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Journal of Bangladesh College of Physicians and Surgeons (JBCPS)

INFORMATION FOR AUTHORS

MANUSCRIPT PREPARATION AND SUBMISSION

Guide to Authors

The Journal of Bangladesh College of Physician and Surgeons, provides rapid publication (quarterly publication) of articles in all areas of the subject. The Journal welcomes the submission of manuscripts that meet 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.

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Submit manuscripts as e-mail attachment to the editorial office at: journal.bcps@gmail.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, as an attachment.

The Journal of Bangladesh College of Physicians and Surgeons will only accept manuscripts submitted as e-mail attachments or triplicate Hard copy with a soft copy

Article Types

Five types of manuscripts may be submitted:

Editorials: 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.

Short Communications: A Short Communication is suitable for recording the results of complete small investigations or giving details of new models or hypotheses, innovative methods, techniques, images in clinical practice, letter to editors, short reports or apparatus. The style of main sections need not conform to that of original article. Short communications are 2 to 4 printed pages (about 6 to 12 manuscript pages) in length.

Reviews: Submissions of reviews and perspectives covering topics of current interest are welcome and encouraged. Reviews should be concise and no longer than 4 to 6 printed pages (about 12 to 18 manuscript pages). It should be focused and must be up to date. Reviews are also peer-reviewed.

Case Reports: 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 weeks. The editorial board will re-review manuscripts that are accepted pending revision. The JBCPS editorial board will try to publish the manuscript as early as possible fulfilling all the rigorous standard journal needs.

I.A. Preparing a Manuscript for Submission to JBCPS

Editors and reviewers spend many hours reading manuscripts, and therefore appreciate receiving 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.

Conditions for submission of manuscript:

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

Ethical aspects:

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

Preparation of manuscript:

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

Preparation:

1. Manuscript should be written in English and typed on one side of A4 (290 x 210cm) 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 on separate page :
 - o Title page
 - o Summary/abstract
 - o Text
 - o Acknowledgement
 - o References
 - o Tables and legends.

Pages should be numbered consecutively at the upper right hand corner of each page beginning with 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 sections: Introduction, Methods, Results, and Discussion. This so-called "IMRAD" structure is a direct reflection of the process of scientific discovery.
- Long articles may need subheadings within some sections (especially Results and Discussion) to clarify their content. Other types of articles, such as case reports, reviews, and editorials, probably need to be formatted differently.
- Electronic formats have created opportunities for adding details or whole sections, layering information, crosslinking or extracting portions of articles, and the like only in the electronic version.
- 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 text line 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 printing for reviewing and editing.
- Authors should number on right upper 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 JBCPS 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 is the EQUATOR Network (<http://www.equator-network.org/home/>) or CONSORT network (<http://www.consort-statement.org>).

I. A. 2. Title Page

The title page should have the following information:

1. Article title. Concise titles are 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.
2. Authors' names and institutional affiliations.
3. The name of the department(s) and institution(s) to which the work should be attributed.
4. Disclaimers, if any.
5. Contact information for corresponding authors. The name, mailing address, telephone and fax numbers, and e-mail address of the author responsible for correspondence about the manuscript .
6. The name and address of the author to whom requests for reprints should be addressed or a Statement that reprints are not available from the authors.

7. Source(s) of support in the form of grants, equipment, drugs, or all of these.
8. A short running head or footline, of no more than 40 characters(including letters and spaces). Running heads are published and also used within the editorial office for filing and locating manuscripts.
9. The number of figures and tables. It is difficult for editorial staff and reviewers to determine whether the figures and tables that should have accompanied a manuscript were actually included unless the numbers of figures and tables are noted on the title page.

I. A. 3. Conflict-of-Interest Notification Page

To prevent potential conflicts of interest from being overlooked or misplaced, this information needs to be part of the manuscript. The ICMJE has developed a uniform disclosure form for use by ICMJE member journals (http://www.icmje.org/coi_disclosure.pdf) and JBCPS has accepted that.

I. A. 4. Abstract

- 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
- The abstract should provide the introduction of the study and blinded state and should state the study's purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect sizes and their statistical significance, if possible), principal conclusions. It should emphasize new and important aspects of the study or observations. Articles on clinical trials should contain abstracts that include the items that the CONSORT group has identified as essential (<http://www.consort-statement.org>).
- Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to be careful that they accurately reflect the content of the article

I. A. 5. Introduction

- Provide a context or background for the study (that is, the nature of the problem and its significance). It should be very specific, identify the specific knowledge in the aspect, reasoning and what the study aim to answer.
- State the specific purpose or research objective of, or hypothesis tested by, the study or observation; the research objective is often more sharply focused when stated as a question.
- 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.

I. A. 6. Methods

The Methods section should be written in such way that another researcher can replicate the study.

I. A. 6. a. Selection and Description of Participants

- Describe your selection of the observational or experimental participants (patients or laboratory animals, including controls) clearly, including eligibility and exclusion criteria and a description of the source population. Because the relevance of such variables as age and sex to the object of research is not always clear, authors should explain their use when they are included in a study report—for example, authors should explain why only participants of certain ages were included or why women were excluded. The guiding principle should be clarity about how and why a study was done in a particular way. When authors use such variables as race or ethnicity, they should define how they measured these variables and justify their relevance.

I. A. 6. b. Technical Information

- Identify the methods, apparatus (give the manufacturer's name and address in parentheses), and procedures insufficient detail to allow others to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and brief descriptions for methods that have been published but are not well-known; describe new or substantially modified methods, give the reasons for using them, and evaluate their limitations. Identify precisely all drugs

and chemicals used, including generic name(s), dose(s), and route(s) of administration.

- Authors submitting review article should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

I. A. 6. c. Statistics

- Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals).
- Avoid relying solely on statistical hypothesis testing, such as *P* values, which fail to convey important information about effect size. References for the design of the study and statistical methods should be to standard works when possible (with pages stated).
- Define statistical terms, abbreviations, and most symbols.
- Specify the computer software used.

I. A. 7. Results

- Present results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Please keep the result the sequence of specific objective selected earlier.
- Do not repeat all the data in the tables or illustrations in the text; emphasize or summarize only the most important observations. Extra or supplementary materials and technical detail can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.
- When data are summarized in the Results section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them.
- Restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables.

- Avoid nontechnical uses of technical terms in statistics, such as “random” (which implies a randomizing device), “normal,” “significant,” “correlations,” and “sample.” Where scientifically appropriate, analyses of the data by such variables as age and sex should be included.

I. A. 8. Discussion

- Emphasize the new and important aspects of the study and the conclusions that follow from them in the context of the totality of the best available evidence.
- Do not repeat in detail data or other information given in the Introduction or the Results section.
- For experimental studies, it is useful to begin the discussion by briefly summarizing the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies, state the limitations of the study, and explore the implications of the findings for future research and for clinical practice.
- Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses when warranted, but label them clearly as such.

I. A. 9. References

I. A. 9. a. General Considerations Related to References

- Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible.
- On the other hand, extensive lists of references to original work of a topic can use excessive space on the printed page. Small numbers of references to key original papers often serve as well as more exhaustive lists, particularly since references can now be added to the electronic version of published papers, and

since electronic literature searching allows readers to retrieve published literature efficiently.

- Avoid using abstracts as references. References to papers accepted but not yet published should be designated as “in press” or “forthcoming”; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication.
- Information from manuscripts submitted but not accepted should be cited in the text as “unpublished observations” with written permission from the source.
- Avoid citing a “personal communication” unless it provides essential information not available from a public source, in which case the name of the person and date of communication should be cited in parentheses in the text. For scientific articles, obtain written permission and confirmation of accuracy from the source of a personal communication. Some but not all journals check the accuracy of all reference citations; thus, citation errors sometimes appear in the published version of articles. To minimize such errors, references should be verified using either an electronic bibliographic source, such as PubMed or print copies from original sources.
- Authors are responsible for checking that none of the references cite retracted articles except in the context of referring to the retraction. For articles published in journals indexed in MEDLINE, the ICMJE considers PubMed the authoritative source for information about retractions.

I. A. 9. b. Reference Style and Format

- References should be numbered consecutively in the order in which they are first mentioned in the text.
- Identify references in text, tables, and legends by Arabic numerals in superscript.
- References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure.

I. A. 10. Tables

- Tables capture information concisely and display it efficiently.

- Use tables /fig that are relevant to study
- Try to limit the number of tables/figure
- Type or print each table with double-spacing on a separate sheet of paper. Number tables consecutively in the order of their first citation in the text and supply a brief title for each.
- Do not use internal horizontal or vertical lines. Give each column a short or an abbreviated heading. Authors should place explanatory matter in footnotes, not in the heading. Explain all nonstandard abbreviations in footnotes, and use the following symbols, in sequence:
*, †, ‡, §, —, ¶, **, ††, ‡‡, §§, —, ¶¶, etc.
- Identify statistical measures of variations, such as standard deviation and standard error of the mean.
- Be sure that each table is cited in the text. If you use data from another published or unpublished source, obtain permission and acknowledge that source fully.

I. A. 11. Illustrations (Figures)

- Figures should be either professionally drawn and photographed, or submitted as photographic-quality digital prints. In addition to requiring a version of the figures suitable for printing, (for example, JPEG/ GIF)
- Authors should review the images of such files on a computer screen before submitting them to be sure they meet their own quality standards. For x-ray films, scans, and other diagnostic images, as well as pictures of pathology specimens or photomicrographs, send sharp, glossy, black-and-white or color photographic prints, usually 127 _ 173 mm (5 _ 7 inches)
- Letters, numbers, and symbols on figures should therefore be clear and consistent throughout, and large enough to remain legible when the figure is reduced for publication.
- Photographs of potentially identifiable people must be accompanied by written permission to use the photograph. Figures should be numbered consecutively according to the order in which they have been cited in the text.
- If a figure has been published previously, acknowledge the original source and submit written permission from the copyright holder to reproduce the figure. Permission is required irrespective of

authorship or publisher except for documents in the public domain.

- For illustrations in color, JBCPS accept coloured illustration but when it seems essential. This Journal publish illustrations in color only if the author pays the additional cost. Authors should consult the journal about requirements for figures submitted in electronic formats.

I. A. 12. Legends for Illustrations (Figures)

- Type or print out legends for illustrations using double spacing, starting on a separate page, with Arabic numerals corresponding to the illustrations.
- When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend. Explain the internal scale and identify the method of staining in photomicrographs.

I. A. 13. Units of Measurement

- Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples.
- Authors should report laboratory information in both local and International System of Units (SI).
- Drug concentrations may be reported in either SI or mass units, but the alternative should be provided in parentheses where appropriate.

I. A. 14. Abbreviations and Symbols

- Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers.
- Avoid abbreviations in the title of the manuscript.
- The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

I. B. Sending the Manuscript to the Journal

- If a paper version of the manuscript is submitted, send the required number of copies of the manuscript and figures; they are all needed for peer review and editing, and the editorial office staff cannot be expected to make the required copies.
- Manuscripts must be accompanied by a cover letter, conflicts of interest form, authorship and declaration, proforma of which is available in JBCPS web site.

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

Submission Preparation Checklist

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.

Check Lists

Final checklists before you submit your revised article for the possible publication in the Journal of Bangladesh College of Physicians and Surgeons:

1. Forwarding/Cover letter and declaration form
2. Authorship and conflicts of interest form
3. Manuscript
 - o Sample of the above documents is available in the following links: <http://www.bcpsbd.org> (registration required for download)
 - o If you have submitted mention document (1, 2, 3) above, when you first submitted your article then you don't need to re-submit but if there is change in the authorship or related then you have to re-submit it.
- General outline for article presentation and format
 - Δ Double spacing
 - Δ Font size should be 12 in arial
 - Δ Margins 5 cm from above and 2.5 cm from rest sides.

- Δ Title page contains all the desired information (vide supra)
- Δ Running title provided (not more than 40 characters)
- Δ Headings in title case (not ALL CAPITALS, not underlined)
- Δ References cited in superscript in the text without brackets after with/without comma (,) or full stop (.)
- Δ References according to the journal's instructions – abide by the rules of Vancouver system. Use this link to get into the detail of Vancouver system.

• **Language and grammar**

- Δ Uniformity in the language
- Δ Abbreviations spelt out in full for the first time
- Δ Numerals from 1 to 10 spelt out
- Δ Numerals at the beginning of the sentence spelt out

• **Tables and figures**

- Δ No repetition of data in tables/graphs and in text
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- Δ Figures necessary and of good quality (colour)
- Δ Table and figure numbers in Arabic letters (not Roman)
- Δ Labels pasted on back of the photographs (no names written)
- Δ Figure legends provided (not more than 40 words)
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- Δ Credit note for borrowed figures/tables provided
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Manuscript Format for Research Article

• **Title**

- Δ Complete title of your article
- Δ Complete author information
- Δ Mention conflict of interest if any

- **Abstract**
 - Δ Do not use subheadings in the abstract
 - Δ Give full title of the manuscript in the Abstract page
 - Δ Not more than 200 words for case reports and 250 words for original articles
 - Δ Structured abstract (Including introduction, methods, results and discussion, conclusion) provided for an original article and (Introduction, results and discussion , conclusion) for case reports.
 - Δ Key words provided – arrange them in alphabetical order (three – five)
- **Introduction**
 - Δ Word limit 150 -200 words
 - Δ Pertinent information only
- **Material and Methods**
 - Δ Study Design
 - Δ Duration and place of study
 - Δ Ethical approval
 - Δ Patient consent
 - Δ Statistical analysis and software used.
- **Result**
 - Δ Clearly present the data
 - Δ Avoid data redundancy
 - Δ Use table information at the end of the sentence before full stop between the small bracket
- **Discussion**
 - Δ Avoid unnecessary explanation of someone else work unless it is very relevant to the study
 - Δ Provide and discuss with the literatures to support the study
 - Δ Mention about limitation of your study
- **Conclusion**
 - Δ Give your conclusion
 - Δ Any recommendation
- **Acknowledgement**
 - Δ Acknowledge any person or institute who have helped for the study
- **Reference**
 - Δ Abide by the Vancouver style
 - Δ Use reference at the end of the sentence after the full stop with superscript
- **Legends**
 - Δ Table
 - Δ Figures

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Zika Virus Infection: Are We Aware?

Zika virus (ZIKV) is an enveloped, single stranded RNA virus which is transmitted by daytime-active *Aedes* mosquitoes. Its name comes from the Zika Forest of Uganda, where the virus was first isolated in 1947. In human, the virus causes a mild illness known as Zika fever, Zika, or Zika disease, which since the 1950s has been known to occur within a narrow equatorial belt from Africa to Asia.

In April 2007, the first outbreak outside of Africa and Asia occurred on the island of Yap in the Federated States of Micronesia, which was initially thought to be dengue, chikungunya or Ross River disease.¹ In 2014, the virus spread eastward across the Pacific Ocean to French Polynesia, then to Easter Island and in 2015 to Mexico, Central America, the Caribbean, and South America, where the Zika outbreak has reached pandemic levels.² In February 2016, the WHO declared the virus outbreak a public health emergency of international concern. A number of countries have issued travel warnings.

The virus is mainly spread by the *Aedes aegypti* mosquito, which is commonly found throughout the tropical and subtropical Americas, but also by *Aedes albopictus*, “Asian tiger” mosquitoes that now have become widespread up to the Great Lakes area of the United States.³ Studies show that the extrinsic incubation period in mosquitoes is about 10 days.⁴ Zika virus can migrate between humans through sexual contact and it can also cross the placenta, affecting an unborn fetus. A mother already infected with Zika virus near the time of delivery can pass on the virus to her newborn around the time of birth, but this is rare. The vertebrate hosts of the virus are primarily monkeys and humans.

The potential societal risk of Zika virus can be delimited by the distribution of the mosquito species that transmit it (its vectors). The global distribution of the most cited carrier of Zika virus, *A. aegypti*, is expanding due to global trade and travel.⁵

Zika virus is related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses. Common symptoms of infection with the virus include mild headaches, maculopapular rash, fever, malaise, conjunctivitis, and joint pains. Within two days, the rash started fading, and within three days, the fever resolved and only the rash remained. Thus far, Zika fever has been a relatively mild disease of limited scope, with only one in five persons developing symptoms, with no fatalities and poses a significant threat only in pregnancy.

It is difficult to diagnose Zika virus infection based on clinical signs and symptoms alone due to overlaps with other arboviruses that are endemic to similar areas.⁶ The methods currently available to test for Zika antibodies cross-react with dengue antibodies. Zika IgM ELISA test should be considered indicative of a recent flavivirus infection. Plaque reduction neutralization tests (PRNT) can be performed to measure virus specific neutralizing antibodies to Zika virus and may be specific.⁷ Zika virus can be identified by RT-PCR in acutely ill patients. However, there are no commercially available diagnostic tests for Zika virus.

Symptoms can be treated with rest, fluids, and paracetamol while non-steroidal anti-inflammatory drugs should be used only when dengue has been ruled out.

Zika virus infections have been confirmed in several infants with microcephaly; Guillain–Barré syndrome and other neurologic conditions may be complications of Zika virus.⁸

Work has begun towards developing a vaccine for Zika virus. It may take two years to develop a vaccine, but 10 to 12 years may be needed before an effective Zika virus vaccine is approved by regulators for public use.⁹

The good news is, the risk for Zika virus infection in Bangladesh is low as the countries affected are far away. But the bad news is, a swarm of *Aedes* mosquitoes are waiting to greet Zika virus if it ever reaches our country.

It is the high time to design a National strategy and policy to identify and prevent Zika virus disease in Bangladesh and ensure emergency preparedness plan.

We have to act in a coordinate way to control the mosquitoes, inform people about the risks, keep a check on cases, step up research to understand the disease and develop vaccines.

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Frequency of Extracranial Complications of Chronic Suppurative Otitis Media

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Summary:

Objectives: To see the way of presentation of extracranial complication, relationship between socio-economic conditions and extracranial complication of chronic suppuration otitis media.

Methods: This is a cross-sectional study carried out in Department of Otolaryngology Head and Neck Surgery, Sir Salimullah Medical College & Mitford Hospital and Dhaka Medical College Hospital from 1st July 2009 to 30th June 2010. The diagnosis was made by detailed history, clinical examination & investigation. Analyzed data was presented by various tables.

Results: In this study male (59%), lower class people (57%), age 11-20 years, rural (66%) and less educated patients were more affected. Having bath in the ponds and rivers suffers more. Clinical presentation of CSOM with complications

were aural discharge (100%), hearing impairment (94%), post auricular swelling (15%), pain in the ear (21%), postauricular discharge (27%) and mass in the EAC (12%). Here found aural discharge mostly malodorous and scanty, attic perforation and cholesteatoma. Post auricular abscess most common (47%) extracranial complication and labyrinthitis was the lowest (3%). Atticoantral variety was more common (89%) than that of tubotympanic disease (11%).

Conclusion: From the review of the series we found the frequency & types of extracranial complications arising from CSOM and known the current epidemiological data. It can produce awareness among all level of medical practitioners and enhance prompt diagnosis and treatment.

Key words: Chronic suppurative otitis media, Extracranial complication.

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Introduction:

Chronic suppurative otitis media (COSM) and its complications are major health problem in Bangladesh

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and other developing countries.^{1,2,3} Though the incidence of CSOM is gradually on the decline, it is still remained an important subject of research both in developing and the developed countries.^{2,3}

CSOM implies a permanent abnormality of the parse tensa or flaccida, most likely as a result of earlier acute otitis medica (AOM), negative middle ear pressure or otitis media externa (OME).⁴ CSOM is usually classified into two main groups- atticoantral disease and tubotympanic disease.^{7,8} Tubotympanic disease is characterized by a perforation of the parse tensa.⁸ Patient with this form of otitis media are generally safe and not considered to be at risk of developing complications.^{1,7,8,9} Atticoantral disease most commonly involve the parse flaccida and is characterized by the formation of a retraction pocket in which keratin accumulates to produces cholesteatoma and considered to a dangerous form of the disease because of development of complications.^{1,7,8} Complications are more common in

atticoantral disease (79.11%) than in tubotympanic disease (20.89%).^{1,7}

The incidence of CSOM appears to some extent on racial and socio-economic factors. Poor living conditions, overcrowding, poor hygiene and nutrition have been suggested as a basis for the widespread prevalence of CSOM in developing countries.^{2,3,7,8} Complications of CSOM are more common in combined with cholesteatoma and granulation tissue.^{10,11} The overall incidence of complications has fallen greatly with antibiotic treatment.¹²

Complications of CSOM are classified into two main categories- extracranial complication (EC) and intracranial complication (IC). Extracranial complications are subperiosteal abscess, labyrinthitis, facial paralysis, petrositis.^{10,13} Intracranial complications are- meningitis, brain abscess, extradural abscess, subdural abscess and lateral sinus thrombosis. Different studies showed that extracranial complication of CSOM is more than that of intracranial complications.^{2,7,10,13,14} Cholesteatomas are potentially dangerous because of their potential to incite resorption of bone, leading to intratemporal or intracranial complications.¹⁵

This study will be conducted to find out the frequency, types of extracranial complications arising from chronic suppurative otitis media and to know the current epidemiological data. It can produce awareness among all level of medical practitioners and enhance prompt diagnosis and treatment, at least early referral and thereby reduce morbidity and mortality of the patients suffering from chronic suppurative otitis media.

Aims and Objectives

General Objectives:

- To find out the types of extracranial complication of CSOM.

Specific Objectives:

- To find out the relationship between socio-economic conditions and the disease process.
- To see the way of presentation of extracranial complication of CSOM.

- To develop awareness among all level of medical practitioners, so that prompt diagnosis and proper management can be achieved.

Study design: Cross sectional, observational study.

Study place: Otolaryngology & Head Neck Surgery department of Sir Salimullah Medical College & Mitford Hospital and Dhaka Medical College Hospital.

Period of Study: 1st July 2009 to 30th June 2010.

Source of Material: Patients admitted in the Otolaryngology & Head Neck Surgery department of the above mentioned hospitals included in the study.

Sample Size: 100 patients

Selection Criteria:

- a) Inclusion criteria: Chronic suppurative otitis media & with extracranial complications like subperiosteal abscess, postauricular discharging sinus, labyrinthitis, facial palsy.
- b) Exclusion criteria: Patients present with acute suppurative otitis media, chronic suppurative otitis media with intracranial complications.

Data collection method: Data was collected by well prescribed data sheet.

Data analysis: All data were statistically analyzed by SPSS method.

Ethical Clearance: Ethical review committee of Sir Salimullah Medical College has given permission to perform the study.

Method:

Whenever a case was selected, detailed history of each of the patient has been taken in a prescribed data sheet with the informed consent of the patient or the patient's guardian. Each of the patients under went thorough clinical examinations. Otological examination also performed under operating microscope. The findings of clinical and microscopic examination were recorded and plotted on the data sheet. Some important relevant investigations were done and recorded. All the collected data are analyzed properly.

Results:**Table-I**

Age distribution of the patients (inclusive)		
Age group (Years)	No. of Patients (n=100)	Percentage (%)
0-10	21	21
11-20	51	51
21-30	18	18
31-40	07	07
41-50	03	03

The age of youngest patient was 4 years and the eldest 50 years. The highest number of sufferers was in the 11-20 years age group (51%).

Table-II

Sex distribution of the Patients		
Sex	No. of Patients (n=100)	Percentage (%)
Male	59	59%
Female	41	41%

Male patients are more sufferers (59%) than the female (41%).

Table-III

Socioeconomic status of the patients		
Socioeconomic status	No. of Patients (n=100)	Percentage (%)
Lower class	57	57%
Middle class	30	30%
Affluent	13	13%

Here shown that lower class people (57%) are more sufferers.

Table-IV

Residential status of the patients		
Residence	No. of Patients (n=100)	Percentage (%)
Rural	66	66%
Urban	34	34%

People living in rural area (66%) are more sufferers.

Table-V

Educational status of the patients		
Educational status	No. of Patients (n=100)	Percentage (%)
Illiterate	24	24%
Primary education	41	41%
Secondary education	21	21%
Higher secondary education	11	11%
Graduation	03	03%

Here shown that the patient with illiterate and less educated group suffers more.

Table-VI

Bathing habit of the patients		
Bathing place	No. of Patients (n=100)	Percentage (%)
River + Pond	66	66
Shower + Tube-well	34	34

The peoples having bath in the ponds and rivers suffers more.

Table-VII

Presenting features of the patients		
Symptoms	Number of patients (n=100)	Percentage (%)
Aural discharge	100	100
Hearing impairment	94	94
Post auricular swelling	45	45
Neck swelling	09	09
Supra & preauricular swelling	05	05
Pain in the ear	21	21
Postauricular discharge	27	27
Mass in the EAC	12	12

Most of the patients were presented with multiple symptoms. Majority of cases had the complaints of hearing impairment and aural discharge.

Table-VIIIa

<i>Physical examination findings: Aural discharge</i>							
Odor (n=100)		Amount of discharge (n= 100)			Nature of discharge (n= 100)		
Odorless	Malodorous	Scanty	Profuse	Mucoid	Muco Purulent	Purulent	Blood Stained
13 (13%)	87 (87%)	85 (85%)	15 (15%)	09 (09%)	31 (31%)	46(46%)	14 (14%)

Here found that aural discharge is mostly malodorous and scanty in amount.

Table-VIIIb

<i>Physical examination findings: others</i>			
		Otosopic findings	Microscopic findings
TM perforation	Attic	64	64
	Posterior marginal	25	25
	Central	11	11
Cholesteatoma		87	91
Aural polyp		12	12
Granulation tissue	Middle ear	07	09
	EAC	04	04
Epithelial in growth		01	09
Ossicles	Intact	32	29
	Eroded	68	71

Attic perforation and cholesteatoma found in majority of the cases. Most important factor is that microscopic examination is more important both in diagnosis of the disease and planning of the treatment.

Table-IX

<i>Distribution of patients in different types of CSOM with complications</i>		
Types of CSOM	Number of patients(n=100)	Parentage (%)
Atticoantral	89	89
Tubotympanic	11	11

Table-X

<i>Extracranial complication of CSOM found in the study</i>		
Complications	No. of patients (n=100)	Percentage %)
Post auricular abscess	47	47%
Post auricular discharging sinus	26	26%
Labyrinthitis	03	03%
Bezold's abscess	07	07%
Facial nerve paralysis	11	11%
Zygomatic abscess	06	06%

Here found that post auricular abscess is the most common (47%) extracranial complication and labyrinthitis is the lowest (03%).

Discussion:

CSOM is a potentially serious disease because of its complications.¹⁰ CSOM is quite common in developing countries.² Peoples of younger age group and low socio-economic classes are more sufferer.^{2,3} This type of disease is also common in our country.¹ This study was carried out to find out frequency of extracranial complications of CSOM.

Despite an overall decline in the incidence of complications of otitis media, some complications are still exist.^{2,12} Studies in different parts of the world found that attico-antral type of disease presented with more complications than the tubo-tympanic type.^{1,7,10,12} Attico-antral disease (89) and its complications were more than that of tubo-tympanic disease (11) in this study (table IX), which are consistent with other global studies.^{1,7,10,12} Cholesteatoma with or without granulation tissue is the commoner causative factor for the development of complication in CSOM.^{2,3,12,13,14} Here cholesteatoma found in most of the cases (table VIIIb) which were in good agreement with the other previous studies.

Incidence of complications are common in children and young adults.^{1,7,11} Highest rates of extracranial complications were found in 11-20 years age group of this study (table I) which were compatible with many studies.^{1,3,7,11} Studies both in home and abroad^{1,3,11} showed that male suffered more than that of female which was in good agreement with this study (table II). Like different studies^{3,11,13} illiterate and primary education groups were more sufferers in this study (table V).

Rural peoples from low socio-economic groups are the common victim of CSOM and its complications, which are evident in many studies.^{2,3,7,11} This study (table III & IV) having similar agreement with the mentioned studies. Similar symptoms and findings were found in these patients (table VII & VIII), which are consistent with some of the standard studies.⁷ Most of the literatures published that attic perforation is the most common otoscopic and microscopic findings^{2,7}, here (table VIIIb) also showed the similar agreement. Post auricular abscess was the most common extracranial complication in this study and post-auricular discharging sinus was the second (table X), keeping agreement with different standard study in home and abroad.^{1,2,7,10,11}

Incision and drainage followed by mastoid exploration should be done to prevent fatal complications. The incidence of facial nerve paralysis (table X) corresponds to the value of other studies.^{2,7,10} In these cases urgent mastoidectomy with facial nerve decompression should be done promptly to recovery the nerve function.

Conclusion:

It is important to identify that the prevalence of CSOM with extracranial complications as it is still high in young age group and low socio-economic classes specially in the rural areas. Here we found that lack of knowledge regarding the disease process and its complications in illiterate and under educated population lead to complications like post-auricular abscess, post-auricular discharging sinus, facial palsy and deafness. So it is recommended that organizing health education program is essential for all classes of people specially in rural and underdeveloped areas. So that the people can be motivated and morbidity due to CSOM could be minimized. Surgeons should have their upgraded knowledge and proper training for modern surgical technique. Adequate medical and surgical intervention in time for treatment of chronic suppurative otitis media can restrict the development of extracranial complications and even prevent the development of irreversible facial nerve damage and hearing impairment.

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Evaluation of Blood Transfusion Practices in Obstetrics and Gynecology in a Tertiary Hospital in Bangladesh

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Summary:

Background: Blood transfusion is a life saving intervention in some obstetric and gynecological cases but is associated with risk of transfusion reaction and transmission of infection. Appropriate use of blood and blood products is of utmost importance for the safety of the patients. During the evaluation of an ongoing study on PPH, it appears that rate of blood transfusion is unexpectedly high in this centre, which raised the inquisitiveness in evaluating the rate and rationality of blood transfusion in present practice.

Objective : To determine the incidence of blood transfusion in admitted and operated cases and is also to evaluate the indication of transfusion among the study patients.

Subject and Method: It was an observational descriptive study, conducted from 1st April 2012 to 30th June 2012 in department of obstetrics and gynecology of Ad-din Women Medical College Hospital, Dhaka. Total 256 cases were included for the study, who received blood and /or blood products during the study period.

Introduction:

Safe blood products, used correctly, can be life saving¹ in cases with major and life threatening obstetric

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Results: Transfusion rate in total admitted patients was 9.23%. Most common indication for blood transfusion in obstetric patients was mild preoperative anaemia with or without excessive bleeding during cesarean section (63.92%) and second common cause was antenatal anaemia (24.05%). In gynecological cases abortion (45.91%) was the commonest indication for blood transfusion and next common conditions were total abdominal hysterectomy (20.40%), vaginal hysterectomy (7.14%), ectopic pregnancy and post coital tear (6.12%) and (6.12%).

Conclusion: In this study it was observed that, blood transfusion was not appropriate in all cases, specially in cases where single unit blood was transfused. So creation of awareness among the junior doctors, obstetricians, nurses – midwives is essential by developing regular education and training programme.

Key words: Blood transfusion, Obstetrics and Gynaecology.

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hemorrhages, which occurs in 3-5%² and .1%³ of deliveries.

Blood transfusion is recognized as one of the eighth essential components of comprehensive emergency obstetric care (CEOC), which has been shown to reduce rates of maternal mortality⁴.

Studies show that there is inappropriate transfusion in 15-45%, either transfusion was done in, not indicated cases or too late or too little done in indicated cases⁵.

The appropriate use of blood and blood products means the transfusion of safe blood product only to treat a condition leading to significant morbidity and mortality that can not be prevented or managed effectively by other means⁶. Medical alternatives to transfusion include iron supplementation and erythropoiesis-stimulating agent(ESA)⁷.

Accurate evaluation of blood loss is important to determine whether transfusion should be performed, but it is difficult in obstetric hemorrhage^{8,9,10}. Transfusions decisions are clinical judgments that should be based on the overall clinical assessment of

the individual patient. It should not be based on laboratory parameters alone¹¹.

Prior to the administration of blood or blood components, the indications, risks and benefits, of a blood transfusion and possible alternatives must be discussed with the patient and documented in medical record¹².

Purpose of the study: The purpose of the study was to identify difficulties and also to find out the rate of unnecessary transfusion in total transfusion management in this hospital, and then proposal for setting up a Hospital Transfusion Committee for proper transfusion management.

Subject and Methods: It was an observational descriptive study conducted in Obstetrics and Gynecology Department of Ad-din Women Medical College Hospital, Dhaka, a tertiary care center for obstetrics and gynae patients. A big population including referred complicated cases are served here coming from whole country. Duration of study was from 1st April 2012 to 30th June 2012. All patients, received blood transfusion in obstetrics and gynecology department were included for the study. Total 2849 patients got admitted during the study period in

Obstetrics and Gynecology Department. Among them 2417 were obstetrics and 432 were gynecological cases. 162 obstetrics and 101 gynae patients received blood or blood component transfusion. In 162 obstetric patients, who received transfusion, 158 cases were included for study and among 101 gynecological patients 98 cases were included and total 7 cases were excluded from is in group due to incomplete data.

Patients were evaluated according to demographic characteristics, indication of blood transfusion, units of blood transfused, pre – transfusion and post transfusion Hb level. Data was collected in a preformed data sheet and result were calculated by scientific calculator.

It was an observational type of study, and due consent was taken from Ethical committee of the Hospital

Results: Transfusion rate in total admitted cases was 9.23%. In obstetric patients

the rate was 6.02%, Patients with cesarean section the rate was 8.68%. Among gynecological cases 23.37% received transfusion and among them 14.49% cases, it was transfused during elective surgery.

Commonest age group among the study patients in obstetrics was between 20 to 30 years of age group. Teen age pregnancy constituted less than 10% of the cases. Among the obstetric cases, who received blood transfusion, 75(47.47%) were booked and 83(52.53%) were unbooked. Multiparous patients constituted 68.35% of the total obstetric patients, received transfusion.

Obstetric and medical condition for blood transfusion were mild preoperative anaemia with or without excessive hemorrhage during cesarean section 63.92% (101), antenatal anaemia 24.05% (38), postpartum hemorrhage 15.19%(24), pre-eclampsia /eclampsia 9.49%(15), placenta praevia 9.49(15), multiple pregnancy 6.33%(10), abruptio placenta 4.33%(7), PROM 4.33%(7), IUD 2.53%(4), vulvovaginal and cervical tear 2.53%(4) and puerperal sepsis .63%(1).

110(69.62%) patients received single unit blood transfusion. Massive blood transfusion (20units) was given in one patient, who was a case of placenta increta. Her uterus was preserved during cesarean section by leaving the placenta insitu. But delayed hysterectomy was done due to severe hemorrhage after two months. FFP(Fresh Frozen Plasma) was transfused to the patients, who received 6 or more unit whole blood according to necessity.

In a case with Thrombocytopenia, one unit Platelet and one unit fresh blood were transfused during her operation.

In obstetric cases pre-transfusion Hb level was <7gm/dl in 22(13.93%) patients. In 72(46.83%) cases Hb level was 7- 9gm/dl. Post-transfusion Hb level was 8-10gm in 56 cases, >10gm in 67 cases.

Among the gynecological patients most common indication of blood transfusion was abortion 45.91%(45), followed by TAH 20.40%(20), VH 7.14%(7), ruptured ectopic pregnancy 6.12%(6), Postcoital tear 6.12%(6), molar pregnancy 5.10%(5), puberty menorrhagia 2.04%(2), Weirtheims hysterectomy 1.02%(1).

Table-I*Socio – Demographic characteristic of the obstetric patients(n-158)*

Age (years)	N(%)
<19	13(8.33)
20-30	121(76.58)
>30	24(15.19)
Parity	50(31.65)
Primi	108(68.35)
Multi	
Booking status	75(47.47)
Booked	83(52.53)
Unbooked	
Socioeconomic status	90(56.96)
Low middle	68(43.04)
Middle	

Commonest age group among the study patients in obstetrics was between 20 to 30 years of age group .Teen age pregnancy constituted less than 10% of the cases. Among the obstetric cases, who received blood transfusion, 75(47.47%) were booked and 83(52.53%) were unbooked. Multiparous patients constituted 108(68.35%) of the total obstetric patients , received transfusion. >50% cases had low middle or lower socioeconomic status

Table-II*Indication of blood transfusion in obstetric patient(n-158)*

Factors	N(%)
Medical condition	
Anaemia including Thalassaemia	38(24.05)
Antenatal factors	37(23.42)
Previous cesarean section	15(9.49)
PIH/PE/ECL	15(9.49)
placenta praevia	7(4.43)
Abruptio placenta	10(6.33)
Multiple pregnancy	7(4.43)
PROM	4(2.53)
Intrauterine fetal death	
Cesarean section	101(63.92)
Postpartum factors	24(15.19%)
Postpartum hemorrhage	4(2.53)
Vulvovaginal and cervical tear	1(.63)
Puerperal sepsis	

Table is showing that 38(24.04%) patients needed blood transfusion during antenatal period due to moderate to severe anaemia.

101 cases received transfusion during their cesarean section due to mild pre-operative anaemia with or without excessive hemorrhage.

24(15.19%) patients were diagnosed case of Postpartum hemorrhage. Among all the obstetrics patients 37(23.24%) had previous cesarean section, 15(9.49%) had pre-eclampsia/eclampsia, 15(9.49%) had placenta praevia, 7(4.43%) had abruptio placenta.

Table-III*Pre transfusion and post transfusion Hb level in obstetric patients*

Pretransfusion Hb level gm/dl	Total patients n-158(%)	Post-tansfusion Hb level gm/dl	Total patients n-158(%)
<7	22(13.93%)	8-10	56(35.44%)
7-9	74(46.83%)	>10	67(42.41%)
>9	62(39.24%)	Not done	35(22.15%)

This table is showing that 39.24% patient received transfusion even they had Hb level >9gm/dl. Among these cases transfusion might have been avoided.

Table-IV*Number of unit of blood transfused in obstetric patients*

Unit of blood	Number of patient-158	Percentage
1	110	69.62
2	26	16.46
3	12	7.60
4	6	3.80
5	1	.63
6	1	.63
10	1	.63
20	1	.63

Table-V

<i>Indication of blood transfusion in gynae patient(n-98)</i>		
Indication	Causes	N(%)
Abortion	Moderate to severe anaemia	45(45.91)
Molar pregnancy	Anaemia and operative blood loss	5(5.10)
TAH	Perioperative anaemia	20(20.40)
VH	Perioperative anaemia	7(7.14)
Ectopic Pregnancy	Moderate to severe anaemia	6(6.12)
Postcoital tear	Moderate bleeding	6(6.12)
Puberty menorrhagia	Severe anaemia	2(2.04)
Weirtheims hysterectomy	Excessive operative blood loss	1(1.02)
Others		6(6.12)

Table-VI

<i>Pre and post transfusion Hb level in Gynecological cases</i>			
Pretransfusion Hb level gm/dl	Total patients n-98(%)	Post –transfusion Hb level gm/dl	Total patients n-98(%)
<7	19(19.39%)	8-10	42(42.86%)
7-9	23(23.47%)	>10	42(42.86%)
>9	56(57.14%)	Not done	14(14.28%)

This table is showing that 57.14% patient had >9gm/dl pre-transfusion Hb . Transfusion could be avoided among these cases.

Discussion:

In total admitted cases in obstetrics and gynecology the transfusion rate is 9.23%, which is more or less comparable to the study done in Nigeria at the Lagos University Teaching Hospital ,where the rate was found 12.1% ¹³ and also correlate with another study done in Khartoum teaching hospital ,where the rate was 11.4% ¹⁴. But it is higher than the rate reported from developed countries ¹⁵.

In cases with cesarean section transfusion rate was 8.68%. It correlates with study done in Nigeria ¹⁶ where the rate was 8.9%. The current rate is relatively higher than study done in Canada ¹⁷ (5.7%) and the rate reported by Duthie et al¹⁸(4.5%) and Rouse et al ¹⁹ (5.4%) .But the rate is much lower than the rate found in studies done in Aga Khan University ²⁰ (15%), University of Nigeria Teaching Hospital ²¹ (25.2%) and also lower than the studies done by Ranaldi MP²² and others 23.5% and by Oluwarotimi et al ²³ 12.5%, by Adity G.et al²⁴(12.21%).

Commonest indication for blood transfusion was cesarean section (63.92%). It correlates with the rate 68.8% ,found in the study done in Lagos University Teaching Hospital , where the most common determinant for blood transfusion was cesarean section ¹³.

Anaemia was the second common cause .Among the cases of cesarean section mild preoperative anaemia with or without mild to moderate peroperative hemorrhage was the commonest indication .Majority of these cases were unbooked .Some studies found that most of the transfusion for anaemia in pregnancy were unnecessary ^{9,13}. Regular antenatal check up, prevention and early detection of anaemia , iron supplementation could avoid blood transfusion for anaemia.

Pretransfusion Hb level was <7 gm/dl in 22(13.93%)cases. In 62(34.24%) cases Hb level was 7 to 9gm/dl in 22(13.93%) cases .In 62(34.24%) cases Hb level was 7 to 9 gm/dl. More than 40% patient had no other symptoms than anaemia .The practice of transfusion at a Hb concentration <10gm/dl is no longer uniformly accepted ^{9,13}.

Predelivery Hb level > 9gm/dl was found in 54% cesarean delivery cases. In these cases blood was transfused during cesarean section or immediate postpartum period due to mild to moderate peroperative hemorrhage .

110 units blood were transfused to 110(69.62%) patients. This rate is comparable to the rate 68.2% of single unit blood transfusion ,reported by Khan et al ²⁰ , in their study in study in Aga Khan University . One unit blood may not have brought about any significant change in the hematocrit but was more than enough to cause all the complications of blood transfusion .In this circumstance one unit of crystalloid or colloid would have achieved the same effect without incurring the costs, risk and complications of blood transfusion ¹³.

One patient received 10 units blood due to placenta increta ,who ultimately needed cesarean hysterectomy .Only one patient needed massive blood transfusion (20units) ,which was also a case of placenta increta.

Transfusion rate is high in gynae cases (23.37%) .This high rate is due to transfusion of blood in abortion and ectopic pregnancy cases , which included more than 50% of the transfused patients in gynae.

Transfusion rate in abortion cases was 24.15% . This rate correlates with rate, found in study done by Stanely et al ²⁵ , where 22% patient required blood transfusion and another study ,in Latin America, where the rate is 18.2% ²⁶.

But in cases of abdominal and vaginal hysterectomy ,transfusion rate was 14.49% . It also correlates with another study done by Naser Edris ¹⁴ , where transfusion rate in cases with TAH was 14.9%. In the present study ,transfusion rate in cases with post coital tear is high (6.12%). It is unusual to give transfusion to these cases . But in our study group 4 patients came with moderate bleeding and 2 patient came in severe bleeding with shock.

Conclusion:

In this study it was observed that, blood transfusion was not appropriate in all cases, specially in cases where single unit blood was transfused . So creation of awareness among the junior doctors, obstetricians,

nurses – midwives is essential by developing regular education and training programme .

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Metabolic Syndrome in Bangladeshi Menopausal Women

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Summary:

Objective: To assess the factors of metabolic syndrome (MetS) in post menopausal women in Bangladesh.

Methods: Menopausal women are at increased risk of metabolic syndrome (MetS). This cross-sectional study on 64 willing post menopausal women from an urban and a rural area of Bangladesh was done. The socio-epidemiologic factors with anthropometric examination, blood pressure recording and fasting blood analysis for triglyceride (TG), high density lipoprotein (HDL), sugar were studied.

Results: Prevalence of MetS was 50.0% (95% CI= 39.9%-60.1%) among menopausal women, seventy five percent of them were urban. Low HDL cholesterol prevailed in almost 96% respondents followed by high TG (51%), obesity (28.0%), high fasting blood sugar (FBS, 27.1%) and hypertension (HTN, 16.9%). On logistic regression, age

(OR=1.6, 95% CI: 1.3-1.9), male sex (OR=2.5, 95% CI: 1.4-4.2) and exercise (OR=1.9, 95% CI: 1.2-2.9) produced significantly higher odds of being associated with MetS; rural area (OR=1.4, 95% CI: 1.0-2.1) and sedentary occupation (OR=1.7, 95% CI: 0.9-3.0) were associated just insignificantly. Though higher income, better education, good physical movement and knowledge of MetS produced protective odds, they were not significant.

Conclusions: The study suggests that MetS is highly prevalent among Bangladeshi menopausal women. Further studies are needed to identify risk factors and for effective preventive measures to control this metabolic disease.

Key Words: Metabolic Syndrome, Epidemiology, Obesity, Lifestyle, Bangladesh

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Introduction:

Menopause is the inevitable event terminating reproductive segment of women's life. Worldwide life expectancy has increased and as a result increasingly more women are now passing a longer period of their life after menopause. The post menopausal life is being associated with an increased risk¹ of metabolic syndrome (MetS) that had been recognized as a public health problem². Defined by different expert bodies³⁻⁶, the criteria of MetS by the Adult Treatment Panel III⁴ (ATP III) of National Cholesterol Education Program (NCEP) had been widely used. The ATP III criteria defines MetS as the presence of 3 of 5 factors namely a) abdominal obesity, determined by waist circumference ≥ 88 cm (35 inch) in women, ≥ 102 cm (40 inch) in men, b) high Triglyceride (TG) ≥ 1.7 mmol/l (150 mg/dl), c) low High Density Lipoprotein (HDL) cholesterol < 1.3 mmol/l

(50 mg/dl) in women, < 1.03 mmol/l (40 mg/dl) in men, d) high Blood Pressure (BP) $\geq 134/85$ mm Hg, e) high Fasting Blood Sugar (FBS) ≥ 6.1 mmol/l (110 mg/dl). The problem of MetS has been shown a steady increase in all populations with a propensity towards older age⁷⁻¹¹ associating with lifestyle, diet, body mass, risky behaviour, abdominal obesity, insulin resistance glucose metabolism, dyslipidemia, increased blood pressure and even non-alcoholic fatty liver.

Of the factors, weight gain had been identified¹²⁻¹³ to be associated with MetS in menopausal women with increasing risk of cardiovascular disease¹⁴ (CVD) and acquiring all of its components¹⁵. As experienced by the Asians¹⁶⁻²⁰, Bangladesh^{21,22} also have similar experience on MetS although there are scopes to assess the situation in menopausal women in a community. Identifying the community risk for MetS in menopausal women could be an important research work to reject the primary null hypothesis that there was no difference of MetS factors in menopausal women in Bangladesh.

Materials and Methods:

The cross sectional study was conducted on 490 willing respondents, 275 of whom were females using Power and Sample Size program software²³ to include a representative sample from one urban and a rural area. The data collection was done after getting ethical

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clearance from Bangladesh Medical Research Council (BMRC) in 2010. Out of total female population, there were 64 post menopausal women on which the secondary analysis of data was done. Respondents' socio demographic and behavioural information was recorded followed by anthropometric and blood pressure (BP) was measurement. Fasting blood was taken for the measurement of TG, HDL and FBS.

Necessary editing and coding of the data was done before final analysis accordingly^{24,25,26}. All the components of metabolic syndrome were categorised by threshold value according to ATP III criteria and MetS was calculated with all possible combination of components together. Collating all the MetS components, dichotomous variable was created as either having MetS or not. The number of combination of components was added for total number of combined components distributed within the respondents.

Univariate analysis of the basic socio-demographic and suspected factors was done using χ^2 test for categorical data and Mann-Whitney U test for continuous data. The data were presented as proportion and mean \pm SD respectively. For variable selection of independent effect measurement in logistic regression, the researcher followed the rule^{27,28} of minimum number of event or non-event divided by 15 (10-20), i.e. number of variable inclusion for adjustment of confounding factors. As there were 32 respondents in no MetS and 32 in MetS group, so both were same, and dividing the number by

10, it was found that the researcher could include a maximum of 4 variables in the equation. Logistic regression was also done for looking at the interaction by discrete interaction model assessment with the significant variables found in univariate analysis. After initial regression, the non-significant variables were removed to look for best fit model in a stepwise fashion. Confidence Interval Analysis (CIA) software was used to calculate the 95% confidence interval (CI) for the prevalence of MetS and its components. A p value ≤ 0.05 was considered statistically significant. The near significant variables with a p value ≤ 0.1 were also quoted with caution.

Results:

The prevalence of MetS was 50.0% (95% CI= 39.9%-60.1%) in the study. Low HDL prevalence was highest (96.9%, 95% CI=91.0-99.0) among the components of MetS followed by TG (51.6% 95% CI= 41.4-61.6), DM (40.6%, 95% CI= 31.1-50.9), HTN (32.8%, 95% CI= 24.0-43.0) and obesity (10.9%, 95% CI= 6.0-19.0). Of the combined components high TG, low HDL and DM concluded a quarter of respondents followed by high TG low HDL and HTN (18.8%). Nearly 11% of the respondents had combination of four components as obesity, high TG, low HDL and DM while another 9.4% had combination of HTN, high TG, low HDL and DM. Table 1 shows the prevalence of components of metabolic syndrome with 95% CI.

Table-I

Prevalence of components of MetS

Components (%)	N (%)	95% CI of %
Obese	7 (10.9)	6.0-19.0
HTN	21 (32.8)	24.0-43.0
-TG	33 (51.6)	41.4-61.6
\bar{HDL}	62 (96.9)	91.0-99.0
DM	26 (40.6)	31.1-50.9
-TG + \bar{HDL} + DM	16 (25.0)	17.2-34.8
-TG + \bar{HDL} + HTN	12 (18.8)	12.0-28.0
DM + \bar{HDL} + HTN	11 (17.2)	10.8-26.3
-TG + HTN + DM	6 (9.4)	4.9-17.1
Obese + \bar{HDL} + DM	4 (6.3)	2.8-13.2
Obese + -TG + \bar{HDL}	3 (4.7)	1.9-11.2
Obese + -TG + HDL + DM	7 (10.9)	6.0-19.0
HTN + -TG + \bar{HDL} + DM	6 (9.4)	4.9-17.1

One interesting feature was observed with the non modifiable risk factor, the age. Figure 1 depicts the preponderance of MetS with advancing age though the association of higher age and MetS has not been statistically significant ($c^2=4.13$, $p=0.25$).

None of the respondents had any knowledge of the term MetS. The socio-demographic and other variables are shown in Table 2. None of age, education, occupation or area of residence was associated with MetS. Though MetS respondents had higher average income than no MetS respondents, it was not significant. Water intake and sleeping duration were also not associated. Height was not related with MetS though MetS respondents were nearly six kg heavier ($p=0.05$) than no MetS respondents as reflected by

significantly higher BMI ($p=0.05$). While looking at the components, MetS respondents had high waist circumference ($p=0.03$), high SBP ($p<0.001$), high DBP ($p<0.001$), high TG ($p<0.001$), high FBS ($p<0.001$). The MetS respondents had lower HDL than no MetS respondents, but the difference just missed the significance level ($p=0.09$).

The significant factors were put into stepwise logistic regression model to check the magnitude of association with MetS added with age. These are shown in Table 3, where DBP (OR=1.24, 95% CI= 1.08-1.41), TG (OR=1.03, 95% CI= 1.01-1.05), obesity (OR=1.12, 95% CI= 1.01-1.25) and DM (OR=1.02, 95% CI= 1.00-1.04) became significant predictor of MetS in the final model.

Table-II

Baseline characteristics¹ of MetS respondents according to ATP III

Variables ²	No (n=32)mean±SD	Yes (n=32)mean±SD	p ³
Age (years)	52.03±9.19	51.38±8.12	0.96
Income (/month)	32.97±62.972637.50±5037.52	121.48±443.199718.75±35454.86	0.94
Water intake(lit/day)	3.45±1.73	2.94±1.31	0.34
Sleep	6.33±2.12	6.30±1.92	0.67
Weight (kg)	53.83±10.49	59.63±12.20	0.05
Height (cm)	153.63±6.06	153.94±5.92	0.89
BMI (kg/m ²)	22.78±4.14	25.06±4.48	0.05
Waist (cm)	86.84±8.80	93.97±13.65	0.03
SBP (mm Hg)	125.44±15.01	144.06±14.53	<0.001
DBP (mm Hg)	75.94±11.42	86.81±9.53	<0.001
TG (mg/dl)	137.28±69.36	214.47±101.25	<0.001
HDL (mg/dl)	37.31±6.84	34.59±5.51	0.09
FBS (mg/dl)	101.66±44.69	151.91±74.80	<0.001
Area			0.11
Urban	18 (42.9)	24 (57.1)	
Rural	14 (63.3)	8 (36.4)	
Education			0.96
Illiterate	9 (47.4)	10 (52.6)	
Some Education	18 (51.4)	17 (48.6)	
Good Education	5 (50.0)	5 (50.0)	
Occupation			0.77
Sedentary	8 (47.1)	9 (52.9)	
Heavy	24 (51.1)	23 (48.9)	

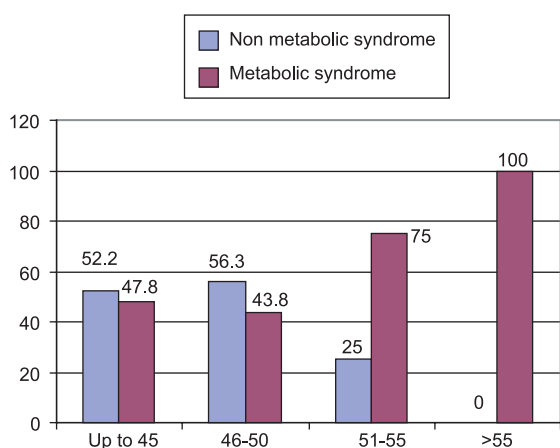
¹Continuous values were presented in means and standard deviations (SD), categorical values in frequencies and proportions.

²Age/age group in years, monthly income in USD converted from Bangladesh Taka (BDT: 1 BDT=1/80USD), water intake in litre/day, sleep in hours of sleep/day, weight in kilogram, height in cm.

³Mann-Whitney U test were done for continuous variables while c^2 or Fisher's exact test was applied for categorical variables.

Table-III

<i>Stepwise logistic regression with suspected factors related to MetS</i>				
Initial model	OR	95% CI for OR		p
		Lower	Upper	
Age	1.01	0.90	1.13	0.91
SBP	1.04	.97	1.12	0.29
DBP	1.20	1.04	1.396	0.02
Obesity	1.13	1.00	1.271	0.05
DM	1.02	0.99	1.05	0.06
-TG	1.02	1.00	1.04	0.02
-HDL	0.98	0.81	1.19	0.85
Final model	OR	95% CI for OR		p
		Lower	Upper	
DBP	1.24	1.08	1.41	0.002
Obesity	1.12	1.01	1.25	0.04
DM	1.02	1.00	1.04	0.045
-TG	1.03	1.01	1.05	0.005

**Fig.-1:** *MetS at different ages***Discussion:**

The prevalence of MetS in this study population was 50% and was largely determined by obesity, high diastolic blood pressure high TG and diabetic status. The finding was similar to other studies^{15,29}. Shihua F et al in china³⁰ and Heideri R et al in Iran³¹ also found hypertension and high TG to be associated with MetS. Jouyandeh et al¹ didn't find any difference of age in their study but they found all the components of MetS were significantly different from those of without MetS. Mahajan N et al³³ showed the proportion of HTN and DM in menopausal women increases after 50 years of

age. The current study also conform similarity to the study of Jouyandeh and Mahajan though the association was not statistically significant. Had the sample size been larger this association would become significant. Carr MC³⁴ in her review article discussed that the prevalence of MetS increases with menopause having the risk of suffering from cardio vascular disease (CVD), increase TG levels, reduced HDL and increased glucose levels. Though she expressed of the unclear idea whether the transition of menopause increases the CVD risk in all women or only those who become the candidate of MetS. Lee JS³⁵ did not find any independent association of HTN or DM with menopause but they found only hypercholesterolemia was associated with menopause.

The study had several limitations. Firstly, the sampling was done from only one urban and one rural area. So it would be hard to ascertain whether the studied prevalence of MetS was an underestimate or overestimate of the true prevalence. Detailed information on lifestyle and eating pattern was not done hence it was not possible to assess the type of food or lifestyle as predictive factors. But as the study assessed both rural and urban population, it can be considered the community-based study in Bangladesh to know the preliminary situation. A well documented protocol for easy diagnosis, management and prevention could be

worked out by the policy makers using this baseline data to manage the syndrome accordingly.

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Diarrhea in Breastfed versus Formulated Baby: A Hospital Based Study in 150 Children

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Summary:

Background: Breastfeeding reduces incidence of common childhood illnesses such as diarrhea and thus reduces infant mortality and morbidity.

Objective: To find out the incidence of diarrhea in breastfed versus formula fed baby.

Methodology: An observational cross sectional study was carried out in the Pediatric department of Northern private medical college hospital, Rangpur from March 2013 to June 2014. Total 150 children aged 1 to 24 months having diarrhea were enrolled in the study.

Result: Mean age of children was 11.6 with SD ± 5.29 months, ranges from 1 month to 23 months in which exclusively breast fed 51.3%, breast fed plus formula fed 39.3%, exclusively formula fed 9.4%; single attack of diarrhea occurred in 72.7%, 40.7%, and 28.6% children in exclusively breast fed, breast fed plus formula fed and exclusively formula fed children respectively. Frequent attack of diarrhea occurred in 27.3%, 59.3% and 71.4% children

in exclusively breast fed, breast fed plus formula fed and exclusively formula fed children respectively; among 59 patients who developed first attack of diarrhea by 6 months of age, 10.2%, 69.5 % and 20.3% were from exclusively breast fed, breast fed plus formula fed and exclusively formula fed children respectively. Patients who developed first attack of diarrhea by 7-12 months of age, 69.8% were from exclusively breast fed, 27.0% from breast fed plus formula fed and 3.2% from exclusively formula fed children. But 28 children whose first diarrhea occurred by 13-24 months of age, 96.4% and 3.6% were from exclusively breast fed, and breast fed plus formula fed group respectively.

Conclusion: Breast feeding reduces incidence of diarrhea, prevents frequent attack and early occurrence of diarrhea in under two children.

Key words: Exclusive breastfeeding, Formula feeding, Diarrhea.

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Introduction:

Breastfeeding is an unequalled way of providing ideal food for the healthy growth and development of infants¹. Breast milk promotes sensory and cognitive development, and protects the infant against infectious and chronic diseases. Exclusive breastfeeding reduces infant mortality due to common childhood illnesses such as diarrhea, and helps for a quicker recovery during illness². Breast milk contains all nutrients as well as antibodies especially Immunoglobulin A (IgA) and protects baby from infections including diarrheal diseases. WHO has recommended, infants should be

exclusively breastfed for the first six months of life to achieve optimal growth, development and health. Breast milk substitutes (such as commercial infant formulas and cow's milk) are considered nutritionally acceptable for few infants, but there is greater risk of developing a number of infections including diarrhea. Breast milk substitutes and other baby foods as well as bottles, teats and utensil are attributable to contamination causing diarrheal diseases in infants who are not exclusively breastfed.

Objectives of the Study

To find out the incidence of diarrhea in breastfed versus formula fed baby.

Methodology:

This observational cross sectional study was carried out in the Pediatric department of Northern Private Medical College Hospital, Rangpur from March 2013 to June 2014. Total 150 children aged 1 to 24 months were included in the study. Children having diarrhea attending in and out patient department were enrolled in this study. Data were collected by face to face interview using a

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structured close ended questionnaire information regarding demographic data; containing detailed feeding history and information of diarrhea. All the parents and attendants were informed about the purpose of the study and verbal consent was obtained. Children aged less than 1 month or more than 24 months and the children whose mother were not agreed to include in the study were excluded. Data were processed by using SPSS-19 program. Frequency distributions and proportions were calculated for the values. Students unpaired *t test* were applied as statistical tools. P value of < 0.05 was considered as significance. There was no ethical problem, as because verbal consent of parents and attendants were taken before conducting interview for the study.

Results:

Age of the study population ranges from 1 month to 23 months. Mean age was 11.6 with SD; ± 5.29 months. Demography of the study population is as follows:

Figure 1 shows, single attack of diarrhea occurred in 56 (72.7%), 24 (40.7%), and 4 (28.6%) children in exclusively breast fed, breast fed plus formula fed and exclusively

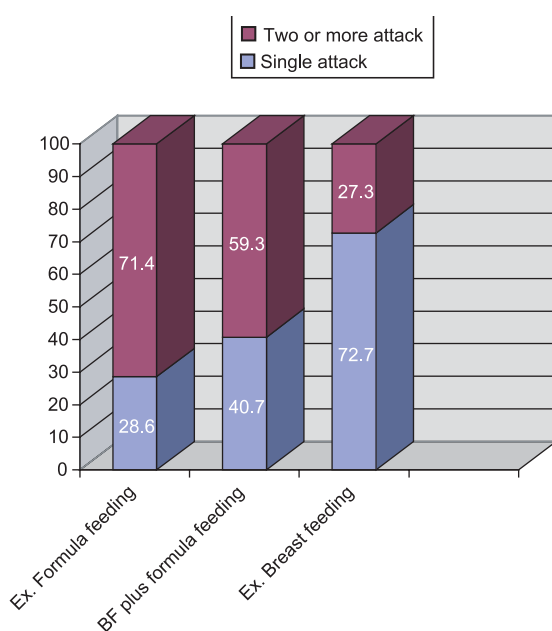


Fig-1: Relationship between feeding and number of diarrhea attack

formula fed group respectively. Frequent (≥ 2) attack of diarrhea occurred in 21 (27.3%), 35 (59.3%) and 10 (71.4%) children in exclusively breast fed, breast fed

plus formula fed and exclusively formula fed group respectively (p value .000).

Table-I

<i>Demography of study population</i>			
Parameters	No. (%)	Parameters	No. (%)
Age group		Sanitation	
1 to 6 month	30 (20.0)	Pacca	94 (62.7)
7 to 12 month	60 (40.0)	Water seal	15 (10.0)
13 to 18 month	47 (31.3)	Kacha	38 (25.3)
19 to 24 month	13 (8.7)	Open air	03 (02.0)
Sex		Residence	
Male	102 (68.0)	Urban	65 (43.3)
Female	48 (32.0)	Rural	79 (52.7)
		Urban slum	06 (04.0)
Fathers' education		Mothers' education	
Illiterate	22 (14.7)	Illiterate	22 (14.7)
Primary	33 (22.0)	Primary	54 (36.0)
Secondary	49 (32.7)	Secondary	54 (36.0)
Above secondary	46 (30.6)	Above secondary	20 (13.3)
Fathers' occupation		Mothers' occupation	
Service	73 (48.7)	Service	08 (05.3)
Business	26 (17.3)	Housewife	142 (94.7)
Farmer	37 (24.7)	Water supply	
Others	14 (09.3)	Tube well	131 (87.3)
		Tap water	19 (12.7)

Table III shows, patients who developed first attack of diarrhea by 6 months of age were 6 (10.2%) from exclusively breast fed, 41 (69.5%) from breast fed plus formula fed, and 12 (20.3%) from exclusively formula fed group. Patients who developed diarrhea by 7-12 months of age, 44 (69.8%), 17 (27.0%) and 2 (3.2%) respectively developed in exclusively breast fed, breast fed plus formula fed and exclusively formula fed group. Twenty eight patients developed diarrhea by 13-24 months of age; among them 27 (96.4%), and 1 (3.6%) were from exclusively breast fed, and breast fed plus formula fed group respectively (p value .000).

Table IV shows, children of illiterate mother had more frequent diarrheal attack (63.6%) than literate mother but educational level did not influenced consistently on occurrence and frequency of diarrheal attack on the study population (p value .02).

Table V shows, there is no significant influence of source of water on diarrheal attack and frequency in different group of patient (p value .407).

Table VI shows, residence of patients did not influenced on frequency of diarrheal attack (p value .084).

Table-II*Feeding information, number of diarrheal attack and age of first occurrence*

Parameters	No. (%)
Feeding	
Exclusively breast fed	77 (51.3)
Breast fed plus formula fed	59 (39.3)
Exclusively formula fed	14 (09.4)
Pre-lacteal fed	50 (33.3)
First occurrence of diarrhea	
1-6 month	59 (39.3)
7-12 month	63 (42.0)
13-24 month	28 (18.7)
Number of diarrheal attack	
1st attack	84 (56.0)
2nd attack	58 (38.7)
3rd attack	2 (1.3)
4th attack or more	6 (4.0)
Formula feeding utensils	
Bottle	55 (76.4)
Cup and spoon	17 (23.6)

Table-III*Type of feeding versus age of first occurrence of diarrhea*

Age of first diarrhea	Feeding			Total
	Exclusive breast feeding (%)	Breast feeding+Formula feeding (%)	Exclusively formula feeding (%)	
0-6 month	06 (10.2%)	41 (69.5%)	12 (20.3%)	59
7-12 month	44 (69.8%)	17 (27.0%)	02 (3.2%)	63
13-24 month	27 (96.4%)	01 (3.6%)	–	28
Total	77	59	14	150

Table-IV*Relation between Mothers' education and number of diarrheal attack*

Mothers' education	Single attack (%)	Two or more attack (%)	Total
Illiterate	08 (36.4%)	14 (63.6%)	22
Primary	31 (57.4%)	23 (42.6%)	54
Secondary	33 (61.1%)	21 (38.9%)	54
Above secondary	12 (60.0%)	08 (40.0%)	20
Total	84 (56.0%)	66 (44.0%)	150

Table-V

Relation between water supply and number of diarrheal attack			
Water supply	single attack (%)	Two or more attack (%)	Total
Tube well	73 (55.7%)	58 (44.3%)	131
Tap water	11 (57.9%)	08 (42.1%)	19
Total	84 (56.0%)	66 (44.0%)	150

Table-VI

Relation between residence and number of diarrheal attack			
Residence	Single attack (%)	Two or more attack (%)	Total
Urban	39(60.0%)	26(40.0%)	65
Urban slum	03(50.0%)	03(50.0%)	06
Rural	42(53.2%)	37(46.8%)	79
Total	84(56.0%)	66(44.0%)	150

Discussion:

Breast milk is the ideal food for an infant's first six months of life. Colostrum and breast milk contains an abundant amount of IgA₂ and other antibodies that can help the baby to resist infections³. Breastfeeding has many health benefits for both the mothers and infants. In addition to providing ideal nourishment, breastfeeding provides infants with protection from many infections, including diarrheal diseases. Breastfeeding can also reduce the severity, duration, and negative nutritional consequences of diarrhea⁴. On the other hand, use of formulas including infant formula is associated with increased health risks such as acute gastroenteritis, otitis media, severe lower respiratory tract infections, atopic dermatitis, asthma and obesity⁵. The infant's intestine is not properly ready to digest non-human milk and this may often result in diarrhea, intestinal bleeding and malnutrition⁶. In our study, we found more than half (51.3%) of the study population were exclusively breastfed and single attack of diarrhea occurred in all children (as per inclusion criteria). But frequent (two or more) attack of diarrhea occurred in non-exclusive breast fed children; in breast fed plus formula fed children 35 (59.3%), exclusively formula fed 10 (71.4%) and exclusively breast fed 21 (27.3%). Abdulbari Bener et al.⁷ study on exclusive breast feeding and prevention of diarrheal diseases showed more than half of the infants (59.3%) were exclusively

breastfed; the risk for presenting diarrhea was higher in formula fed (48.7%) and partially breastfed children (37.3%) when compared to exclusively breast fed (32.5%). Black RE et al.⁸ study on Maternal and child under nutrition showed, the relative risk for prevalence of diarrhea was more in predominant and partial breastfeeding (1.26 and 3.04 respectively) as compared to exclusive breastfeeding.

World Health Organization (WHO) recommends exclusive breast feeding for first six months of life and continuation of breast feeding for two years or beyond^{9,10}. We found 59 patients developed first attack of diarrhea by 6 months of age, of whom most children were from non-exclusively breast fed group; there were breast fed plus formula fed children 41 (69.5%), exclusively formula fed 12 (20.3%) and exclusively breast fed only 6 (10.2%). This finding reflects exclusive breastfeeding has influence on prevention of early occurrence of diarrhea. On the other hand, patients who developed first attack of diarrhea by 7-12 months and 13-24 months of age mostly were from exclusively breast fed group (69.8%, and 96.4%) respectively indicating later occurrence of diarrhea in exclusively breast fed children than non- exclusively breast fed one. Our finding correctly supports current WHO recommendation on breast feeding. Laura M Lamberti et al.¹¹ study on breastfeeding and the risk for diarrhea morbidity and mortality showed excess risk of diarrhea

in non-exclusively breast fed 0-5 months aged infants; relative risk of diarrheal incidence was 1.26, 1.68, and 2.65 in predominant, partial, and non-breastfed group children respectively. Similarly, the estimated relative risk of incident diarrhea was elevated when comparing non-breastfed to breastfed 6-11 months aged infants.

We have observed the relationship of diarrheal incidence with other demographic parameters also. But residence, water supply, sanitation and parent's educational level had no significant influence on incidence and frequency of diarrhea.

Conclusion:

Breast feeding reduces incidence of diarrhea, prevents frequent attack and early occurrence of diarrhea in under two children. Residence, water supply, sanitation and parent's educational status may not have significant influence on incidence of diarrhea.

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Recent Update in The Management of Childhood Nephrotic Syndrome

MIKAYES

Summary :

Nephrotic Syndrome (NS) is a common renal disease seen in children. Children who go into complete remission following treatment with corticosteroids are classified as having steroid sensitive NS. In developed countries over 80% of children with idiopathic NS have steroid sensitive disease. The exact pathogenesis of this condition remains elusive. Podocyte injury and proteinuria are the two main issues in the pathogenesis. Recent studies suggest release of cytokines by T-cells as well as a strong contribution of B-cell immunity. Genetic studies have reported human leucocyte antigen (HLA) class II antigens DR and DQ associations linked to steroid sensitive NS. Most children with steroid sensitive NS have multiple relapses and a significant percentage also develop steroid dependent NS. Diuretic-resistant edema also a clinical problem to manage

Introduction:

Nephrotic Syndrome (NS) is a common renal disease seen in children. Children who go into complete remission following treatment with corticosteroids are classified as having “steroid sensitive” NS. In developed countries over 80% of children with idiopathic NS have steroid sensitive disease¹. The nephrotic syndrome is characterized by heavy proteinuria (> 40 mg/h/m² or protein/creatinine ratio > 200 mg/mmol); hypoalbuminemia (< 25 g/L); generalized edema² and hypercholesterolemia are almost always present³. It should be noted that this definition is distinct from a nephritic ‘syndrome’ (i.e. glomerulonephritis), which is defined by glomerular hematuria +/- hypertension. It is possible for a patient to be nephrotic, nephritic or nephrotic/nephritic depending on the underlying cause². The incidence of all forms of nephrotic syndrome in childhood is 2-4 per 100000 population, whereas in

these patients. These children receive multiple courses of steroids and are at high risk of developing steroid toxicity. Patient with frequent relapses who develop steroid dependency thus require alternative treatment. Steroid resistant NS considers when failure to response within 8 weeks of steroid therapy. Steroids sparing agents used include levamisole, cyclophosphamide, mycophenolate mofetil (MMF), calcineurin inhibitors (cyclosporine and tacrolimus), rituximab and vincristine; these agents have greatly reduced the adverse effects seen with long-term use of steroids; so therapy needs to be individualized to achieve optimal care of each child.

Keywords: Nephrotic Syndrome(NS),Relapse ,Steroid sensitive, Steroid dependency, Steroid sparing agents.

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the Indian subcontinent it is estimated at 9-10 per 100000 population³, but this figure will vary according to the ethnic mix of the population. For instance, the incidence amongst Asian children in two cities in the UK was reported to range from 9 to 16 per 100000, respectively⁴. Most children (90%) with nephrotic syndrome have a form of the idiopathic nephrotic syndrome. Causes of idiopathic nephrotic syndrome include minimal change disease (85%), mesangial proliferation (5%), and focal segmental glomerulosclerosis (10%). The remaining 10% of children have secondary nephrotic syndrome related to systemic or glomerular diseases such as membranous nephropathy or membranoproliferative glomerulonephritis⁵. The predominant pathology is minimal change disease (MCD), with contributions from other pathologies such as focal segmental glomerulosclerosis (FSGS) and mesangial proliferation. This applies only in Caucasian populations, as around the world the pathology varies. For instance, in Africa it has long been thought that ‘tropical nephropathy’ (malaria, HIV, hepatitis B etc.) predominates, though this has been challenged⁶ with schistosomiasis being responsible for the majority of the cases in South America. Nephrotic

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syndrome could be subdivided into congenital, idiopathic (primary) or secondary³.

In general, secondary nephrotic syndrome should be suspected in patients with age > 8 yr, hypertension, hematuria, renal dysfunction, extrarenal symptomatology (rash, arthralgias, etc.), or depressed serum complement levels. In certain areas of the world, malaria and schistosomiasis are the leading causes of nephrotic syndrome. Henoch- Schönlein purpura nephritis, lupus nephritis, acute post-streptococcal nephritis, sickle-cell disease, and amyloidosis also may be the cause of nephrotic syndrome. Other infectious agents associated with nephrotic syndrome include hepatitis B virus, hepatitis C virus, filaria, leprosy, and HIV. Nephrotic syndrome has also developed during therapy with numerous drugs and chemicals. The histologic picture may resemble membranous glomerulopathy (penicillamine, captopril, gold, nonsteroidal anti-inflammatory drugs, mercury compounds), minimal change disease (probenecid, ethosuximide, methimazole, lithium), or proliferative glomerulonephritis (procainamide, chlorpropamide, phenytoin, trimethadione, paramethadione)⁷⁻¹¹.

Idiopathic nephrotic syndrome

Minimal change disease accounts for most of the cases presenting in childhood. The other histological types of mesangial proliferative and FSGS may well represent the spectrum of a single disorder with varying histological features. The cause of minimal change nephrotic syndrome (MCNS) remains unknown. It is more prevalent in families with an atopic history, and some studies have suggested an abnormality of T cell function. Although broad-spectrum immunosuppressive drugs have been used to control the disease, there is lack of evidence for classical mechanisms of immunological injury. In minimal change disease, the glomeruli appear normal or show a minimal increase in mesangial cells and matrix. The immunofluorescence studies are negative, and electron microscopy reveals gross podocyte foot process fusion, which is a nonspecific finding in any patient with heavy proteinuria².

Clinical presentations

Minimal change nephrotic syndrome is more common in boys than girls (2:1) and usually occurs between the ages of 2 and 6 years³. There may be an antecedent

history of an upper respiratory tract infection and, certainly, these are well known to precipitate relapses in this condition. The presenting feature is usually edema, which is first noticed around the eyes. The edema may become generalized, with swollen limbs, ascites and pleural effusions with diminishing urine output. There may be lethargy, poor appetite, mild diarrhea and, sometimes, abdominal pain². Hematuria (mostly microscopic), hypertension and raised blood urea levels are occasionally observed³.

Dignosis

The diagnosis is suggested by simple urinalysis, which will show heavy proteinuria (3-4 +) by heat test or dipstick test. Measurement of 24 hour urinary protein is not essential. Careful and repeated microscopic urine examination should be done for red cell, persistent microscopic hematuria suggest the likelihood of significant histologic lesion³. About 30% of patients will have transient microscopic hematuria, but gross hematuria is rare. Heavy proteinuria can be confirmed by early morning urine protein/creatinine ratio (> 200 mg/mmol). Renal function is usually normal, but there will be a low serum albumin (< 25 g/L), with raised serum cholesterol (>250 mg/dl) and triglyceride levels. Swabs should be taken from the throat and any skin lesions, as well as a urine culture. An X-ray of chest and Mantoux test should be done. Overt or covert infection can be the cause of steroid resistance. Serological tests such as complement (C3) studies, an ASO titer, hepatitis B surface antigen and antinuclear factor antibodies need only be measured in patients when there is a mixed nephritic/nephrotic picture. Children between the ages of 1 and 10 years are very likely to have steroid-responsive minimal change disease and so prednisolone therapy is usually initiated without a renal biopsy.

A biopsy may be considered in children with nephrotic syndrome if²:

1. onset of NS occurs between 6 and 12 months of age,
2. onset over 12 years of age (other pathology may be more likely),
3. persistent hypertension, microscopic hematuria, or low plasma C3,
4. renal failure - persistent and not attributable to hypovolemia; Secondary nephrotic syndrome and steroid resistance cases require renal biopsy³.

Complications

The major complication is infection. Spontaneous bacterial peritonitis is the most frequent type of infection. Although *Streptococcus pneumoniae* is the most common organism causing peritonitis, gram-negative bacteria such as *Escherichia Coli* may also be encountered. Other infections such as sepsis, pneumonia, cellulitis and urinary tract infections may also be seen¹². A high prevalence of tuberculosis has been reported in children with nephrotic syndrome, especially those receiving immunosuppressive drugs for a long period³. The reasons for the susceptibility may be multifactorial and include decreased immunoglobulin levels, ascitic fluid acting as a culture medium and immunosuppressive therapy. While on corticosteroids the clinical findings may be masked, and so any child with nephrotic syndrome and abdominal pain should be carefully evaluated. Nephrotic children also have a tendency to arterial and venous thrombosis. The nephrotic syndrome is a hypercoagulable state with high levels of fibrinogen, factor VIII:R:AG and alpha-2-macroglobulin with a decrease of both functional and immunological antithrombin III¹³.

Treatment:

Hospitalization should only be required for the initial attack, when the diagnosis can be established, treatment initiated and the response evaluated. It will also give an opportunity to educate the patient and the family in what may be a frustrating chronic illness. Good education and efficient communication should enable further problems to be assessed and treated on an outpatient basis. Bed rest does not need to be enforced, as the child will determine their appropriate activity level. The traditional high-protein, no-salt-intake diet should be abandoned in favor of trying to maintain the recommended daily allowances of calories and protein in a child whose appetite is likely to be markedly diminished until on steroids¹⁴.

Edema

When edema is present, no-added-salt diet is advised, with avoidance of foods known to be high in sodium, particularly snack or processed foods. In severe edema, in addition to sodium restriction, fluid restriction may be necessary¹⁵. The water intake may be limited to replacement of insensible losses plus urine output minus a planned weight loss³. Patients with nephrotic

syndrome are prone to hypovolemia and drastic change in the daily weight should be avoided. Diuretics should be used with caution in plasma-volume-depleted nephrotic patients, as they may be predisposed to fluid and electrolyte disturbances. Thiazide diuretics have little effect. Cautious use of loop diuretics such as furosemide (frusemide) (1-2 mg/kg/24 h), in combination with an aldosterone antagonist such as spironolactone 0.5-5 mg/kg/24 h (which may take several days to act), can be used to control the edema, until there is a diuretic response to the corticosteroids. Occasionally, metolazone (0.2-0.4 mg/kg/24 h), in combination with furosemide (frusemide), may be needed to induce a diuresis, but careful biochemical monitoring is required. If there are signs of hypovolemia, such as abdominal pain (due to a contracted plasma volume), hypertension, oliguria, low urinary sodium excretion (<10 mmol/L) or evidence of renal insufficiency, then an i.v. 4.5% albumin infusion (1 g/kg) given over 3-4 h with careful monitoring and followed by furosemide (frusemide) (1-2 mg/kg) may replenish intravascular volume. For diuretic-resistant symptomatic edema, 20% albumin infusion (1 g/kg) can be added if intravascular volume is adequate, to promote loss of peripheral fluid. Albumin infusions are both expensive and potentially hazardous, as pulmonary edema could be precipitated if the volume status has been misjudged. Since most of the infused albumin is rapidly lost in the urine, there is little place for their routine use. Mannitol (5 ml/kg of 20% solution) and furosemide (frusemide) (2 mg/kg/dose) have also been used to treat diuretic-resistant edema¹⁶. 'Resistant oedema' was considered based on failure to achieve therapeutic response to diuretics or a weight loss of <1% body weight daily. In a study¹⁷ reported that response to mannitol-furosemide (intravenous mannitol 0.5-1 gm/kg/day in single daily dose over 1-2 hrs followed by intravenous furosemide 1 mg/kg/day for 5 days) combination is as effective as albumin with furosemide in the treatment of diuretic resistant oedema in children with nephrotic syndrome. However, new combination is less costly and may be more useful in developing country like Bangladesh.

Corticosteroid therapy 95% will respond to steroid therapy within the first 4 weeks. The consensus regimen proposed by the British Association for Paediatric Nephrology was prednisolone 60 mg/m²/d until the urine was protein-free for 3 d, followed by 40 mg/m² for 4

weeks¹⁸. Daily prednisolone 60 mg/m² for a full 4 weeks followed by a further 4 weeks of alternate day therapy at 40 mg/m² proposed by ISKDC (International Study of Kidney Diseases in Children) is not recommended³. The increase in the initial steroid dose acknowledges the evidence that the relapse rate is reduced with increased duration of initial therapy¹⁹. Now the initial episode is treated with prednisolone 60 mg/m²/day in 2-3 divided doses for 6 weeks followed by 40 mg/m² on alternate days as a single morning dose for 6 more weeks, after which it is discontinued^{3,15}. Children in their first episode should be treated for at least three months therapy recommended by Hodson et al²⁰. Cessation of prednisone after 12 weeks without a taper has no disadvantage and may limit the negative effects of prolonged courses of prednisone. A 24-month sustained remission rate of 49% and frequent-relapse rate of 29% is expected with this regimen¹⁵. Nephrologists remain concerned about the possibility of steroid side-effects, with this large initial dosage, and their effect on the hypothalamic pituitary axis. Surprisingly, there is usually little gastric upset from the use of soluble prednisolone in children, and the more expensive enteric coated forms or drugs to control gastric acidity are not routinely prescribed²¹. Children who have problems with vomiting or diarrhea should receive i.v. methylprednisolone in an equivalent dose to the oral prednisolone dosage and additional care should be taken to monitor blood pressure. It is important to exclude occult infection such as urinary tract infection as a cause of steroid resistance. The parents should be told daily steroids may well alter the child's behavior as well as increasing the appetite. General dietary advice about avoiding excess consumption of snacks, etc. should be given. A steroid warning card should be issued, and the parents should report if the child is exposed to infections such as measles or chickenpox, while on daily steroids. Immunization using live vaccines should be avoided until the child has been off daily steroids for at least 3 months, but are permissible if the child is on alternate-day steroids (< 0.5 mg/kg body weight/d).

Relapse

When there is a relapse of proteinuria (3 consecutive days of heavy proteinuria [+++ or greater]), treatment may be withheld for up to 5 d (or possibly 10 if variable proteinuria) unless the child becomes edematous. This is because some children will spontaneously remit

during this period. If proteinuria persists, then remission is induced with daily steroids as before until the urine is protein free for 3 d, and then alternate-day corticosteroids are continued for 28 d. More than 75% of children with minimal change nephrotic syndrome will have at least one relapse.

Frequent relapses or steroid dependency

If the child has two or more relapses within 6 months of initial treatment, or four or more relapses within any 12-month period (frequent relapser), then a slow weaning dose of alternate-day prednisolone may be considered, after inducing remission with daily steroids as mentioned earlier. The prednisolone may be weaned off over 6 months, and by this means steroid toxicity may be minimized.

Steroid dependency may be defined as those who relapse on two consecutive occasions as prednisolone is being decreased, or within 2 weeks of it being discontinued. If a child requires more than 0.5 mg/kg of prednisolone on alternate days to remain protein free, and particularly if there are signs of steroid toxicity, then alternative therapy should be considered. Such steroid side-effects would include stunting of growth, cataracts, obesity and behavioral changes, but alternative therapy to corticosteroids and/or the advice of a pediatric nephrologist or pediatrician will, preferably, have been sought before many of these side-effects are manifest. Alternative therapy consists of levamisole, cyclophosphamide, chlorambucil and cyclosporine which all reduce the risk of relapse in children with relapsing steroid-sensitive nephritis compared with prednisolone alone²². Steroids sparing agents used include levamisole, cyclophosphamide, mycophenolate mofetil (MMF), calcineurin inhibitors (cyclosporine and tacrolimus), rituximab and vincristine. Time to first remission is a strong predictor of the need for these agents²³. The steroid-sparing effects of these agents have greatly reduced the adverse effects seen with long-term use of steroids. Despite the wide arsenal of agents available, therapy needs to be individualised to achieve optimal care of each child¹.

Levamisole

It is an immunomodulatory agent, has been successfully employed in patients with frequent relapse (FR) and steroid dependent (SD) nephrotic syndrome. A dose of 2-2.5 mg/kg given on alternate days for 1-2 years or

longer is effective in 50-60 percent cases. Initially prednisolone 0.75 to 1 mg/kg is given along with levamisole. In 20-30 percent cases prednisolone can be gradually stopped and levamisole alone is sufficient. Side effects of levamisole are infrequent and mild gastrointestinal upset may occur³.

Cyclophosphamide

Steroid-dependent patients, frequent relapsers, and steroid-resistant patients may be candidates for alternative agents, particularly if the child suffers severe corticosteroid toxicity (cushingoid appearance, hypertension, cataracts, and/or growth failure). Cyclophosphamide has been shown to prolong the duration of remission and to reduce the number of relapses in children with frequently relapsing and steroid-dependent nephrotic syndrome. The potential side effects of the drug (neutropenia, disseminated varicella, hemorrhagic cystitis, alopecia, sterility, and increased risk of future malignancy) should be carefully reviewed with the family before initiating treatment. The dose of cyclophosphamide is 2-3 mg/kg/24 hr given as a single dose, is given after remission has been induced with daily steroids, for a total duration of 8-12 wk. Alternate-day prednisone therapy is continued during the course of cyclophosphamide administration³. An additional option for the child with complicated nephrotic syndrome is high-dose pulse methylprednisolone. Methylprednisolone is usually given as a 30-mg/kg bolus (maximum 1,000 mg), with the first 6 doses given every other day, followed by a tapering regimen for periods up to 18 mo. Cyclophosphamide may be added to this regimen in selected patients¹. It was once customary to perform a renal biopsy on all nephrotic children prior to cyclophosphamide therapy. However, this is probably no longer justifiable if the patient is still steroid responsive.

Cyclosporine: Prolonged administration of cyclosporine (3-6 mg/kg/24 hr) has also been effective in maintaining a prolonged remission in children with nephrotic syndrome and is useful as a steroid-sparing agent. Children must be monitored for side effects, including hypertension, nephrotoxicity, hirsutism, and gingival hyperplasia¹.

Mycophenolate Mofetil (MMF) This is now being increasingly used as an alternate to cyclophosphamide,

particular when there are concerns about long-term gonadal toxicity. The major limitation to its use in the developing world is its high cost. The dose is 600-1000 mg/m²/day or 20-25 mg/kg/day in two divided doses for 12-36 months. Prednisone is maintained at a dose of 1-1.5 mg/kg given on alternate days during treatment and then tapered over 4-6 weeks. Leukopenia is a common side effect and leucocyte counts should be monitored every 1-2 months and treatment stopped if it drops below 4000/mm³¹.

Cyclosporine and tacrolimus

This treatment is usually reserved for children who fail treatment with the agents above. Cyclosporine A is given in a dose of 4-5 mg/kg/day for 12-24 months while tacrolimus dose 0.1-0.2 mg/kg/day. Prednisone is continued using a dose of 1mg/kg on alternate days and tapered over 6-9 months once remission is achieved. Both agents have the potential for acute and chronic nephrotoxicity, so renal function should be monitored closely¹.

Rituximab

Its use is reserved for patients with marked steroid dependency who fails to respond to other drugs or in patients with toxicity secondary to other drugs. A significant proportion of patients relapse after rituximab treatment. Most relapses occur simultaneously with the recovery of B-cell lymphocyte counts²⁴. Maintenance therapy using mycophenolate mofetil is effective in preventing relapses after treatment with rituximab in many cases²⁵. Side effects include infusion related reactions (hypotension, fever and rigors), serious infections, and progressive multifocal leukoencephalopathy²⁶.

Vincristine

There has been one report in 2005 of patients treated with vincristine for steroid dependent NS who were relapsing despite cytotoxic or calcineurin treatment²⁷. Vincristine was used in a dose of 1-1.5 mg/m² that was given weekly for 4 weeks intravenously, followed by monthly courses for 6 months. Adverse effects were minimal. The median sustained remission was 5 months. Another study in 2006 that also showed positive results with the use of vincristine²⁸. Future controlled studies are needed to carefully evaluate the role of this drug in NS¹.

Choice of steroid sparing agents in practice:

Given the more favourable toxicity profile of mycophenolate mofetil compared to other agents; many centres are using this agent as first choice for a steroid-sparing agent. In countries where levamisole is available, this is also being increasingly used. Some experts however have suggested the use of cyclophosphamide in patients with frequently relapsing, but not steroid dependent NS, the long-term remission rate is much lower and doses used do not warrant the significant potential toxicity²³. Cyclosporine, although effective in maintaining remission requires prolonged treatment which increases the risks of nephrotoxicity. Hence its use is mainly restricted to patients that fail to maintain remission after a course of mycophenolate mofetil (MMF) or cyclophosphamide without a significant steroid dose. In a study found that treatment with cyclosporine A and combination of cyclosporin A plus MMF was useful for steroid dependent and for remission induction in steroid resistant cases²⁹.

Vitamin D and Calcium Prophylaxis

Corticosteroids are known to increase the risk for fractures however; no studies have demonstrated that corticosteroid treatment of steroid sensitive NS increases fracture risk. In a randomized controlled trial comparing vitamin D and calcium prophylaxis with no prophylaxis, bone mineral density was significantly lower in treated than non-treated patients³⁰. Hypercalciuria occurred in both groups. Adequate dietary calcium intake is necessary; most such patients also benefit from vitamin D3 supplements³. Recently a systematic review based on randomized controlled trials and observational studies concerning children >18 years with renal diseases requiring steroids is recommended calcium combined with vitamin D to prevent bone disease³¹.

Psychosocial support

It is helpful to provide the family of a child with nephrotic syndrome with an information booklet about the condition, as a great deal of anxiety can result with the clinical course of relapse and remission. In addition, the parents have benefited from attending a local parents' group, where they can discuss and share many of their anxieties³². If a nephrotic child has been free of relapses for 5 years, then there is a strong chance of a long-term remission. However, some children may continue to

relapse into adult life, and those who develop nephrosis earlier in life are likely to relapse more often³³.

Conclusion:

Many children with nephrotic syndrome have frequent relapses or become steroid dependent. The precise etiology and pathogenesis of this disease remains elusive although some progress is being made, particularly regarding its genetic origins, in elucidating its cause. Now highly potent drugs available to treat children with frequent relapses and steroid dependency, remission should be the ultimate goal in the management of this disease. Steroids remain the mainstay of treatment and with the introduction of newer therapeutic agents; the prognosis of this disease has greatly improved. The steroid-sparing effects of these agents have greatly reduced the adverse effects seen with long-term use of steroids.

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Bilateral Paget's Disease of Nipple

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Summary:

Paget's disease of nipple is a rare entity of malignant lesion of breast and bilateral Paget's disease is very uncommon. It presents as eczema like condition of the nipple areola which persists despite local treatment. As it is a superficial manifestation of underlying breast carcinoma high degree of suspicion is essential for proper recognition of this condition, so that early diagnostic work up can be initiated for differentiating it from other benign inflammatory skin

Introduction:

Paget's disease of nipple is uncommon type of breast carcinoma. More than 95% of patients also have underlying invasive or noninvasive breast carcinoma.¹ A palpable mass in breast may or may not be present. Usual presentation is as a chronic eczematous eruption of the nipple progressing to ulcerated, red weeping lesion. Paget's disease is frequently confused with eczema which tends to occur in younger people having signs of eczema elsewhere in the body. Eczema primarily involves the areola and only secondarily affects the nipple and mostly bilateral. Whereas Paget's disease is

disorder and for detecting an underlying breast carcinoma, thereby delay in proper treatment can be avoided in order to avoiding dismal consequences. Here we report a case of bilateral Paget's disease of nipple with invasive left breast carcinoma in a 40 year old lady diagnosed in Medical College for Women and Hospital, Uttara, Dhaka.

Key words: Paget's disease, Breast carcinoma.

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usually unilateral, always affects the nipple first then involves the areola as a secondary event.² Although rare, Paget's disease of nipple can occur in both breasts. In our case report the patient developed Paget's disease in one breast and treated as benign skin lesion for 3 years. She noticed a lump in same breast 3 & ½ years later and developed Paget's disease in other breast. This report focuses on the fact that though this condition is often innocuous and limited to a surface appearance, actually indicative of a very serious underlying breast carcinoma.³ So early diagnosis and prompt treatment is the basis for better outcome.

Case report:

A 40 year old lady, housewife with lower middle socio economic background presented to us on June 2010 with recurrent itching and excoriation of left nipple areola for 4 years. Lesion started at nipple then extended to areola. She experienced same at right nipple for 4 months. She also noticed a painless lump in left breast for 4 months which was gradually increasing in size. She had no nipple discharge and did not give any previous history of breast diseases. The patient had no history of eczema or dermatitis elsewhere in the body. She received treatment as eczema and fungal disease but did not improve completely. She was a premenopausal lady and her menarche started at her 13 years of age. She was a mother of 3 children; all were breast fed, her age was below 25 years during first baby;. She did not take any contraception. She was normotensive and nondiabetic. Her appetite was good and she had no

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recent weight loss. She had no history of cough, haemoptysis and jaundice or bone pain. She had no family history of breast cancer or any other cancer. She is neither a smoker nor an alcoholic. She used to take average Bengali foods.

Examination of her breasts revealed moderate excoriation of nipple with erythema in right breast without any palpable lump and severe excoriation of nipple areola in left breast with swollen areola. A well defined hard, nontender, irregular lump of about 3x3cm was found in upper and outer quadrant of left breast encroaching to areola with no fixity to underlying structures or overlying skin. Surrounding skin of her both breast appeared normal. A mobile hard, nontender lymph node of about 2x2cm was palpable in left axilla. Her right axilla and supraclavicular fossa were free of palpable lymph nodes.



Fig.-1: Right breast



Fig.-2: Left breast

She was of average weight and height with sound mental status and unremarkable general status. Her breath sound was normal; she had no hepatomegaly or ascites. No abnormality was found by digital rectal and per vaginal examinations.

FNAC of her left breast lump showed invasive duct cell carcinoma, FNAC of her left axillary lymph node revealed no malignant cell. Histopathological examination of incision biopsy from right nipple and left nipple areola confirmed Paget's disease. Ultrasound scan of both breasts detected a echogenic irregular mass in left breast. Bilateral mammography suggested a suspicious mass lesion in left breast with left axillary lymphadenopathy. Her chest skiagram was normal, ultrasound scan of whole abdomen showed cholelithiasis. Her CA 15-3 level was within normal limit. She had normal bone scan. Other routine investigations were unremarkable.

She underwent simple mastectomy with axillary dissection on left side and simple mastectomy on right side. Histopathology of tissue from left breast lump showed invasive ductal carcinoma(NOS) with invasion into surrounding tissue, grade – 3, Bloom- Richardson score 8/9. Resection margins were free of tumor, 3 Lymph nodes out of 8 showed metastatic adenocarcinoma with involvement of adjacent fibrofatty tissue. No underlying malignancy was found in excised right breast. Receptor analysis of specimen revealed negative for estrogen & progesterone receptor with positive for HER – 2.

Her post operative period was uneventful. Subsequently she delayed in receiving adjuvant therapy. After 4th cycle of chemotherapy her general condition was deteriorating; multiple secondary lesions in liver were evident on ultrasonogram. She survived for 9 months after operation.

Discussion:

Paget's disease of breasts represents approximately 1-3% of all breast malignancies; Sir James Paget, an English surgeon first described it in 1874.³ It is usually associated with Duct cell carcinoma in situ or invasive carcinoma. More than 50% of patient have lump in breast. It is most common in women in their 50s but can occur at a younger or older age. Involvement of male breast is rarely reported.⁴ Only a few cases of bilateral Paget's disease of the breast have been described world wide.⁵ To our best knowledge no such case was reported in

Bangladesh. In a study in Japan Paget's disease accounts for 1.2% of all breast cancer.⁶ In a case report, Bijian xie et al described bilateral paget's disease of the breast without underlying cancer in a 45 year old Chinese lady having gastric cancer.⁵

Exact cause of Paget's disease is still unknown. But in this connection two theories have been suggested in literature. One theory proposes that cancer cells called paget cells break off from a tumour inside the breast and move through the milk ducts to the surface of the nipple resulting in Paget's disease of nipple. The theory is supported by the fact that more than 97% of the patient with Paget's disease also have underlying breast carcinoma or duct cell carcinoma in situ. Other theory suggests that skin cells of nipple spontaneously become Paget cell. This theory is supported by the rare case of Paget disease in which there is no underlying breast carcinoma and the cases in which the underlying breast carcinoma is found to be a separate tumour from paget's disease.¹

Initially Paget's disease presents as mild eczematous rashes or scaling with redness & itching affecting usually only one nipple. Then the condition spreads outward onto areola & surrounding skin of the breast.⁷ More advanced disease may show more serious destruction of skin with straw coloured or bloody nipple discharge; nipple becomes flattened or inverted or is eroded slowly and eventually disappear leaving a weeping ulcer.⁸ Underlying breast carcinoma sooner or later becomes clinically evident. Patient may have pain, tingling, itching, burning and increase sensitivity. It is common for the symptoms to disappear for a while which misguides the patient.

The clinical differential diagnosis of this condition includes eczema, contact dermatitis, psoriasis and post radiation dermatitis.⁷

An incision biopsy from the lesion can confirm the diagnosis by the presence of paget's cell – large, pale, vacuolated cells in the epidermis. Paget's cells do not invade through dermal basement membrane therefore are a form of carcinoma in situ.⁷ Other useful diagnostic tools are imprint or scrap cytology or superficial epidermal shave biopsy or punch biopsy of nipple lesion. Sample of nipple discharge may also be examined microscopically for presence of paget's cell.⁹ Fine needle

aspiration cytology of the lump confirms the underlying breast cancer where lump is present. Mammography may be helpful for better delineation of any abnormalities like skin thickening, nipple retraction, presence of subareolar mass, subareolar or diffuse malignant calcification, a discrete or multifocal mass.¹⁰ Supplementary ultrasonogram of breasts is helpful for further evaluation of abnormal mammographic findings. Detection of early stage of cancer by Magnetic resonance imaging is also reported.¹¹

Surgical treatment is the mainstay of treatment. Simple mastectomy with or without an axillary node procedure is recommended for noninvasive carcinoma. Extensive duct cell carcinoma in situ or invasive carcinoma is treated by modified radical mastectomy. Anticancer drugs, radiation therapy, hormone therapy or immunotherapy are the other modalities of adjuvant treatment.

Survival rate in paget's disease alone at 5 year is 85% when lymph node is negative whereas in cases of positive lymph node it is about 32%. Patient with an underlying breast carcinoma have survival rate of 38 – 40% at 5 years. Death rate of metastatic breast carcinoma in patient with paget's disease & underlying carcinoma is about 61.3%.¹² Our patient got the dismal outcome probably due to delay in diagnosis and subsequently delay in starting chemotherapy.

Conclusions:

According to cancer research UK, paget's disease is found in one or two out of every 100 cases of breast carcinoma.¹³ There are fewer than 10 cases of bilateral involvement described in the literature.⁵ It is difficult to diagnose due to its resemblance to dermatitis & eczema. Histopathological study is the only gateway. Awareness of women is vital. Early diagnosis ensures better outcome. So the women experiencing any changes in nipple areola always should get examined by their General practitioner and who should not delay to refer the suspicious cases to specialist doctor.

Acknowledgement:

Late Prof. AKM Mahbubur Rahman, Honorary professor, Dept. of surgery, Medical college for Women & Hospital, Uttara, Dhaka.

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Thymoma Presenting as a Giant Intrathoracic Mass

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Summary:

Thymoma is an epithelial neoplasm of the thymus, which commonly lies in the anterior mediastinum. Thymomas comprise about 1% of all mediastinal tumours. The current treatment of invasive thymoma is often multidisciplinary. This report presents a case of giant thymoma arising in the anterior mediastinum.

Surgical resection was scheduled based on the radiological and fine needle aspiration cytology findings. The tumor

was completely resected. The weight of the tumor was 2000g. The tumor was histologically diagnosed to type B1 thymoma. Patient was discharged from hospital with advice to attend the oncology department for next treatment.

Keywords: *Intrathoracic mass, Giant thymoma, Type B1 thymoma.*

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Introduction:

Thymomas are epithelial neoplasm of the thymus. The overall incidence of thymoma is rare, which approximately 0.15 cases per 100,000 of the population per year¹. Thymoma account for about 20 percent of mediastinal neoplasm. Localization of thymoma resembles that of thymus itself with 75% of thymoma originating in anterior mediastinum, 15% originating in both anterior and superior mediastinum, 6% originating in the superior mediastinum. Other 4% occur ectopically². In general, thymomas are indolent tumors with local recurrence rather than metastasis. Thymic carcinomas, however, are typically invasive, with high risk of relapse and death^{3,4}. Most thymomas patients are between 40 to 60 years of age, and there is slight male predominance. Invasive thymomas and thymic carcinomas are relatively rare tumors, which together represent about 0.2-1.5% of all malignancies⁵. The major

histological classifications of thymoma by World Health Organization⁶ is: A-Medullary, AB-Mixed type, B1-Predominant cortical, B2-Cortical, B3-Well differentiated thymic carcinoma, C-Undifferentiated carcinoma.

Symptoms from thymoma or thymic carcinoma may be due to the presence of a tumor in the mediastinum or may be a manifestation of a paraneoplastic syndrome. Clinical signs and symptoms are related to the size of the tumor and its effects on adjacent organs (eg, chest pain, shortness of breath, cough, phrenic nerve palsy, Superior vena cava obstruction). Pleural or pericardial effusion are the most common manifestations of metastatic involvement. Extrathoracic metastases occur in less than 7% of patients⁷.

Thymomas are associated with a wide variety of paraneoplastic disorders, the most common of which is myasthenia gravis. These syndromes are seen in 50 to 60 percent of patients, and more than one syndromes may be present⁸. Upto one-half of thymomas are diagnosed incidentally, based upon a radiographic abnormality in an asymptomatic patient⁹.

Although surgery is the most effective treatment modality for thymomas. In some cases, it is difficult to excise due to involvement of surrounding organs or tumor size. This report presents a case of thymoma that presented as a giant intrathoracic tumor, histologically diagnosed as type B1 thymoma.

Case presentation:

A 52-year-old male presented with left sided chest pain, breathlessness and weakness in both upper limb.

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Thorough clinical examinations and laboratory tests were done according to symptoms and history. In the examination of motor system, muscle tone and power were reduced whereas bulk was normal in both upper limbs. On chest examination breath sound diminished on left side and other examinations revealed normal. Antiacetylcholine receptor antibody level 1 ± 79 nmol/L. Other laboratory data were normal. Chest X-RAY P/A view shows a large soft globular opacity was seen in left mid and lower zone, perihilar and pericardial region, suggestive of anterior mediastinal mass of chest (Figure-1). Chest Computed tomography revealed a sizable well-delineated soft tissue mass (10.4x8.1cm) was seen at anterior to ascending aorta and pulmonary trunk, extended downward along the aortic arch down till left hilum (Figure-2). This soft tissue mass shows inhomogeneous enhancement after contrast administration. A Computed tomography guided fine needle aspiration cytology revealed moderate cellular material containing a good number of epithelial cells and a moderate number of lymphocytes of different size with some histiocytes in the background of blood. No malignant cell was seen. An intrathoracic benign tumor was suspected, therefore surgical resection was decided and performed. Surgical access to the mass was



Fig.-1: Chest x-ray P/A view shows anterior mediastinal mass of chest with left phrenic nerve palsy.

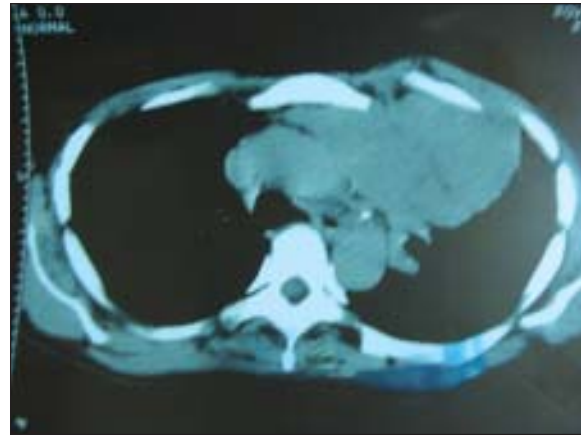


Fig.-2: Computed Tomography scan shows lobulated mass in the anterior mediastinum.

accomplished through a vertical midline incision beginning from sternal notch and extended to the xiphoid with median sternotomy, had some adhesion to the pericardium, pleura of both lungs and left lung. A well-defined giant mass measuring $10 \times 12 \times 8$ cm was found in the mediastinum and left thoracic cavity. The tumor was completely resected without combined resection of the other organs. Some broncho-pleural fistula developed and repaired accordingly. The weight of the tumor was 2000g. On gross examination it was a well encapsulated mass, outer surface was bosselated. The cut surface of tumor revealed mostly white and partly brownish. Histopathological examination showed a benign tumor composed of densely packed population of small lymphocytes giving rise to starry-sky appearance. Pale areas of medullary differentiation are seen. The neoplastic epithelial cells having pale round to oval nuclei with occasional small nucleoli are also present dispersely. These histopathological findings indicated that the tumor was a type B1 thymoma according to the World Health Organization classification. The postoperative course was uneventful (postoperative management up to discharge). Then patient was referred to oncology department to Dhaka Medical College Hospital for next treatment.

Discussion:

Approximately half of all thymomas never produce symptoms, and are discovered incidentally, either on a routine chest X-RAY or at autopsy⁹. Our patient had anterior mediastinal mass on chest X-RAY. In large retrospective study, approximately 47% of thymoma

cases (excluding thymic carcinoma) were found to be associated with myasthenia gravis¹⁰. This is manifested by the presence of measurable antibodies to acetylcholine receptors as demonstrated in our patient. The symptoms of myasthenia gravis usually precede the discovery of a thymoma. Reports indicate the association of myasthenia gravis with thymoma to be about 15% but increase to 35% in older patients¹¹. Our patient 52 years old male presented with left sided chest pain. Ocular symptoms like diplopia and ptosis are the commonest clinical presentations in myasthenia gravis seen in more than 50% of patients¹². In this case there was no such features.

Thymomas develop in the thymus and are usually located in the anterior mediastinum, only 4% of the tumors are ectopic tumors¹³. Thymus develops from the ventral portion of the third and fourth pharyngeal pouches and then descends into the anterior mediastinum by the sixth week of gestation. Thymic ectopia results from failure of this migration¹⁴. Ectopic thymomas have been reported in the neck, middle or posterior mediastinum, lung and pleura, a few reports have described giant intrathoracic tumors¹⁵. In this case thymus was situated in the normal place (intra-thoracic).

As we suspected this as a case of thymic growth on X-ray, we undertook various imaging procedures, among which, Computed Tomography scan was more informative. Keen and Libshitz reported that the presence or absence of intervening fat planes on Computed Tomography accurately predicts vascular and/ or pericardial invasion¹⁴. However, Fon GT et al. reported that although the presence of preserved fat planes between a thymoma and the adjacent vascular structures reliably excludes macroscopic invasion, the absence of such fat does not consistently indicate an invasive tumor¹⁶. In this case we performed chest Computed Tomography scan which revealed well delineated soft tissue mass seen at anterior to ascending aorta and pulmonary trunk, extended downward along the aortic arch down till left hilum.

Although the oncological prognosis of thymoma is reported to be more favorable in patients with myasthenia gravis than in patients without myasthenia gravis¹⁷. Treatment with thymectomy may not significantly improve the course of thymoma associated myasthenia gravis¹⁸. Standard primary treatment for

these types of tumors is surgical with en bloc resection for invasive tumors, if possible. This report suggests our line of management^{19,20}. Thymoma and thymic carcinoma should be differentiated from a number of nonepithelial thymic neoplasm, including neuroendocrine tumors, germ cell tumors, lymphomas, stromal tumors, tumor like lesions (such as true thymic hyperplasia), thymic cysts, metastatic tumors and lung cancer²¹. In our case after thymectomy we send for histopathology. Findings indicating the tumor was type B1 thymoma. Depending on tumor stage, multimodality treatment includes the use of radiation therapy and chemotherapy with or without surgery^{22,23}. After surgery we referred our case to oncology department to Dhaka Medical College Hospital for further management. Thymoma has been associated with an increased risk of second malignancies, which appears to be unrelated to thymectomy, radiation therapy, or a clinical history of myasthenia gravis^{24,25}. In this case we decided to follow up the patient at regular interval to rule out second malignancies.

The widely accepted staging system is used for thymoma is that proposed by Masaoka et al. based on a postoperative staging procedure, since capsular invasion, a key staging system, is best evaluated by pathologic examination²⁶. Recently, the World Health Organization classification of thymic tumours²⁷ based on the histological assessment of the morphology of the neoplastic epithelial cells has received increasing acceptance, and it has been shown to be of prognostic significance^{28,29}. Thymomas are classified as type A, AB, B and C in the World Health Organization classification, and exhibit organotypic (thymus-like) architectural features.

Nevertheless, the prognostic relevance among type B thymoma subtypes is still controversial. They did not find any significant differences in the incidence of recurrence and survival among the three subtypes of type B thymomas³⁰. The tumor was diagnosed to be type B1 thymoma according to the World Health Organization classification.

The presence of myasthenia gravis in patients with thymoma had been regarded as an indicator of poor prognosis, recent evidence suggests that this is not the case. There are reports of improved survival rates for patients with myasthenia gravis with thymoma³¹.

Indeed prognosis may be improved because thymomas are diagnosed at an earlier stage. In addition, the recurrence rate of patients with myasthenic thymoma is lower than that of patients with nonmyasthenic thymoma³².

Although thymomas can present as huge masses, the symptoms and stage may not always correlate with tumor size. A large tumor size is a significantly poor prognostic factor of thymomas³³. Limmer et al. reviewed previously reported giant thymomas³⁴. Interestingly, although a large tumor size is a poor prognostic factor, the resected giant thymomas tended to be low-grade thymomas.

Conclusion:

This report presented a very rare case of an intrathoracic giant thymoma, histologically diagnosed as type B1. Extended thymectomy followed by radiotherapy must be considered in this type of lesion.

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A Case of Wolfram Syndrome Presenting with Restlessness

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Summary:

Wolfram Syndrome (DIDMOAD) is a rare genetic disorder presenting with Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, Deafness and some other neurological , reproductive , hormonal, urological and psychic problems. About 200 cases have been reported so far. Here we present a 25 years old Bangladeshi male having early onset Diabetes Mellitus, optic atrophy, deafness and many other features consistent with Wolfram Syndrome. We examined the patient thoroughly and did necessary

investigations to confirm our diagnosis. As there is no cure of this disorder, we gave symptomatic and supportive treatment to the patient to make his life easier. Although the outcome is unrewarding , such patients will be kept in regular follow up for early detection of new complications and possible solutions.

Keywords: *Wolfram Syndrome, Diabetes insipidus, Diabetes mellitus, optic atrophy.*

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Introduction:

Wolfram Syndrome is a rare neuro-degenerative disorder involving central nervous system, peripheral nerves and neuro-endocrine tissue. This rare genetic disorder , also known as DIDMOAD (Diabetes Insipidus , Diabetes Mellitus, Optic Atrophy, Deafness) presents with early onset diabetes mellitus and optic atrophy. Patients are most likely to develop diabetes insipidus, deafness , urinary tract and neurological abnormalities.¹ It is an autosomal recessive disorder and the causative gene maps to chromosome 4p16.1. The mutation causes loss of function of the protein, wolframin that has important role in the homeostasis of endoplasmic reticulum. Recently, another causative gene, CISD2, has been identified in patients with a type of Wolfram Syndrome (WFS2) resulting in early optic atrophy, DM, deafness, decreased life span but no diabetes insipidus². Treatment is mostly supportive . Prognosis is very poor with the highest life expectancy of 35 years in 60% of the patients³. This case report describes a 25 years old male of Wolfram Syndrome with an affected sibling.

Background:

Wolfram Syndrome was named after a physician D J Wolfram who reported 4 cases in 1938⁴. Frequency is 1 in 100000 to 1 in 700000³. Parental consanguinity is often present in affected siblings. This rare complex hereditary disorder manifests as Young onset non immune insulin dependent diabetes mellitus and progressive optic atrophy in all patients. In 70% patient diabetes incipidus and sensory neural deafness is added where it is referred to as DIDMOAD³. The natural history of Wolfram syndrome was described in 45 individuals from 29 families in UK ⁵. By the age of 20 years, 64% had hearing impairment and 60% of all (mean age 16 years, range 5-32 years) had one or more of the following: cerebellar ataxia, peripheral neuropathy, intellectual disability, dementia, psychiatric illness and urinary tract atony. Constipation, chronic diarrhea and other bowel dysfunction is reported in 25% cases⁶.

Case Report:

Our case is a 25 years old Asian male from Tongipara, Munshigonj, born to consanguineous parents, presented with restlessness for 1 day, and gradual loss of vision for 7 years. He was a diagnosed case of diabetes mellitus and was on insulin for 18 years. He also had ployuria , polydypsia, occasional episodes of altered consciousness and poor control of diabetes mellitus. The patient developed hearing difficulty for 3 years and his intellectual function was below average.

The patient has one affected sister of 16 years having diabetes mellitus for 5 years and dimness of vision for 1.5 years. She also has hearing difficulty.

Examination revealed a height of 56.5 inches, weight 45 kg, BMI 21.51, decreased axillary hair, absence of chest hair, normal pubic hair and presence of gynecomastia.

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Cranial nerve examination showed- decreased smell perception, visual acuity decreased to perception of light, funduscopy revealed- pseudophakia of both eyes, liquefied vitreous, bilateral primary optic atrophy and microaneurysm. Sensory neural hearing impairment was noted. Testicular atrophy with soft testes was found.

The patient underwent some investigations. CBC showed Hb % -9.1 gm/dl, WBC- 20.9×10^3 /cmm, RBC- 3.82×10^6 /cmm, DC- N-91.1%, Hct- 29.7%. Urine R/E showed Albumin: +, Pus cell: 5-10/HPF, Epithelial cells: 4-6/HPF, RBC: 2-4/HPF, presence of granular casts. Serum sodium was high (150 mmol/L) initially but later it became normal. USG of whole abdomen revealed cholelithiasis, bilateral hydronephrosis and cystitis. Audiogram showed – bilateral moderate sensory neural hearing loss. Some hormonal studies were done with the following results- Follicle Stimulating Hormone (FSH): 37.06 mIU/ml (Very High), Leutinizing Hormone (LH): 12.49 mIU/ml (Slightly Raised), Testosterone: 0.40 nmol/L (Very low, Normally 10.4-35.71 nmol/L for 20-30 years male). Plasma Osmolality: 282, Urinary Osmolality: 283, urinary specific gravity was 1.008. MRI of brain was normal.

Discussion:

Wolfram syndrome usually presents with non autoimmune, non HLA linked diabetes mellitus with optic atrophy in 1st decade, diabetes incipidus and sensory neural deafness in 2nd decade, renal tract abnormalities in the 3rd decade and multiple neurological abnormalities like cerebellar ataxia, myoclonus and psychiatric illness early in the 4th decade⁵. In our case, the patient was first diagnosed as having IDDM at the age of 7 years that is in the 1st decade and developed gradual dimness of vision for 7 years that is approximately at the age of 18 years. He had no evidence of diabetic retinopathy. And for the last 3 years he can only differentiate light from darkness.

The patient had polyurea and urinary osmolality was slightly decreased. Water deprivation test could not be done as the patient and relatives refused after explaining the procedure. So the presence of diabetes incipidus could not be proven.

Our patient developed hearing difficulty around the age of 22 years. It was also proven by audiogram. Audiograms show a down sloping progressive pattern of hearing loss in WS⁷.

A wide range of urological abnormalities are seen in patients with Wolfram Syndrome including varying degrees of upper urinary tract dilatations, recurrent bladder infection, and bladder dysfunction⁴. USG of our patient revealed bilateral hydronephrosis and cystitis.

The presence of decreased hair, gynaecomastia, testicular atrophy and high gonadotropin levels proves gonadal failure in our patient. Hypogonadism in Wolfram syndrome is more common in males, while females usually retain their ability to become pregnant⁸. A few episodes of aggressive behavior was noted in our patient.

Our patient has an affected sister and his parents are 1st cousins. This type of family history is very common in patients of Wolfram Syndrome.

There is no definitive treatment of these patients. Supportive care like insulin for DM, vasopressin for DI, hearing aids and hormone replacements along with prevention of secondary complications like those of DM and regular surveillance to detect manifestations early – are the principles of management. Genetic counseling must be provided that at conception, each sib of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier and a 25% chance to be unaffected. The prognosis is very poor with a premature death before the age of 35 years in 60% patients³. Common causes of death are hypoglycemic coma, status epilepticus, ESRD and suicide⁸.

Conclusion:

Wolfram Syndrome is a rare genetic disorder but whenever a young patient presents with early onset diabetes mellitus and optic atrophy, the possibility of Wolfram Syndrome should always be kept in mind. Subtle symptoms such as attitude change, growing reading difficulties in the history of children or adolescents with antibody negative and ketone negative DM should alert the treating physician for further evaluation⁹. Although the outcome is unrewarding, steps should be taken to improve the quality of life and to prevent complications. Multidisciplinary approach should be instituted as early as possible to make the patient's short span of life worthwhile.

Consent:

Written informed consent was obtained from the patient's father for publication of the case report and accompanying images. A copy of the written consent is available for review by the Editor in Chief of this journal.

Conflict of Interest:

The authors declare that they have no conflict interests.

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Precocious Puberty with Primary Hypothyroidism due to Autoimmune Thyroiditis

SB KASEM

Summary:

Children with hypothyroidism generally have delayed pubertal development. Rare association with precocious puberty may occur especially in long standing untreated patients. The cardinal features of hypothyroidism induced pseudoprecocious pubertal development include thelarche, galactorrhoea & menarche. Other characteristic features are absence of sexual hair & retardation of linear growth. In this report a rare case of vaginal bleeding, large multicystic ovaries, precocious puberty, slow physical & mental growth

in a seven and half years old girl with hypothyroidism due to autoimmune thyroiditis is described. It is important to recognize this syndrome because initiating simple thyroid hormone replacement completely resolves symptoms and hormone abnormalities, avoiding unnecessary investigations for malignancies or surgical intervention.

Key words: Precocious puberty, Hypothyroidism, Autoimmune thyroiditis.

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Introduction:

Sexual precocity is the onset of sexual maturation at any age that is 2.5 standard deviations earlier than the normal age for that population, being usually before the age of eight years. It may be classified as central, or GnRH dependent, precocious puberty (true precocious puberty) or peripheral, or GnRH independent precocious puberty (pseudo precocious puberty)¹. Endocrine disorders such as hypothyroidism may accelerate hypothalamic pituitary axis maturation, resulting in precocious puberty¹. Hence, precocious puberty secondary to hypothyroidism behaves like an incomplete form of gonadotropin dependent precocious puberty².

Juvenile hypothyroidism is a common disorder which usually presents with short stature and delayed puberty. Rarely sexual precocity can occur due to severe hypothyroid in young children. In girls precocity manifests as breast enlargement, uterine bleeding and multicystic ovaries³. In 1960, Van Wyk and Grumbach first described a syndrome characterized by breast development, uterine bleeding and multicystic ovaries in the presence of long standing primary hypothyroidism⁴. Looking for hypothyroidism in girls with ovarian masses and precocious puberty is

important in order to avoid surgery on the ovaries⁵. This condition is very important to recognize as it is completely treatable with levothyroxine³. In this case hypothyroidism occurs due to autoimmune thyroiditis. Autoimmune thyroid disease (ATD) is the most common autoimmune condition, affecting approximately 2% of the female population & 0.2% of the male population⁶. In females it usually occurs early to mid puberty. Optimal quantities of thyroid hormone are critical to neurodevelopment and growth⁶. ATD arises due to complex interactions between environmental and genetic factors, that are yet to be completely defined. Even with identical twins the concordance rate is only about 50%, emphasizing environment play a role in disease pathogenesis⁶. Most cases of syndrome in the literature are secondary to autoimmune thyroid disease but there are some case reports where the syndrome is secondary to unrecognized congenital hypothyroidism⁴. Although rare, the exact incidence of pseudoprecocious puberty attributable to hypothyroidism is unknown⁷.

Case report:

A seven and half years old girl was attended in Gynae outpatient department in Sir Salimullah Medical College Hospital because of a history of single episode of pervaginal bleeding for 5 days and slight enlargement of breast for one year. Bleeding was average in amount (use 2-3 pads/day). There was no history of local trauma or discharge, foreign body insertion, bleeding from any other site and difficulty in micturation. The patient did not have a history of convulsions, meningitis,

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encephalitis, head injury or hormonal therapy. She was born at term pregnancy without any complication in a lower middle class family. Her parents noticed that she had slow mental and physical development compared with her brother. They also complain that she has low memory, fatigue, cold intolerance and constipation and excessive weight gain. There is no family history of similar condition.

On examination, Patient looked lethargic, pale with puffy face. Her temperature was 98.4°F. Height was 115cm (<10th percentile), body weight was 32kg (>90th percentile). Her blood pressure was 95/55mm of Hg, pulse was regular with a rate of 68/min. Thyroid gland was slightly enlarged, which was diffuse & non tender. Lymph nodes- not enlarged. Heart and chest were normal. Her breast buds were developed as Tanner stage 2-3 (fig-6) without galactorrhoea or other external signs of sexual maturation. Abdomen was distended, no abnormal pelvic and abdominal mass was palpated. No pitting oedema. On genital examination no abnormalities were detected. No pubic or axillary hair growth. She was intolerant to cold.

Initial laboratory data showed: Haemoglobin-11.5g/dl, ESR- 15mm/1st hr, total WBC count- 7500/mm³, platelet -280,000/mm³, MCV- 88.4fl, MCH-30.3pg, RDW-CV-14.6%, RBS- 5.3mmol/L, Alkaline phosphatase- 156 U/L, Total cholesterol- 200mg/dl, Tryglyceride- 232mg/dl, HDL cholesterol- 33mg/dl, LDL cholesterol -120mg/dl, Urine RME- NAD.

Anti-Thyroglobulin Ab- 82.50IU/ml (normal<34), Anti-Thyroid Peroxidase Ab-163.70IU/ml (normal <12).

Endocrinological evaluation revealed: T3- 0.54ng/ml (normal 0.86-2.70), T4- 4.36ng/dl (normal 5.50-15.00), FT4- 0.40ng/dl (normal .77-2.08), TSH>100.00mIU/ml (normal 0.70-5.70), LH- 0.62mIU/ml (prepuberty female <0.20), FSH 2.06 mIU/ml (prepuberty female <2.00), Prolactin 50.10ng/ml (normal 2.8-29..2),

Estradiol- 10.63pg/ml (child<10.00), Progesterone- 0.02nmol/l, Testosterone- 0.10nmol/L, Cortisol- 2.56ug/dl, GH- 0.19ng/ml (normal 0.06-50), DHEA -S04 21.30ug/dl (normal 35-450), Ca125- 12.50U/ml (normal <35.00).

Pelvic ultrasound: Uterus is anteverted in position. Longitudinal, side to side and anteroposterior diameter are about(6.2×3.1×2.6)cm. Myometrial and endometrial echotexture is uniform. Endometrial thickness is about

5-6mm. There are enlarged cystic mass in both adnexal region. Cyst in right ovary measures about 9.3×6.7cm. Cyst in left ovary measures about 9.1×5.3cm. Both cysts are closely applied with each other, wall of both cysts are thin and multiple thin septations are seen in both cysts (Figure-2).

Thyroid Ultrasound: Thyroid gland slightly enlarged.

Xray skull: Enlarged pituitary fossa. Sella turcica is widened and deep.

These results were consistent with diagnosis of Precocious puberty with primary hypothyroidism as a result of chronic autoimmune thyroiditis.

After establishment of diagnosis, L-thyroxin 75µg once daily was given. Within few days after treatment vaginal bleeding was stopped and there was no recurrence. In addition the patient was improved both physically and mentally and her weight decrease to 22Kg (<50th percentile). Over the last six months of follow up the post treatment laboratory data become normal except antithyroid antibodies remain raised. Pelvic ultrasound revealed normal uterus and ovaries.

Discussion:

The cause of vaginal bleeding must be sought when bleeding occurs in young girl and clinical presentation may help in establishing the correct diagnosis⁸. We report a typical case of vaginal bleeding that is caused by hypothyroidism & its successful treatment with thyroxin replacement therapy. Here hypothyroidism occurs due to autoimmune thyroiditis.

Generally hypothyroidism is associated with delayed sexual maturation and delayed puberty. However, rarely it is associated with paradoxical precocious puberty, especially in longstanding untreated acquired hypothyroidism, a strikingly unphysiological association. This entity of hypothyroidism with precocious puberty was first described by Kendle in 1905⁹. Etiology of acquired hypothyroidism could be undiagnosed autoimmune thyroiditis. Van Wyck-Grumbach first reported the association of hypothyroidism with multicystic ovaries and precocious puberty. This is also called the Van Wyck Grumbach syndrome. There is no axillary and pubic hair development in both sexes. Exact pathophysiology for this paradoxical phenomenon is not clear⁹. But there are several explanations: A convincing explanation of sexual precocity and bilateral ovarian enlargement is that high levels of TSH seen in profound hypothyroidism could act through the FSH-r (FSH receptor) and cause gonadal

stimulation. This causes breast development, uterine bleeding, multicystic ovaries in girls⁸. The glycoproteins TSH, FSH, LH and hCG share a common alpha subunit but have a unique beta subunit that is specific to each hormone. They each act through transmembrane GPCRs to activate adenylate cyclase and stimulate c-AMP production⁴. Anasti et al¹⁰ showed that recombinant human TSH elicited a dose-dependent response at the human FSH receptor. The TSH concentration required was several orders of magnitude higher than FSH, demonstrating that the FSH-like activity of TSH is very low⁴. Prolactin concentration was high as this hormone (prolactin) and TSH share the same hypothalamic releasing factor TSH releasing hormone (TRH). Continuous and high TRH concentrations have been shown to stimulate FSH secretion as well¹¹.

On the otherhand, hyperprolactinemia reduced gonadotrophic clearance and decrease dopaminergic and opioid tone at the hypothalamic pituitary axis. Pituitary enlargement with long standing profound hypothyroidism results from prolonged and or target organ failure in the absence of the appropriate hormone replacement, the loss of negative feedback of hypothalamus and secondary hypertrophy or hyperplasia of the thyrotrophic cells in the anterior lobe of pituitary gland⁸. Sometimes there is hyperplasia of not just thyrotrophs, but lactotrophs as well causing hyperprolactinemia¹¹. Pubic and axillary hair is absent due to non arousal of adrenal gland. Unlike other precocious puberty, height acceleration does not occur in this condition and bone age gets retarded³. Thyroid hormone (TH) may actually be considered a growth factor, and TH deficiency impairs child growth and development, even when the growth hormone is present¹². Providing TH is adequately replaced, and there is enough time for catch up growth before true puberty occurs, it is conceivable that patients can achieve a final height within normal limits¹.

Conclusion:

Where vaginal bleeding occurs in young girls, hypothyroidism should be considered especially when vaginal bleeding is accompanied with additional clinical presentations such as short stature, delayed bone age and multicystic ovaries⁸. Early recognition of thyroid dysfunction is necessary to prevent the negative effects of hypothyroidism on growth and metabolic function and to prevent deranged pubertal development⁶. Thyroxin replacement therapy lead to complete resolution of such disorder and promote normal physical and mental development of young girls⁸. Parents of

children with AT should be advised that the hypothyroidism is likely to be permanent and monitoring of thyroid function for all patients should be lifelong⁶.

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IMAGES IN MEDICAL PRACTICE

Janeway Lesions in Systemic Lupus Erythematosus

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(*J Bangladesh Coll Phys Surg 2016; 34: 48-49*)

A 19-year-old male presented with rapidly progressing shortness of breath for three days. He noticed puffiness of face and swelling of feet, developing over three weeks, and some painless reddish lesions on the palms and soles [Image A & B], for two months. Examination revealed “butterfly-rash” on the face, sparing the



Image A: Janeway lesion in palm and finger-tips.

nasolabial folds [Image C]. The lesions on palms and soles were identified as “Janeway lesions”. Pericardial and bilateral pleural effusions were evident clinically, and also on imaging [Image D]. Antinuclear (ANA) and



Image B: Janeway lesion in sole.

anti-ds-DNA antibodies were strongly positive, complements (C3 & C4) were low, and there was nephrotic range proteinuria with altered renal function. He was diagnosed as Systemic Lupus Erythematosus (SLE) according to the SLICC classification criteria.¹ Subsequent endocarditis, either infective, or “Libman-Sacks” was excluded by trans-esophageal and trans-thoracic echocardiography and multiple sets of negative blood cultures (aerobic and anaerobic). So the Janeway lesions were attributed to not as peripheral stigma of endocarditis, but as a vasculitic manifestation of SLE. After stabilization and control of acute features, he was referred to the specialized SLE clinic at the medical university for further management.

Janeway lesions are erythematous or haemorrhagic nontender macules found on palms and soles, commonly known as a stigma of infective endocarditis (IE).^{2,3} Earlier, it was thought to be a result of small-vessel vasculitis,³ but recent publications describe it as

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dermal septic micro-emboli.^{3,4} They were commonly seen in IE in the pre-antibiotic era, but now, are very rare in clinical practice.^{2,3} SLE is a female predominant (female : male = 9:1), multifactorial disease, with diverse clinical features.¹ Janeway lesion has been described as a vasculitic manifestation in SLE. Although non-specific, they may have prognostic significance.⁵ SLE is usually associated with Libman-Sacks endocarditis, but IE is not unusual.⁶ Presence of Janeway lesions in SLE patients may indicate coexisting IE. So clinicians should be vigilant for such findings, even if they are less common clinically now-a-days.

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LETTER TO THE EDITOR

(*J Bangladesh Coll Phys Surg 2016; 34: 50-51*)

The Editor-in-Chief

Journal of Bangladesh College of Physicians & Surgeons.

Subject: A letter to the Editor on an article titled "Jarcho-Levin Syndrome-A case Report".

Dear Sir,

This is my pleasure to inform you that I am a senior fellow (Fellow No.-388) and a regular reader of the Journal of Bangladesh College of Physicians & Surgeons. Reading a journal article helps us to keep updated and to learn about the standard format for publication of a scientific article in a Biomedical Journal. Keeping these views in mind I have gone through the above mentioned article 'Ref.: J Bangladesh Coll Phys Surg 2015; 33:222-224'.

I must thank you and the authors of the article for giving me the opportunity to learn about a very interesting and rare case "Jarcho-Levin Syndrome". I appreciate the authors for reporting such an interesting case. As I was going through the article, I have experienced some lacking in different parts of it which I would like to share with you and the authors.

The overall setup of the article is excellent. The introduction is nicely written but citation of reference is missing from an important information "Occasional abnormalities may be cleft palate, hydronephrosis with ureteral obstruction, anal atresia and neural tube defects (33%)". Any information used in a scientific article (which is not the words of the authors' own) needs a specific reference.

The description of the case in the Case Report section seems to be quite good but it has some flaws and missing information as follows: The description of the case could have been started as "An 8-hour-old female term newborn presented with.....since birth" inspite of 'A female term 8 hour old newborn presented with.....since birth'. 'Baby was delivered normally and cried immediately after birth' - the place of delivery of a newborn is very important for presenting a case, which is missing here.

The presentation of the findings are incomplete and not sequential. "Vital signs were normal though chest cage was abnormal" what abnormality was present in chest

cage that should have been mentioned. The examination of the swelling is not sequential. Site of the swelling should be more specific (whether whole lumber region or a part of it). Measurement of the swelling should be placed next to the site. Reflexes should be the last part of newborn examination, which is placed before the examination of swelling. Lower limb measurement should have been placed along with neck and trunk as a part of anthropometry. Interestingly nothing has been written about the upper limbs.

As a rule - if there is a congenital malformation we have to search for anomalies in other organs. But, nothing has been mentioned about heart, lungs or kidneys in this report. Even in a case report it must have a provisional diagnosis (on the basis of clinical presentation) before performing investigations for confirmation which is missing here.

Discussion is very thorough but not focused on the reported case. It should have been more concise and focused. Pictures are well presented. Although the references are old, I have been benefited from the literature review and discussion.

Finally, I appreciate the authors for their hard work and would request them to be generous to accept my constructive criticism to keep it up.

With regards

Prof. Syeda Afroza

Professor & Head,

Dept. of Paediatrics

Shaheed Suhrawardi Medical College, Dhaka.

Author's reply

The Editor-in-Chief,

Journal Of Bangladesh College of Physicians and Surgeons

Dear Sir,

Thank you very much, for going through the article meticulously. I also appreciate your decision, to share your suggestions and for pointing out the lackings in

different parts of the article. I fully agree with you that citation of reference is missing in the introduction, which would be as follows:

Jones KL. Jarcho Levin Syndrome. Smith's Recognizable Patterns of Human Malformation. 5th ed. Philadelphia: Sanders. 1997;p598.

The place of delivery was SSMC Mitford Hospital. The abnormality that was present on the chest cage was anterior bulging of the chest. Site of swelling was lumbosacral region. Upper limbs were normal. Of Course reflexes should be the last part of Newborn Examination. This was mentioned earlier by

mistake. Provisional diagnosis was Meningomyelocele with chest deformity. Clinically heart, lungs and kidneys were normal.

Again, I thank you for your constructive criticism. I hope my corrections will be helpful for the readers.

Yours Sincerely,

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FROM THE DESK OF EDITOR in CHIEF

(J Bangladesh Coll Phys Surg 2016; 34: 52)

Dear Fellows,

A very Happy New Year 2016. May the new year bring good health, prosperity and happiness to us all. 2015 has been overall a successful year with a number of well applauded publications and launching of our journal website. I am truly thankful to the authors, the members of the editorial board, the office staffs, the press and all concerned.

We are working relentlessly to uphold our journal especially in the international arena and look forward to index the journal in PubMed in the near future. I request our valued authors to follow the updated guideline thoroughly for better uniformity and international

acceptability. It is also worthy to mention that the more we submit our papers online through the website, the more the user number increase and it becomes more vibrant in the web. I look forward for your active participation and support as always.

I am concerned for the delayed publication and trying to speed up various processes like timely review and printing. I hope for your cordial gesture.

Thank you.

Prof. Khan Abul Kalam Azad

Editor-in-Chief

Journal of BCPS