Total cholesterol	+0.857	< 0.001
HDL-C	-0.838	< 0.001
LDL-C	+0.841	< 0.001
Triglycerides	+0.783	< 0.001

Spearman’s ranks correlation coefficient test were done to measure the level of significance.

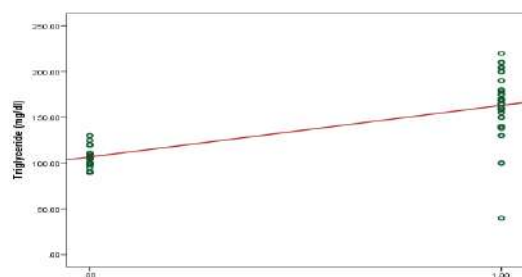
Group A: Psoriasis patients.

Level of significance at p value < 0.05

**Table 2** shows correlation of serum lipid profile with psoriasis. Serum prolactin, TC, LDL-C and TG were significant positive correlation with psoriasis and HDL-C was significant negative correlation with psoriasis.



**Figure 2:** Scatter diagram showing correlation of serum total cholesterol with psoriasis ( $r = +0.857$ ,  $p < 0.001$ ).



**Figure 3:** Scatter diagram showing correlation of serum triglyceride with psoriasis ( $r = +0.783$ ,  $p < 0.001$ ).

**Discussion:**

This cross sectional study was aimed to evaluate the relation of serum lipid profile in patients with psoriasis. In this study compared some baseline demographic, clinical and anthropometric characteristics of study subjects as well as their few laboratory features were compared between psoriatic patients and apparently healthy individuals. There were no differences among groups in terms of these characteristics and features which reflected the homogeneity among the groups. In present study, mean  $\pm$  SD of total cholesterol, TG, LDL-C, HDL-C of the group A were  $218.65 \pm 26.90$ ,  $163.09 \pm 30.40$ ,  $147.05 \pm 19.18$  and  $38.27 \pm 2.61$  mg/dl respectively. The mean  $\pm$  SD of serum total cholesterol, TG, LDL-C, HDL-C of group B were,  $140.73 \pm 19.89$ ,  $106.71 \pm 9.88$ ,  $98.42 \pm 10.48$  and  $46.56 \pm 2.82$  mg/dl respectively. Serum TC, TG, LDL-C were found significantly higher ( $p < 0.001$ ) where serum HDL-C was found significantly lower ( $p < 0.001$ ) in group A when compared to group B. These results were in agreement with the studies done by Amita et al, Vaishalidhat et al, Mervate et al and Akhyani et al<sup>19,22-24</sup>. They observed significant increase of serum total cholesterol, LDL-C, TG and significant decrease of serum HDL-C in patients with psoriasis compared to controls.

Spearman’s rank correlation coefficient test was also done to observe the relationship of serum total cholesterol, triglycerides, LDL-C and HDL-C levels with psoriasis. Serum total cholesterol, triglycerides, and LDL-C levels of psoriasis patients show significant positive correlation with psoriasis ( $r = + 0.857$ ,  $r = + 0.783$ ,  $r = + 0.841$  respectively and  $p < 0.001$  for each). HDL-C level shows significant negative correlation with psoriasis ( $r = - 0.838$ ,  $p < 0.001$ ). These results were in harmony with the study done by Amita et al<sup>22</sup>, Xiaowen et al<sup>25</sup> and Mehdi et al<sup>26</sup>. They reported a significant positive correlation of serum total cholesterol, triglycerides and LDL-C with psoriasis and also reported a significant negative correlation of HDL-C with psoriasis. But present results differ with the study done by Chetana et al<sup>27</sup>.

In their study the authors did not find any significant correlation between lipid profile with psoriasis due to the relatively smaller sample size which means further studies with larger numbers of patients are required to confirm of these findings.

### Conclusion:

In the conclusion, the study demonstrates dyslipidemia are related with psoriasis. Therefore, it is advocated that regular screening of serum lipid profile in psoriatic patients to reduce the risk of exacerbation of psoriasis and help to prevent the complication of dyslipidemia.

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## A Study on Determination of Prescription Writing Errors in Private Practitioners in Bangladesh

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### Abstract:

**Introduction:** Prescriptions enable patients to receive medications that are unsafe for sale directly and also ensure precision in the interests of safety and efficacy and prevention of fraudulent misuse. The present study was conducted to evaluate the prescription writing errors. **Material and Methods:** It was a prospective observational study. Random 300 samples of prescriptions were collected from different patients from January 2021 to October 2021 over the period of 10 months. All prescriptions 300 were analyzed using a pro forma based on the standard of WHO prescription writing parameters. prescription writing errors such as errors of omission related to prescriber (Patients name, Age, O/P Number, Date, Prescribers name, Prescribers signature, Clinic/department, Weight, Diagnosis and illegible prescriptions); errors of omission related to drugs (Route of administration, Dose, Frequency, Strength, Dosage form, Duration/number of doses, Quantity to supply) and errors of commission (Wrong strength, Wrong dosage form, Drug-drug interactions, Wrong drug name) were documented and percentage (%) of various errors related to the errors of omission and errors of commission were calculated and analyzed. **Results:** Out of 300 prescriptions a total of 345 errors of omission related to prescriber were reported with an average of 1.15 errors per prescription and 265 errors of omission related to drugs were reported with an average of 0.88 errors per prescription and also a total of 98 errors of commission were reported with an average of 0.32 error per prescription. Among 610 errors of omission, 345 errors of omission related to prescriber (1.15 errors per prescription) were reported due to failure to mention prescribers name 194 (64.67%) followed by weight 39 (13%), illegible prescriptions were 28 (9.33%), signature of prescriber 25 (8.33%), diagnosis 24 (8%), respectively, and 265 errors of omission related to drugs (0.88 errors per prescription) were reported due to failure to mention duration/no of doses 132 (44%), quantity to supply 55 (18.33%), strength 43 (14.33%), and frequency 15 (5%) respectively. Among 300 prescriptions, 98 errors of commission were found. Among them errors regarding wrong dosage form were 55 (18.33%) followed by wrong strength 19 (6.33%), wrong drug name 14 (4.67%) and drug-drug interactions 10 (3.33%) prescriptions. **Conclusion:** Error reduction strategies, such as an error reporting system and computerized prescription system, may be implemented to avoid preventable medication errors and monitoring of the prescribers' prescription trends is also recommended.

**Keywords:** Prescription writing errors, errors of omission, errors of commissions

### Introduction:

The prescription is the means by which patients receive medicines that are considered unsafe for sale directly to the public. Its format is officially regulated to ensure precision in the interests of safety and

efficacy, and to prevent fraudulent misuse; full details appear in national formularies, and prescribers have a responsibility to comply with these<sup>1</sup>.

Drugs play an important role in protecting in maintaining and resorting health. The goal of drug therapy is to improve a patient's quality of life. Medicine plays a vital role in drug therapy. The drug should be used in the right way knowing what medicine is right for a patient at the right dose for adequate periods as per clinical need<sup>2</sup>. The prescription is a legal document comprising instructions for medication by a licensed medical

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practitioner to the pharmacist<sup>3</sup>. In general, self-medication, polypharmacy, inappropriate use of antibiotics, overuse of injectable medication and the prescribing of medicines without following clinical practice guidelines are common causes of inappropriate use of medicines<sup>2</sup>. A prescription order should clearly communicate with a pharmacist/dispenser what therapy a particular patient is to get: how much of a specific medicine should be taken, how often and for how long. It should also clearly identify the prescriber, be signed in ink, and be dated<sup>4</sup>.

A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use<sup>5</sup>. The National Coordinating Council for Medication Error reporting and prevention (NCCMERP) reported that, 15% of the medication errors occurred because of illegible handwriting, problems with leading and trailing zeroes, misinterpreted abbreviations, and incomplete medication orders<sup>6</sup>. The prescription errors are mainly of two types, errors of omission and errors of commission. Errors of omission mean prescription missing essential information, while errors of commission mean wrongly written information in the prescription<sup>7</sup>. The errors of prescribing are the commonest form of avoidable medication errors and are considered to be the most important target for improvement<sup>8</sup>. Prescriptions containing writing errors communicate incompletely or inadequately to the pharmacist and may have various detrimental consequences. Some errors will require the pharmacist simply to use additional professional judgment in the interpretation and execution of the prescription.

The errors of omission may cause the pharmacist, physician, and patient to waste time while the pharmacist calls the physician to complete the prescription. Unfulfilled legal requirements prevent the prescriptions from being executed or may transfer liability to the pharmacist if the prescription is dispensed<sup>9</sup>.

Hence the present study was conducted to evaluate the prescription writing errors; by way of this the need of educating the prescribers in prescription writing will be determined. This will help to reduce the medication errors due to prescription writing.

### **Materials and methods:**

It was a prospective observational study carried out from January 2021 to October 2021 over the period of 10 months. Samples of prescriptions (by private practitioners) were collected from patients randomly. Mode of collection was copied prescriptions by photocopy or by digital camera after taking consent of patients. A total of 300 prescriptions were the study sample. No attempt has been made to categorize the prescriptions according to patient's age, sex or disease profile. Afterwards all prescriptions (300) were analyzed using a pro forma based on the standard of WHO prescription writing parameters<sup>10</sup>.

The prescription writing errors such as errors of omission related to prescriber (Patients name, Age, O/P Number, Date, Prescribers name, Prescribers signature, Clinic/department, Weight, Diagnosis and illegible prescriptions); errors of omission related to drugs (Route of administration, Dose, Frequency, Strength, Dosage form, Duration/number of doses, Quantity to supply) and errors of commission (Wrong strength, Wrong dosage form, Drug-drug interactions, Wrong drug name) were documented in a suitably designed documentation form.

### **Data analysis:**

From the data collected the percentage (%) of various errors related to the errors of omission and errors of commission were calculated and analyzed.

**Results:****Prescription writing errors**

Out of 300 prescriptions a total of 345 errors of omission related to prescriber were reported with an average of 1.15 errors per prescription and 265 errors of omission related to drugs were reported with an average of 0.88 errors per prescription and also a total of 98 errors of commission were reported with an average of 0.32 error per prescription (Table 1).

**Table 1. Prescription writing errors**

S. No	Types of errors	Total errors (E= 708)	Error per prescriptions
1	Error of commission	610	2.03
	Related to:		
	Prescriber	345	1.15
	Drugs	265	0.88
2	Error of commission	98	0.32

**Errors of omission:**

Among 610 errors of omission, 345 errors of omission related to prescriber (1.15 errors per prescription) were reported (Table 1) due to failure to mention prescribers name 194 (64.67%) followed by weight 39 (13%), illegible prescriptions were 28 (9.33%), signature of prescriber 25 (8.33%), diagnosis 24 (8%), (Table 2) respectively, and 265 errors of omission related to drugs (0.88 errors per prescription) were reported due to failure to mention duration/no of doses 132 (44%), quantity to supply 55 (18.33%), strength 43 (14.33%), and frequency 15 (5%) respectively (Table 3).

**Table 2. Errors of omission related to the prescriber.**

Types of errors	Number of errors	Percentage of errors
Patients name not mentioned	0	0%
Age not mentioned	35	11.67%
O/p number not mentioned	0	0%
Date not mentioned	0	0%
Prescribers name not mentioned	194	64.67%
Prescribers signature not mentioned	25	8.33%
Clinic / department not mentioned	0	0%
Weight not mentioned	39	13%
Illegible	28	9.33%
Diagnosis not mentioned	24	8%

**Table 3. Errors of omission related to the drugs.**

Types of errors	Number of errors	Percentage of errors
Route not mentioned	0	0%
Dose not mentioned	0	0%
Frequency not mentioned	15	5%
Strength not mentioned	43	14.33%
Dosage form not mentioned	20	6.67%
Duration or number of doses not mentioned	132	44%
Quantity to supply not mentioned	55	18.33%

**Errors of commission:**

Among 300 prescriptions, 98 errors of commission were found. Among them errors regarding wrong dosage form were 55 (18.33%) followed by wrong strength 19 (6.33%), wrong drug name 14 (4.67%) and drug-drug interactions 10 (3.33%) prescriptions (Table-4).

**Table 4. Errors of commission.**

Types of errors	Number of errors	Percentage of errors
Wrong strength	19	6.33%
Wrong dosage form	55	18.33%
Drug-drug interactions	10	3.33%
Wrong drug name	14	4.67%

**Discussion:**

A prescription is the reflection of prescriber's attitude towards the disease being treated and the type of health care system in the community<sup>10</sup>. Out of the total 300 prescriptions none was found to have all the standard prescription attributes and parameters. The study revealed that there was an average of 2.36 errors per prescription. All the prescription (100%) was having one or other prescription writing errors. There is no single prescription without errors.

In this study among 610 errors of omission, 345 errors of omission related to prescriber (1.15 errors per prescription) were reported, these were due to failure to mention age (11.67%) followed by prescribers name (64.67%), signature of prescriber (8.33%), diagnosis (8%) and 9.34% were due to illegible hand writing and 265 errors of omission related to drugs (0.88 errors per prescription) were reported and are due to failure to mention duration/no of doses (44%), strength (14.33%), dosage form (6.67%), quantity to supply (18.33%) and frequency (5%). A total of 98 errors of commission were reported with an average of 0.32 errors per prescription. These commission errors were due to drug-drug interactions (3.33%) followed by wrong dosage form (18.33%), wrong drug name (4.67%) and wrong strength (6.33%).

Similar study conducted by Ather A et al (2013) reported that among 819 errors of omission, 635 errors of omission related to prescriber (2.18 errors per prescription) were reported, these were due to failure to mention age (0%) followed by prescribers name (90%), signature of prescriber (9.31%), diagnosis (9.31%) and 10.34% were due to illegible hand writing and 184 errors of omission related to drugs (0.63 errors per prescription) were reported and are due to failure to mention duration/no of doses (30.68%), strength (14.13%), dosage form (7.93%), quantity to supply (6.20%) and frequency (4.4%). A total of 82 errors of commission were reported with an average of 0.28 errors per prescription. These commission errors were due to drug-drug interactions (9.65%) followed by wrong dosage form (7.93%), wrong drug name (6.55%) and wrong strength (4.13%)<sup>11</sup>.

Whereas study conducted by Abdella and Wabe (2012) reported that prescribers name and signature not written in 83.6%, and 23.7% of prescriptions. Duration of treatment and strength were not written in 37.8% of prescriptions followed by frequency 23.67%, where dose and route of administration were not written in 61.2% and 32.6%<sup>12</sup>.

Another study conducted by Al Khaja KA et al' reported that there were 54.1% of prescriptions with omission errors, length of therapy was not specified in 27.7%, and in 12.8% the dosage form was not stated. In 43.5% of prescriptions with errors of commission, dosing frequency (20.8%) and dose/strength (17.7%)-related errors were most common. Errors of integration such as potential drug-drug interaction comprised 2.4% of all prescribing<sup>13</sup>.

A study conducted by Kuan Mun Ni et al' reported 397 Errors of omission related to prescriber and were due to failure to mention age (32.7%) followed by date (17.1%), clinic or department (16.4%), registration number (0.5%), prescriber's name (1.8%), prescriber's signature (0.3%) and illegible hand writing (7.1%) and 862 errors of omission were due to failure to mention route of administration (80%),

strength (56.3%), dosage form (36.4%), duration or number of doses (8.8%), dose (8.7%), quantity to supply (5.8%), frequency (5.3%) and drug name (0.2%)<sup>14</sup>.

Complete information concerning the medicines being prescribed is crucial in promoting rational use of medicines and minimizing prescription errors. Incomplete information on prescribed medicines may lead to under- or over-dosing. Similarly, incomplete treatment may increase morbidity, while unnecessarily extended treatment may cause harmful effects and subsequently be catastrophic for the patients and their families. The results of this study demonstrate commission errors in almost all prescriptions. The errors of commission represent greater threat to the patient's health than the errors of omission; hence they should be identified and corrected. The commission error such as wrong dosage form and wrong strength may lead to serious consequences as the same drug is available in various dosage forms and also in various strengths.

### Conclusion:

Appropriate error reduction strategies, such as an error reporting system and computerized prescription system, may be implemented to avoid preventable medication errors. For continuous improvement, monitoring of the prescribers' prescription trends is also recommended.

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## Suicidal Hanging: A Retrospective Study of Post Mortem Findings during 2 Years Period in ShSMC Morgue

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### Abstract:

**Background:** Hanging is the most common form of suicide, where death is the ultimate result due to violent asphyxia. Easy availability, simple method and presence of wide ranges of ligature materials at our close surrounding, make hanging a preferred method committing suicide over other methods. Every year around 08 lacs people die as a result of hanging, worldwide. Scenarios in Bangladesh also same **Objective:** The objective of the study was to understand various socio-demographic profiles, characteristics of the victim and various aspects of death due to hanging, so as to suggest some remedial measures. **Methods and Materials:** A cross-sectional study was performed at Shaheed Suhrawardy Medical College (ShSMC) morgue, during the period of January'2019 to December'2021. During this 02 years period, data were collected from 2425 cases of medico legal autopsies by purposive sampling. **Result:** A total of 2425 medico legal autopsies were analyzed, of which 1087 (44.82%) were death due to Hanging. Out of these 1087 cases, maximum 786 (72.49%), death due to hanging were age group of 21-30 years. Majority of the cases 728 (67%) were observed in female and others male 359 (33.25%). More than half of the total victims, 565 (51.95%) had used Dopatta (Orna), as ligature material. Cyanosis of the finger tips and nail beds was the commonest finding, 1044 (95.96%), in cases of Asphyxial death due to hanging. **Conclusion:** Suicidal hanging is observed in the study, mostly within the young age group of 21-30 years. Most of them preferred indoor closed locations for committing suicide. Physical, psychiatric disorders, poverty, Quarrel with spouse, extra marital affairs, drug addiction were the major causative factors.

**Keywords:** Hanging, suicide, asphyxia, ligature, cyanosis

### Introduction:

Hanging is a form of violent asphyxial death, caused by body suspension by a ligature encircles the neck, constricting force being the weight of the body. The body needs not to be suspended completely, as death may result from hanging even in sitting, kneeling or Halfling position<sup>1</sup>. It is called partial hanging, where constricting force is the weight of the head. In hanging cases the manner of death is almost always suicidal and accidental, rarely homicidal.

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Hanging is the most popular mode of suicide in Bangladesh<sup>2</sup>, for its simplicity, availability of objects, less cost effective and in term of efficacy<sup>3</sup>. It produces painless death. Precise mechanism of death in hanging is incompletely understood, causes of death include asphyxia, apoplexy, cerebral ischemia, reflex vagal inhibition, fracture or dislocation of cervical vertebra<sup>4</sup>. Fracture cervical vertebrae is very uncommon except in long drop hanging<sup>5</sup>.

In absence of classical signs of asphyxia, death may occur very rapidly in case of reflex vagal inhibition. In these cases meticulous postmortem examination can confirm or rule out asphyxia owing to hanging. Thus this descriptive retrospective study was performed to assess data on hanging cases and document the characteristics death cases resulting from hanging.

### Materials and methods:

This retrospective cross-sectional study was done in Shaheed Suhrawardy Medical College morgue, Dhaka, Bangladesh during the period of January' 2019 to December'2021. In the mentioned period, data were collected from 2425 cases of medicolegal autopsy; Data were collected on socio-demographic characteristics, nature of ligature materials and postmortem findings. Data were presented by a descriptive frequency and percentage in figure and tables.

### Results:

A total of 2425 medicolegal autopsies were conducted during the period of January, 2019 to December'2021, of which 1087 (44.82%) were death due to hanging. Majority of cases hanging 728 (67%) were observed in female and others 359 (33%) were male. Among all hanging cases 565(51.95%) of victim had used Dopatta (or Orna) as ligature materials and 326 (29.95%) used Nylon rope. Common autopsy findings in case Asphyxial death due to hanging were cyanosis of the finger tips and nail beds present in 1043.32 (96%) and pale white and glistening of subcutaneous tissue underneath the ligature mark 1032 (95%) followed by dried mark of saliva dribbling from mouth were present in 428 (39.36%) cases.

**Table 1: Sex wise distribution (n=1087)**

Sex	Frequency	Percentage
Male	359	33.03
Female	728	66.97
N=1087	1087	100

It shows that majority of the victims were female,728 (67%)

**Table 2: Age wise distribution (n=1087)**

Age group (Years)	Frequency	Percentage
10-20	159	14.62
21-30	524	48.20
31-40	282	25.94
41-50	76	06.99
51-60	46	4.25
n=	1087	100

It shows that most vulnerable age group was 21-30 years with total cases 524 (48%).

**Table 3: Distribution according to ligature materials used**

Material used	Frequency	Percentage
Dupatta (Orna)	565	51.98
Nylon rope	325	29.89
Sharee	79	07.27
Electric wire	23	02.11
Bedsheet	21	01.93
Gamcha	46	04.23
Lungi	11	01.19
Cloths	17	01.40
n=	1087	100

Ligature materials used, was Dopatta (Orna) 565 (52%).

**Table 4: Socio-economic status**

Socio-economic status	Frequency	Percentage
Low	964	88.64
Middle	123	11.36
n=	1087	100

It shows that incidence in low socio-economic status is higher than middle class.

**Table 5: Distribution of circumstances how dead body was found**

Valid	Frequency	Percentage
In house with locked door	830	76.36
In house with open door	203	18.67
Out of the house	54	4.97
n=	1087	100

It shows that inside the house with locked door is more common circumstance.

**Table 6: Manner in autopsy report**

Valid	Frequency	Distribution
Suicide	1087	100%
Homicide	00	0%
Accidental	00	0%
n=	1087	100

It shows that Manner of death was suicide in all cases.

**Table 7: Specific cause of death determined by autopsy**

Valid	Frequency	Distribution
Suicide	1087	100%
Negative/Obscure	00	0%
n=	1087	100

It shows cause of death was hanging in all case.

**Table 8: Point of suspension**

Valid	Frequency	Distribution
Ceiling fan	261	24.01%
Angle of roof	826	75.99%
n=	1087	100

It shows that angle of roof is the commonest point of suspension

**Table 9: Type of ligature**

Valid	Frequency	Distribution
Oblique	1087	100%
Non-continuous	1087	100%
High-up of neck	1087	100%

The ligature mark was oblique, non-continuous and high up of the neck in all cases.

**Table 10: Position of ligature mark**

Valid	Frequency	Percentage
Above the thyroid cartilage	1073	98.71%
Over the thyroid cartilage	14	1.29%
n=	1087	100

The commonest level of the ligature mark was above the thyroid cartilage.

**Table 11: Peri ligature Injury presents:**

Valid	Frequency	Percentage
Abrasion	1073	98.71%
Bruise	14	01.29%
n=	1087	100

It shows Commonest peri ligature injury were abrasions (99%).

**Discussion:**

Now a day, suicide has become a major health issue throughout the world, despite all legal, moral, social and religious barriers. It is often a neglected issue to researchers, health policy makers and health professionals<sup>6</sup>. According to WHO, suicide is the second leading cause of death globally. Hanging cases are increasing worldwide<sup>7</sup> and most of these cases are suicidal. In our study, most of suicidal hanging cases were found in the age group of 21-30 years. In developed countries like UK, suicide is three to four times more common in men than women of any age group<sup>8</sup>. On the contrary, suicide rate is higher in women in our country<sup>9</sup>, which reflected in our study. Due to inequity of gender, familial and social maltreatment, marital disharmony, lack of economic freedom, early marriage, low literacy, sexual abuse, poverty, lack of job, defamation and drug abuse are main causative factors for suicide by hanging. Majority of the victims use Dopatta (Orna), followed by Nylon (rope), Sharee and electrical wire as ligature material. In various previous studies also shows Orna, Sharee, cloths were preferred material for hanging, and hard materials like iron wire, cable wire etc. were rarely used. A similar observation also has shown in our study. In present study, Cyanosis of the finger tips and nail bed of both hands was the commonest finding followed by pale, white, hard glistening subcutaneous tissue underneath the ligature mark (Parchmentization) and dried mark of saliva dribbling from mouth. These findings are most important signs of asphyxia and are mentioned in every literature available<sup>10</sup> and also reflected in our study.

**Ethical considerations:**

The confidentiality of cases (Dead bodies), information was maintained when the data were obtained from the post mortem records.

**Acknowledgement:**

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**Conclusion:**

Hanging as a method of suicide is difficult to prevent. However careful screening of susceptible persons, close watch and monitoring of their behavior and psychological counseling can reduce the rate of suicide. A well designed and comprehensive program is required to identify the causative factors and prevent suicidal impulse. As suicide is stigmatized, it remains under reported. Public health authorities must prioritize this big issue. Vulnerable group identification, appropriate education, gender equity, female education with empowerment, prevention of early marriage may help to reduce suicide by hanging<sup>11</sup>. Increasing social awareness against suicide with the active use of print and electronic medias well as religious leaders like 'Imam', 'Purohit' and the involvement of young generation in suicide prevention campaigns may reduce the rate of suicide by hanging in future<sup>12</sup>.

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## Association of Mental Stress with Fertility Related Factors Among Infertile Women

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### Abstract:

**Background:** Infertility is a major life crisis that contributes to mental stress. Mental stress is regarded as a potential factor for decreasing fertility related quality of life among infertile women, as women are more vulnerable in this dynamism. **Objective:** The aim of the study was to assess the association between mental stress and fertility related quality of life among infertile women **Methods:** This cross-sectional study was conducted from January to December 2019 with 225 infertile women selected from Mohammadpur Fertility Services & Training Center. Infertile Women aged 18 to 49 years were enrolled by convenience sampling technique after approval of Research Review Committee and Ethical Review Committee. **Result:** The mean age ( $\pm$ SD) for the infertile women was (26.32 $\pm$ 5.08) years. Majority, 79.6% were primary infertile and remaining 20.4% were secondary infertile. Majority (80.8%) of the participants had moderate stress and more than half (56.9%) had neutral fertility related quality of life. Association between mental stress and fertility related quality of life was very highly significant ( $p<0.001$ ). Association between mental stress and type of infertility was highly significant ( $p<0.01$ ). The difference between mean of fertility related quality of life (59.31+10.814) and mental stress (20.98+4.05) was statistically very highly significant (One way ANOVA,  $p<0.001$ ). The study reveals that mental stress was strongly associated with quality of life of infertile women. To empower infertile women, appropriate measures should be taken to prevent mental stress and improve fertility related quality of life and wellbeing.

**Keywords:** Mental stress, infertile women

### Introduction:

Infertility is an important component of reproductive health. It is “a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual

intercourse”<sup>1</sup>. Although male infertility contributes to significant part of global cases of infertility, it is more of a women’s burden socially<sup>2</sup>. It can cause significant amount of mental or psychological distress. World Health Organization (WHO) estimated 1 in 8 couples or 12% of married women suffer from infertility<sup>3</sup>. stated that infertile women are more likely to experience higher levels of distress than comparison groups, based on an overview of 10 years of research. Inability to give birth naturally could cause feelings of shame and low self-esteem in infertile women. Infertile patients are subjected to greater mental stress and emotional tension than their fertile counterparts.<sup>3</sup> These findings emphasized the need to treat infertility related mental stress<sup>4</sup>. Mental stress affects all aspects of life and normal functioning<sup>5</sup>.

In many societies, especially in China, infertility and the consequent childlessness are often correlated with stigma and guilt<sup>6</sup>. As a result, infertile women may have a strong sense of loneliness and social stress. The actual rate of infertility in Bangladesh is still unknown but World Infertility Survey revealed that in South

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Asia infertility rate is 4% and 15% based on women at the end of their reproductive lives in the age of 45 to 49 years. In Bangladesh, age-standardized primary and secondary infertility prevalence's estimates 1.7 % and 20.5% women aged 20 to 49 years as calculated using standard Demographic and health surveys in 2004<sup>7</sup>. Infertility remains a neglected issue in Bangladesh's reproductive health policy. The prevalence rate in Bangladesh, according to global review of infertility from world fertility survey, is highest among all south Asian countries<sup>8</sup>.

The rising trend of infertility is gaining importance in the field of public health. The impact of mental stress on infertility related quality of life is an increasingly important topic in recent scientific research. Therefore, the objective of the study is to find out association between mental stress and fertility related quality of life of infertile women in context of Bangladesh. The study may be helpful to prevent mental stress and improve quality of life of infertile women.

### Materials & methods:

This was a cross-sectional study carried out at Mohammadpur Fertility Services and Training Center (MFSTC), Mohammadpur, Dhaka-1207; to find out mental stress with related factors impacting infertility related quality of life among infertile women aged 18 to 49 years. Total study required one year from January 2019 to December 2019. The study actually started with protocol preparation and finished with final report submission. By using conventional method of cross-sectional study sample size was determined. Although maximum effort was given by the researcher feasible sample size was 225 due to the fact of unavailability of infertile women. Convenience sampling technique was followed for data collection with informed written consent of selected infertile women at the center. A pre-tested semi-structured questionnaire was developed in the light of objectives and variables of the study for data collection ensuring clarity and accuracy.

A checklist was used to collect data based on reviewing medical records. Data were collected ensuring the privacy and confidentiality by face-to-face interview of the infertile women.

### Result:

#### Comparison of Means (t-test):

**Table 1: Comparison of mean score of mental stress by selected attributes:**

Attributes		Mean ( $\pm$ SD)	Significance
Occupation	Service	20.85 $\pm$ 4.344	t=1.202 p=0.230
	Housewife	19.92 $\pm$ 4.353	
Family Type	Nuclear	20.09 $\pm$ 4.566	t=0.008 p=0.994
	Joint	20.08 $\pm$ 3.782	
Residential Status	Own Residence	20.23 $\pm$ 4.553	t=0.370 p=0.712
	Rented Apt.	20.01 $\pm$ 4.263	
Family history of infertility	Yes	20.64 $\pm$ 2.341	t=0.495 p=0.621
	No	20.05 $\pm$ 4.458	
Alive child (at present)	Yes	18.43 $\pm$ 4.829	t=-2.772 p=0.006
	No	20.46 $\pm$ 4.161	
Type of infertility	Primary	20.41 $\pm$ 4.183	t=2.216 p=0.028
	Secondary	18.83 $\pm$ 4.813	

Table 1 shows the difference of mean score of mental stress with occupation, family type, residential status, family history of infertility, presence of alive child and type of infertility. The mean of total score of mental stress of those who had no alive child (20.46 $\pm$ 4.161) was higher than those who had alive child (18.43 $\pm$ 4.829). This difference was statistically significant. (t-test, P = 0.006) The mean of total score of mental stress in primary infertility (20.41 $\pm$ 4.183) was higher than secondary infertility (18.83 $\pm$ 4.813). This difference was statistically significant. (t-test, P =0.028)



**Comparison of Means (one-way ANOVA):****Table 2: Comparison of mean of mental stress with selected attribute**

Attributes		Mean ( $\pm$ SD)	Significance
Age	18 – 25	19.92 $\pm$ 4.240	F=1.487 p=0.228
	26 – 32	19.91 $\pm$ 4.353	
	33 – 49	21.57 $\pm$ 4.888	
Educational qualification	Illiterate	19.60 $\pm$ 4.356	F=0.572 p=0.683
	Primary Class (1-5)	20.50 $\pm$ 4.450	
	Secondary Class (6-9) & SSC/ Equivalent	19.64 $\pm$ 3.564	
	HSC/Equivalent	19.95 $\pm$ 5.021	
	Graduation & Post Graduation	20.62 $\pm$ 4.744	
Total Family Member (Number)	1 – 3	20.07 $\pm$ 4.655	F=0.020 p=0.980
	3 – 5	20.21 $\pm$ 3.240	
	5 – 15	20.031 $\pm$ 4.162	
Family monthly income (BDT)	5,000 - 25,000	20.06 $\pm$ 4.350	F=0.245 p=0.783
	25,000 - 50,000	20.34 $\pm$ 4.378	
	50,000 - 100,000	19.43 $\pm$ 4.586	
Duration of infertility (yrs.)	0 – 5	19.84 $\pm$ 4.424	F=2.144 p= 0.120
	5 – 10	21.20 $\pm$ 3.806	
	10 – 17	21.86 $\pm$ 3.676	
Duration of treatment (years)	0 – 5	19.92 $\pm$ 4.399	F=1.807 p=0.167
	5 – 10	21.20 $\pm$ 3.806	
	10 – 15	21.86 $\pm$ 3.676	
Fertility related quality of life	Negative	21.63 $\pm$ 3.543	F=9.8431 p=0.000
	Neutral	20.98 $\pm$ 4.056	
	Positive	18.99 $\pm$ 4.093	
	Very positive	11.75 $\pm$ 7.411	

Table 2 shows the difference of mean score of mental stress with age, educational qualification, number of family members, family monthly income, duration of infertility, duration of treatment, type of treatment taken and fertility related quality of life. Regarding mental stress, the highest (mean  $\pm$  SD = 21.63 $\pm$ 3.543) was those who had negative fertility related quality of life. The rest of the (mean  $\pm$  SD) is shown in table 3. This difference was highly statistically significant. (One-way ANOVA, p = 0.000).

## Discussion:

In the current study, association of mental stress with socio demographic attributes showed no significant association. The present study revealed that the mean age for the infertile women was  $26.32 \pm 5.085$  years. Another cross-sectional study was conducted in China in 2018 among 498 infertile women, age ranged between 19 to 40 years and mean age was  $32.19 \pm 3.83^9$ . A cross-sectional study in Hungary revealed that infertile younger women with mean age  $33.30 \pm 4.85$  years had worse psychological ( $p < 0.001$ ) wellbeing.<sup>10</sup> In contrast to the findings of the current study, a study carried out in Malaysia revealed that infertility related stress was significantly ( $p < 0.05$ ) associated with education level<sup>11</sup>. In a prospective Cohort study in Canada, it was revealed that infertile women with education beyond high school had significantly lower Global stress than those with high school education<sup>12</sup>. In the present study, majority 79.6% were diagnosed with primary infertility and the rest 20.4% were diagnosed with secondary infertility. In another cross-sectional study in Morocco among 120 infertile women 79.2% were primary infertile and rest 20.8% were secondary infertile<sup>13</sup>. Mental stress was associated with type of infertility ( $p = 0.18$ ) and presence of alive child among secondary infertile women ( $p = 0.004$ ). A study conducted in Pakistan with 52.10% primary infertile and 47.91% secondary infertile women revealed that there was statistically significant association ( $p < 0.05$ ) between type of infertility and level of stress<sup>14</sup>. A study conducted in Morocco among 120 infertile women revealed higher stress (16.3%) among primary infertile women.<sup>13</sup> In the present study, it was revealed that, mental stress was highly and significantly associated with quality of life ( $p < 0.0001$ ).

The average mean score of mental stress of primary infertile women ( $20.41 \pm 4.183$ ) was higher than secondary infertile women ( $18.83 \pm 4.813$ ), which was statistically significant (t-test,  $p = 0.028$ ). The average mean of mental stress of infertile women who did not have a living child, was higher ( $20.46 \pm 4.161$ ) than those who had a living child ( $18.43 \pm 4.829$ ) present.

This was highly statistically significant (t-test,  $p = 0.008$ ). A study carried out in Turkey reports anxiety subscale and Hospital Anxiety and Depression Scale score was significantly ( $p < 0.05$ ) higher in infertile group than fertile.<sup>15</sup> Among the participants in the present study, majority 84.9% had infertility for less than 5 years. In a cross-sectional study in Morocco, the mean duration of infertility in 120 couples was ( $7.55 \pm 3.480$ ). Majority had duration of infertility lower than 7 years<sup>13</sup>.

The difference of mean score of mental stress was highly significant with level of quality of life, (One-way ANOVA Test,  $p = 0.000$ ). This was due to mental stress was related to quality of life. The difference of mean score of mental stress was highly significant with duration of infertility and duration of treatment (One-way ANOVA Test,  $p > 0.05$ ). This was due to mental stress was related to these attributes. A study conducted in Brazil revealed that higher infertility related stress in females (One-way ANOVA,  $P < 0.05$ ) than males<sup>16</sup>.

The current study findings reflected a snapshot of the existing scenario prevailing in the country regarding mental stress and quality of life among infertile women. The study revealed that most of the infertile women had neutral quality of life and had moderate stress. There was significant association between quality of life and type of infertility ( $p = 0.000$ ). The presence of an alive child was significantly ( $p < 0.05$ ) related to quality of life and absence of alive child was significantly related to mental stress.

As a whole, the study revealed that there was highly significant ( $p = 0.000$ ) association between mental stress and quality of life among infertile women. The study findings suggest intervention and ongoing research is required to better manage mental stress of infertile women and improve their fertility related quality of life and wellbeing.

**Conclusion:**

There is intricate relationship between mental stress and quality of life among infertile women. Infertility has much public health importance. The vulnerable group- women are at greater risk of all sorts of stigma, neglect and social isolation. Majority of infertile women were diagnosed with primary infertility. Majority of infertile women had moderate stress and majority had neutral quality of life. The current study revealed that there was strong association between mental stress and quality of life. Mental stress was also significantly associated with type of infertility. Available data on this topic in Bangladesh is rare due to scarcity of relevant study in Bangladesh. Infertile women are suffering in silence. Appropriate measures and policy level interventions must be taken for the betterment of their mental health, fertility related quality of life and wellbeing.

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## A Review on Tuberculosis Associated Acute Interstitial Nephritis (AIN)

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### Abstract:

**Summary:** Renal tuberculosis is not uncommon in developing countries like Bangladesh. Among different types of clinical presentation, acute tubulo-interstitial nephritis (AIN) with or without granulomas and central caseating necrosis have been reported. However, a high index of clinical suspicion is necessary for diagnosis. Identification of AFB and DNA in urine show marked variation in sensitivity due to sporadic bacilluria. Renal biopsy may show tubulointerstitial nephritis, epithelioid cells, Langhan's giant cells, granulomas with or without caseation and fibrosis. AFB may or may not be seen with Ziehl – Neelsen stain, but can be grown in liquid and solid culture media. Gene Xpert test can detect DNA in renal biopsy tissue. The treatment regimen is RIPE (Rifampicin, INH, Pyrazinamide, Ethambutol) for 2 months, followed by RI (Rifampicin, INH) for 4 months, in addition of pyridoxine 25 to 50 mg/day for 6 months and prednisolone 1mg/kg/day for 1 month. Patient may need concomitant dialysis. After completion of treatment for renal tuberculosis, patient may or may not recover from renal failure.

**Keywords:** Tuberculosis, acute interstitial nephritis, granuloma.

### Introduction:

Extra pulmonary TB has been reported in as many as 60 to 80% of cases, either alone or associated with pulmonary TB<sup>1</sup>. The most common forms of presentation are lymphadenitis, gastrointestinal, genitourinary, bone, peritonitis, pleural effusion, pericardial effusion, military TB and pyrexia of unknown origin<sup>2</sup>. Urogenital tuberculosis occurs in around 15-25% cases of extra-pulmonary tuberculosis<sup>3</sup>. Renal injury is generally due to urinary tract scarring, and less commonly due to glomerulonephritis or secondary amyloidosis, but interstitial nephritis could be the sole manifestation with or without granulomas<sup>4</sup>.

Acute interstitial nephritis (AIN) is most commonly encountered due to drugs such as non-steroidal anti-inflammatory agents or antibiotics, infections (leptospirosis, legionella, streptococcus) or immunological diseases (Sarcoidosis, Sjogren's syndrome).

A less common form of AIN is granulomatous interstitial nephritis (GIN)<sup>5</sup>. GIN may be a presentation of renal TB<sup>6</sup>. This form of renal TB is easily overlooked due to absence of classical symptoms.

### Pathogenesis:

Currently, the pathogenesis of TB-associated tubule-interstitial nephritis (TIN) is unknown. Like other TIN tuberculosis associated TIN might also be due to immunological mechanism involving tubules and interstitium both kidneys simultaneously, rather than direct bacterial (AFB) invasion only. Therefore, the use of corticosteroids could reduce interstitial fibrosis<sup>7</sup>. Shribman et al. showed a case of miliary TB complicated by an immune complex nephritis, which might favor the immunological mechanism in TB-associated renal injury<sup>8</sup>. If acute tubulo interstitial nephritis is not treated properly, it will progress to irreversible chronic tubulo interstitial nephritis.

### Pathology:

There is tuberculous involvement of the renal interstitium in absence of typical renal destruction with calcification, fibrosis or urinary tract obstruction in interstitial nephritis.

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Tubules show focal lymphocytic infiltration of the epithelium. The tubular lumina shows hyaline casts, granular debris and a neutrophilic collection. The interstitium may appear edematous without or with multiple granulomas composed of epithelioid histiocytes and few Langhan's type of giant cells. Granulomas may or may not show caseous necrosis. Interstitium may also show a mixed inflammatory infiltrate composed of lymphocytes, plasma cells, eosinophils and neutrophils<sup>6</sup>. AFB may or may not be seen with appropriate stain<sup>9</sup>.

Glomeruli are normal in size with or without focal and mild mesangial hyper-cellularity. There is no endocapillary proliferation or crescents formation.

### **Clinical presentation:**

This is an insidious form of renal tuberculosis which may be easily missed due to lack of classical symptoms.

In one report, three patients presented with advanced renal failure, in whom imaging showed equal sized smooth kidneys<sup>10</sup>. Renal biopsy revealed interstitial granulomas with caseation and AFB by conventional stain<sup>10</sup>.

Another case report showed, the patient noticed general sickness, weight loss, nocturnal fever 2 months after her last delivery. Physical examination was unremarkable. Renal ultrasonography was normal. Urinalysis revealed low tubular proteinuria, sterile leukocyturia and no hematuria<sup>4</sup>. Renal biopsy showed tubulointerstitial nephritis without granuloma. Because all lab tests- failed to isolate Mycobacterium tuberculosis in the kidney, a targeted biopsy guided by PET- CT was done on mediastinal LN, revealing a positive culture. After 6 months of treatment, no recovery of renal injury has been observed<sup>4</sup>.

Another report showed rapidly progressive glomerulonephritis (RPGN) like presentation, who was initially treated with hemodialysis. After adequate dialysis, renal biopsy was done that showed multiple granulomas composed of epithelioid histiocytes, few Langhan's type giant cells.

One granuloma showed caseous necrosis<sup>6</sup>. The presence of tuberculous DNA in the biopsy specimen was demonstrated. The patient was treated with anti-tuberculous therapy and steroids, besides 11 sessions of hemodialysis. He recovered at last and became dialysis independent<sup>6</sup>.

Khilji et al showed a case of an immigrant female patient who developed acute renal failure with clinical and biochemical features suggestive of lupus nephritis. But a timely renal biopsy showed caseating granuloma in the renal parenchyma consistent with renal tuberculosis. Despite treatment with antituberculosis drug and resolution of TB on repeat renal biopsy, the patient remained hemodialysis dependent<sup>11</sup>.

Do Vale et al showed eight patients presented with dyspnea, weakness and vomiting. Three patients had uremic encephalopathy and six patients had severe high anion gap metabolic acidosis. One patient showed cervical, axillary and inguinal lymphadenopathy. All patients were afebrile with normal urinary output, but eGFR <20ml/min1.73m<sup>2</sup>. Five patients had sterile pyuria. Three patients had bacterial urinary tract infections with positive urine culture<sup>12</sup>.

After appropriate antibiotics, patients had persisted pyuria with negative culture. All patients had proteinuria & four had nephrotic range proteinuria. In all patients, tuberculosis was confirmed by gene Xpert, tissue smear and culture.

Four patients had kidney biopsies, one revealed an interstitial nephritis and three revealed granulomatous interstitial nephritis. One was positive for AFB on ZN stain<sup>12</sup>.

Diagnosis of tuberculous interstitial nephritis needs a high degree of suspicion, especially if there is only kidney involvement without lung involvement & fever<sup>13</sup>.

**Diagnosis:****1. CBC:**

Some cases may show eosinophilia, although this is not constant<sup>14</sup>

**2. Urine R/M/E:**

A pattern of tubulointerstitial nephritis (TIN) is preserved diuresis with mild to no proteinuria, no microscopic hematuria. A common abnormality of TIN is sterile pyuria associated with deteriorated kidney function<sup>4</sup>. Some studies show 1 to 2+ albuminuria and normal leukocyturia (<10/hpf) in tuberculous intestinal nephritis<sup>6</sup>. Serial early morning urine samples may be examined and cultured for the presence of AFB.

**3. Smear:**

Diagnosis based on identification of AFB in the urine through Ziehl – Neelsen (ZN) staining or mycobacterial culture have limited sensitivity. Urine culture is particularly hindered by a long turnaround time and a wide variation in sensitivity. Urine PCR techniques appear to be promising. However, there is marked variation in the sensitivity which appears to be due to sporadic bacilluria<sup>15</sup>.

**4. Culture:**

The most accurate way to diagnose TB-the gold standard- is through culture. The two types of culture –liquid and solid, need 2 weeks and 2 months, respectively to grow the organism. Specimens may be urine or kidney biopsy tissue. Culture can detect 30-50% more cases than microscopy and also provide drug susceptibility testing (DST). Therefore, culture can detect drug-resistant TB (DR-TB).

**5. Chest X-ray:**

It should be done to find out the primary lesion, which may or may not show evidence of tuberculosis. Both conventional and digital X-rays can be used to screen for TB. However, an abnormal chest X-ray may indicate other diagnoses, like lung cancer, pneumonia etc. Follow up tests are required. Normal chest x-ray cannot rule out extrapulmonary TB.

**6. Tubercular skin test (TST)/ Mantoux test (MT):**

This skin test is the oldest method for detecting latent TB infection. The test uses PPD, a mixture of more than 200 different compounds from different mycobacterial cells. TST shows poor sensitivity in immunocompromised individuals (false negative results) and poor specificity for BCG vaccinated people (false positive results). TST shows false positive results in the first ten years of vaccination<sup>16</sup>.

**7. QuantiFERON TB gold test:**

It is an interferon gamma release assay (IGRA) based test where a blood sample is used to measure a person's immune reactivity to MTB. It is performed by mixing fresh blood samples with antigens and the results are based on the amount of interferon gamma released. Actually, it is used to diagnosed latent TB infection and should not be used for the diagnosis of active disease.

IGRA test may be indeterminate or negative if patient gets high dose of glucocorticoids<sup>17</sup>, or if patient suffers from CKD<sup>18</sup>.

IGRA uses antigens that are relatively specific to MTB. Therefore, IGRA has higher sensitivity and specificity than TST<sup>19</sup>.

IGRA is faster and do not yield false positive results from previous BCG vaccination, unlike TST.

**8. Renal biopsy:**

Renal biopsy may show tubulo interstitial nephritis, epithelioid cells, Langhan's giant cells, granulomas with or without caseation and fibrosis. AFB may or may not be seen with appropriate stain (ZN stain)<sup>9</sup> Some studies showed that, light microscopy revealed tubulointerstitial involvement with significant inflammatory infiltrate, predominantly eosinophils. Granulomas only develop in 20-30% cases. Identification of acid-alcohol-fast bacilli may be difficult. Immunofluorescence is typically negative and electron microscopy doesn't usually show abnormalities<sup>14</sup>.

Furthermore, in granulomatous interstitial nephritis, differential diagnoses should be made with other possible aetiologies: drugs, sarcoidosis, bacterial infection, viral infection, parasitic infestations, etc<sup>20</sup>.

### 9. PCR for DNA / Nucleic acid amplification test (NAAT):

NAAT is a method used to detect DNA molecules in the samples, therefore it is also called genotypic or molecular testing. NAAT can also do genotypic drug susceptibility testing (DST) to find out resistance to drugs. It is much faster than culture because this technology multiplies the DNA (or RNA) to detect it more easily, rather than waiting for the organism to grow. NAAT is less likely to be affected by contamination. There are three different kinds of WHO-recommended NAAT testing currently:

- I. Gene Xpert MTB / RIF,
- II. Line probe assay (LPA) for TB,
- III. Loop mediated isothermal amplification (LAMP) for TB.

Gene Xpert can detect pulmonary TB, extrapulmonary TB, extrapulmonary TB and rifampicin resistance rapidly (less than 2 hours).

DNA of *Mycobacterium tuberculosis* may be isolated from the renal biopsy in patients with granulomatous interstitial nephritis (GIN) causing rapidly progressive renal failure. PCR for tuberculosis has been shown to have an overall sensitivity, specificity, positive predictive value and negative predictive value of about 97%, 100%, 100% and 94%, respectively<sup>6</sup>

PCR for *M. tuberculosis* in urine is preferred and has greater sensitivity in comparison to microbiological tests. It yields results more quickly.

### 10. CT and PET / CT scanning:

CT and PET / CT scanning are useful in diagnosing spreading of tuberculosis<sup>4</sup>. PET/CT may show uptakes in lymph nodes, kidneys and other foci of tuberculosis. Targeted Biopsy followed by histopathology of the affected organ may show granuloma formation with central necrosis<sup>4</sup>.

CT scan of the thorax, abdomen and pelvis can be performed to see enlarged lymph nodes, e.g., mediastinal, retro gastric or retroperitoneal lymph nodes. Lymph node biopsy may reveal granulomas with or without caseation with or without AFB<sup>11</sup>. After completion of anti-tuberculous therapy, a follow up CT scan can be done to see the resolution of the previously detected lymphadenopathy.

### 11. Nonapproved tests for detection of active TB:

All currently available serological tests for detection of pulmonary and extra-pulmonary/ TB (IgG, IgA, IgM) are not WHO-recommended for use due to low sensitivity (high false negative results) and low specificity (high false positive results). Similarly, WHO does not recommend the use of IGRA, for diagnosis of active TB<sup>20</sup>.

12. Other laboratory tests should be done according to patient's need, like serum creatinine, electrolytes, uric acid, etc. Serum Creatinine may be high requiring dialysis.

### Treatment:

The treatment regimen is based on four anti-tuberculosis drugs, generally, rifampicin (R), isoniazid (I), pyrazinamide (P) and ethambutol (E) – RIPE. This includes 2 months of intensive phase consisting of RIPE, followed by 4 months of continuation phase with RI. Dose reduction is not required for these drugs in renal failure except ethambutol whose dose has to be reduced due to risk of irreversible optic neuritis<sup>14</sup>. If the organism is fully susceptible to isoniazid and rifampicin in drug susceptibility testing (DST), ethambutol can be safely discontinued before completing the first 2 months<sup>21</sup>. In addition, it must be kept in mind that, concomitant treatment with oral steroids 1mg/kg/day for 4 weeks reduces tubulointerstitial inflammation and hence reduces the risk of progression to fibrosis<sup>20</sup>. It is important to start treatment quickly as this favors kidney survival with no need for renal replacement therapy (RRT) in future. Pyridoxine (Vitamin B6) should be administered (25-50 mg/day) to all patients to prevent isoniazid induced peripheral neuropathy and encephalopathy, which can occur in patients with renal failure<sup>22</sup>.



The WHO currently recommends that tuberculosis patients with renal failure should be treated for 6 months with daily rifampicin and isoniazid throughout and thrice weekly ethambutol (15mg/kg) and pyrazinamide (25mg/kg) for the first 2 months. Streptomycin should be avoided. If its use is essential, 15 mg/kg should be injected two to three times weekly, with regular monitoring of drug levels.

The anti-tuberculous drugs should be taken after the hemodialysis session and on an empty stomach on the non-hemodialysis day to minimize loss of medicine in hemodialysis<sup>23</sup>.

Empiric treatment should be used if the test results are negative, but there is still high clinical suspicion, and should be reviewed within one week of treatment to test whether the patients are responding to treatment<sup>24</sup>.

### Prognosis:

Diagnosis must be done as early as possible, preferably when eGFR is >15 ml/min. In subject with an eGFR>15 ml/min at diagnosis, kidney function usually remains stable or improves after treatment<sup>4</sup>. About 66% of patients presenting with an eGFR<15ml/min need to start dialysis within 12 months after diagnosis<sup>14</sup>. Khilji et al showed that after completion of treatment for renal tuberculosis, patient failed to recover renal function and become dialysis dependent. Repeat renal biopsy showed tubulo interstitial fibrosis without any caseating granuloma<sup>11</sup>.

### Conclusion:

Renal tuberculosis usually presents as gross hematuria, sterile pyuria or obstructive uropathy, but can also present with acute kidney injury due to acute tubulo interstitial nephritis with or without granulomas or central caseating necrosis. Tuberculous granulomatous interstitial nephritis may also present with different degrees of proteinuria. High index of suspicion is necessary for the clinician. For confirmation, renal biopsy is necessary prior to starting anti-tuberculosis medicine and steroids. We conclude that massive proteinuria, acute renal failure and granulomatous interstitial nephritis is a

triad of relatively less common manifestation of renal tuberculosis.

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## Case Report

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## Carcinoma Penis in A Patient with Chronic Non-Retractile Foreskin – A Case Report.

Matin ABMA<sup>1</sup>, Hossain SMA<sup>2</sup>, Sarker KK<sup>3</sup>, Samad S<sup>4</sup>, Sheikh MA<sup>5</sup>, Nahar N<sup>6</sup>**Abstract:**

Carcinoma penis is the most rarely observed carcinoma of male urogenital system. But it is commonly seen in the developing countries like South America, Africa & certain parts of Asia. It occurs predominantly in elderly men although the disease may also present in young men. The mean age for diagnosis of penile cancer is 60 years. Risk of penile cancer increases significantly with age, uncircumcision, poor personal hygiene & also HPV infections. The majority of lesions are found on the glans penis (45%), followed by the prepuce (16%), both the glans & prepuce (15%), coronal sulcus (6%) and shaft (<2%). Clinical presentation of squamous cell carcinoma of penis is variable. Patient may present with ulceration or mass or infiltrative lesion. Our patient presented with a longstanding partially retracted preputial foreskin with ulceration at the muco-cutaneous junction of penis. There were discolorations near the glans penis and root of the penis for 4 months. From the history the patient was not circumcised. Patient is married for 45 years. He has 2 off-springs. The patient has no family history of cancer. He has no history of exposure or other personal history. Patient had wide excision of the ulcerative lesion. Confirmation of diagnosis was done as squamous cell carcinoma and excision margin was not free. After Consultation with oncologist partial penectomy was done. The post operative period was uneventful. Patient is on follow up.

**Keywords:** Penile cancer, circumcision, para-phimosis, partial amputation of penis.

**Introduction:**

Penile cancer is an unusual occurrence affecting only 1 in 100000 men world-wide in a year<sup>1</sup>. 1% of male cancers is constituted by penile cancer and most common histological type is squamous cell carcinoma (SCC) in 95% of cases. It is more common in developing countries. It commonly occurs in 6<sup>th</sup> decade <sup>2</sup>.

Most cases of penile cancer are present in uncircumcised males. It is believed that poor hygiene with the buildup of smegma and chronic inflammation of the foreskin and glans contribute to the carcinogenesis of penile cancers. Male circumcision of the foreskin has been shown to be a protective factor in the development of penile cancer<sup>1,3</sup>.

The objective of this work was to report about the occurrence of SCC of the penis in a 68 years old uncircumcised patient with long standing partially retracted preputial foreskin<sup>4</sup>.

**Case presentation:**

**Clinical history:** A 68-years-old Muslim male came with a history of poorly controlled diabetes and hypertension. He presented to the hospital with the chief complaints of ulceration at the penis and white discoloration at root of the penis. The patient reported that the ulcer is persistent for many years but increasing in size since 4 months. On query, he added that, he was not circumcised. Patient has a history of sudden trapping of foreskin behind the glans penis.

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That could not be pulled back completely which causes persistent discomfort. Patient took Ayurveda treatment for many years. Ulcer was subsided by taking pain killers and antibiotics. He has no urinary complaint, no history of exposure. He did not receive HPV vaccination.

He added that, the ulcer was associated with whitish discharge. Discharge was purulent in nature and was neither blood stained nor malodorous.

On examination, patient was anxious looking and anemic. Urinary system found normal. On genital system, Ulcer was located at the muco-cutaneous junction of shaft and glans penis. Size of the ulcer was about (1.5 \*1.0) cm<sup>2</sup> and shape was irregular. It involved the whole circumference of muco-cutaneous junction. Ulcer was slightly tender, with rolled out & everted edge. Margin was irregular. Floor was covered by inflammatory necrotic tissue and base was indurated with firm consistency. Inguinal lymph nodes were not palpable.

Pathological investigation: Wide local excision was done and sent for histopathology that revealed well differentiated squamous cell carcinoma. Excision margin was not free of cancer.

Computed tomography (CT) of the abdomen, and pelvis was done for the staging of the patient's cancer. The imaging revealed: no metastasis in either organ, no ascites, no abdominal or pelvic lymph node enlargement. The patient was staged as a stage I, T1NoMo. After consultation with an oncologist planned for partial amputation of penis. After operation excised specimen was sent for histopathological examination. That revealed no residual tumor. Patient is on follow up.

### Discussion:

Squamous cell carcinoma of the penis is a relatively rare malignancy, accounting for approximately 0.4-0.6% of all malignancies diagnosed among men in the USA and Europe and 10% of cases diagnosed in some African and South American countries<sup>5</sup>.

The lowest incidence has been reported in Israeli Jews, who are routinely circumcised at birth<sup>6</sup>. Penile cancer is most commonly diagnosed in men aged 50-70 years<sup>7</sup>. However, in 22% of cases SCC is diagnosed in men younger than 40 years<sup>8</sup>. The first sign of penile cancer is usually a localized penile lesion on the foreskin or glans. Skin changes include areas of thickening, ulceration, warty growth or discharge and bleeding under foreskin<sup>9</sup>. Ca. Penis is usually a localized disease with metastasis occurring in <3-5% of patients. Inguinal nodes followed by iliac nodes are commonly involved. Most common sites of distal metastasis are retroperitoneal lymph nodes but bone metastasis is rare. Occurrence of bone metastasis is usually localized to axial skeleton<sup>(10,6)</sup>. Factors known to be associated with a higher risk of penile carcinoma include age, poor socio-economic status, smoking, multiple sexual partners, chronic balanitis, inflammation, phimosis and redundant prepuce. Circumcision carried out early in the patient's childhood is considered a protective factor<sup>(11,12,13,14)</sup>. The pathogenesis of penile cancer can be divided into HPV-dependent and HPV-independent pathways. Penile SCC has been associated with high risk HPV infections. HPV-independent penile cancers are commonly associated with a pre-malignant precursors lesion related to chronic inflammation. Further investigations showed that the pathogenesis of penile carcinoma could be correlated with human papilloma virus specially sub-types 16 and 18<sup>15</sup>.

### Conclusion:

Squamous cell carcinoma of the penis is a rare male malignancy and has a heterogeneous presentation. It carries a poor prognosis overall. In a patient with personal history of uncircumcision and a lack of previous HPV vaccination, it is believed that this cancer is HPV-related. It is important for clinician to be aware of the subtle signs of cancerous growths of the penis, as early detection and recognition afford a better prognosis. Initial symptoms are often non-specific. Management is multi-disciplinary following pathologic confirmation and typically involves both surgery and chemo-therapy.

It is important to recognize the psychological impact of the disease, specially with penectomy and the resulting disfigurement of the normal male anatomy. Self-esteem issues, anxiety, depression and lack of sexual satisfaction are all associated with penile carcinoma. These psychological associations should also be taken into consideration by the patient.

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## Medical Quiz

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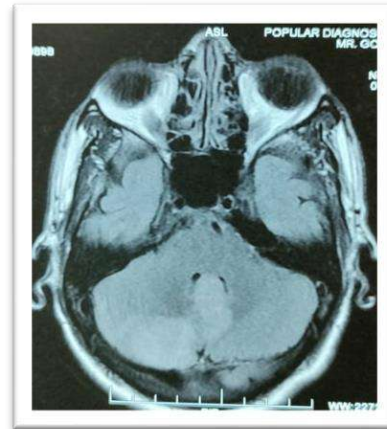
## Medical Quiz: Images

Mamun KAA

A 38 years old male presented with ataxia and vomiting for 10 days. He was treated with ondansetron and betahistine hydrochloride without significant improvement. He was suggested MRI Brain.



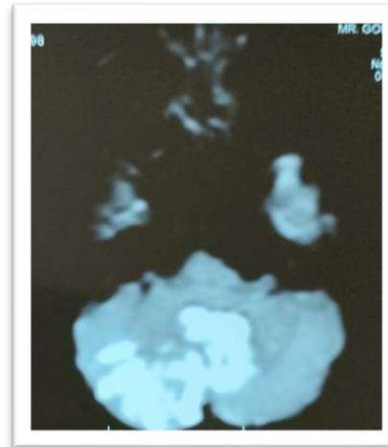
**Figure 1:** MRI brain T1 image showing hypointense lesion occupying both sides of cerebellum.



**Figure 2:** MRI brain T2 image showing hyperintense lesion occupying both sides of cerebellum.



**Figure 3:** MRI brain FLAIR image showing hyperintense lesion occupying both sides of cerebellum



**Figure 4:** MRI brain DWI showing restricted diffusion on both sides of cerebellum

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- ❖ Q1. Mention abnormal findings in MRI brain.
- ❖ Q2. What is the diagnosis?
- ❖ Q3. What further investigations should be done?
- ❖ Q4. What are the treatment options?

### Discussion:

Cerebellar infarcts are relatively uncommon and represent about 2% of all ischemic strokes<sup>1,2</sup>. Potential pathogenesis include hypertension, diabetes mellitus, cardiac emboli, large-vessel atherosclerosis, vertebral artery dissection and less commonly hypercoagulable conditions, vasculitis and venous sinus thrombosis<sup>1-4</sup>. Cardinal features include vertigo, headache, vomiting, and ataxia<sup>3</sup>.—Cerebellar infarcts require special attention because of the danger of cerebral edema within the posterior fossa<sup>4</sup>. The cerebellum and brain stem are tightly constrained by the tentorium cerebelli superiorly and the occipital bone and foramen magnum posteriorly<sup>5</sup>. Within the posterior fossa, cerebral edema can rapidly obstruct the fourth ventricle, causing hydrocephalus. In addition, cerebral edema can compress the brain stem causing potentially fatal transtentorial herniation of the superior vermis through the tentorial notch or downward herniation of the cerebellar tonsils through the foramen magnum<sup>6</sup>. Hydrocephalus may require VP shunting or external ventricular drainage<sup>7</sup>.

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### Answer to Medical Quiz: Images

- ✓ MRI brain shows T1 Hypointense, T2 and FLAIR hyperintense lesion in cerebellum bilaterally. DWI showed restricted diffusion.
- ✓ Bilateral Cerebellar Infarct
- ✓ CBC, RBS, Serum creatinine, ECG, Echocardiography
- ✓ Anti platelet, Statin, Anti vertigo drugs, Antiemeti

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