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The Journal of Bangladesh College of Physicians and Surgeons is a peer reviewed Journal. It is published four times a year, (January, April, July and October). It accepts original articles, review articles, and case reports. Complimentary copies of the journal are sent to libraries of all medical and other relevant academic institutions in the country and selected institutions abroad.

ADDRESS OF CORRESPONDENCE

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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.

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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.

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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.
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Ethical aspects:

- Ethical aspect of the study will be very carefully considered at the time of assessment of the manuscript.
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- 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.
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- Authors need to work closely with editors in developing or using such new publication formats and should submit supplementary electronic material for peer review.
- Double-spacing all portions of the manuscript—including the title page, abstract, text, acknowledgments, references, individual tables, and

legends—and generous margins make it possible for editors and reviewers to edit the 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.
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9. The number of figures and tables. It is difficult for editorial staff and reviewers to determine whether he 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.

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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 specify 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.
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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.
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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 (.)
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    - 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
    - Δ Actual numbers from which graphs drawn, provided
    - 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)
    - Δ Patients' privacy maintained (if not, written permission enclosed)
    - 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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EDITORIAL

Dangers of Infant Formula

Breastfeeding top the list of effective preventive interventions for child survival. Together with appropriate complementary feeding these have more impact even then immunization, safe water and sanitation. There is no food more locally produced, affordable and sustainable than breast milk. Breastfeeding reduces the risk of diarrhea, chest infections (the biggest killer of children) and non-communicable diseases (NCDs) such as diabetes, obesity, cardiovascular disease and cancers. It is also an important in child spacing for the millions of women who have no access to modern forms of contraception.

Twenty one dangers of Infant formula:

Risks for Infants:

Asthma: incidence of asthma increases with formula feeding. Exclusive breastfeeding provides protection in early childhood up to age 6.[1]Allargy: Although the interaction with exposure to allergens and development of allergies is complex, unlike of formula feeding exclusive breastfeeding appear to provide some protection in development of allergies in infants, regardless of familial history of allergy[2].Ear infections: Infants feed formula during the first 6 months of life have more ear infections[3].High blood pressure& Heart Disease:Small – for-gestation and normal-weight infants who gained weight quickly on formula had higher risk of developing hypertension later in life than did breastfeed infants. Additionally, although the physiological /biological mechanisms underlying measurable cardiovascular differences are unclear, infants receiving formula diets have poorer micro vascular function as teenagers[4].Respiratory Infections:Formula fed infants suffer more frequently and more severely fromrespiratory infections, both viral and bacterial.[5]Reduced IQ & Cognitive Development: Formula fed infants consistently score lower on IQ and cognitive test, even when study results are controlled for all possible socioeconomic confounders[6].Obesity: Formula feeding in infancy is associated with increased incidence of childhood and adolescent obesity, and higher BMI in adults[7]. Iron-Deficiency Anaemia: Formula fed infantshave higher rates ofiron-deficiency anaemia due to low bioavailability of ferrous sulfate in cows milk based formulas[8].SIDS(Sudden Infant Death Syndrome): Formula feeding increases the risk of dying from SIDS up to 50% throughout the first year of life. Diabetes (both types 1&2): Formula fed infants have greater risk for developing both type1 and type2 Diabetes irrespective of parents Diabetic status. Additionally when mother has gestational type1 and type2 diabetes. Digestive problems: Diarrheal disease is twice as high in formula fed infants, in both industrialized and resource dependent countries, and the increased risk of diarrheal disease when formula fed extends through the first 2 years of life. Infants fed formula have greater chance of developing Crohn's disease and ulcerative colitis in adulthood. Childhood Cancers: Formula fed infants are at greater risk for developing childhood cancers, and the benefits of breastfeeding are dose-dependent, increasing with length of duration and exclusivity. Exposer to Environmental Contaminants: When expose to contaminants in utero, children who are subsequently formula fed perform poorer on neurological tests up to 9 years of age compared to similarly exposed breastfed children. Sleep Apnea: Formula fed infants are at higher risk for developing sleep disordered breathing problems. Dental problems requiring orthodontia: Formula fed children have a significantly higher chance of having dental malocclusions, (particularly anterior overbite and cross bite problems.

Risks for Mothers:

Diabetes: Compared to women who do not have children, women who give birth but do not breastfeed their children have a significantly higher incidence (14%) of developing type-2 diabetes than women who breastfeed.[9]Overweihgt & Obesity: Formula feeding mothers retain their pregnancy weight longer and are at risk to keep weight gain between pregnancies.[10] Osteoporosis: Formula feeding mothers are at greater risk to experience hip fractures and other problems related to osteoporosis in the postmenopausal period.

Breast Cancer, Ovarian Cancer &Uterine Cancer: Formula feeding mothers have increased risk of developing breast ovarian and uterine cancers later in life. Hypertension & Cardiovascular diseases: Formula feeding mothers have higher BP levels in the initial postpartum period. They are also at increased risk to develop hypertension, hyperlipidemia and cardiovascular disease later in life. Reduced Natural Child Spacing: Formula feeding mothers are at increased risk of having less space between pregnancies, thereby placing both mother and children (already living as well as future pregnancies) at increased risk of mortality, morbidity and malnutrition.

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Delayed Surgical Site Infection by Tuberculosis – A Rising Cause of Concern ?

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Summary:

Background: Surgical site infections causes significant morbidity and mortality of patients and causes more difficult to treat if unexpected cause behind the infection like tuberculosis. Delayed surgical site infection after initial healing are uncomfortable for both surgeons and patient.

Methods: Wound tissue from 18 patients with delayed surgical site infection not responding to antibiotics used for pyogenic infection were collected and examined histopathologically.

Results: Of the 18 patients, 9 revealed histologically tuberculosis, 7 non-specific chronic inflammation and others showed foreign body granulomma. Association between histopathological report and incidence of tuberculosis is significant ($p<0.001$) and association between onset of infection and incidence of tuberculosis also significant ($p<0.05$).

Conclusion: A high degree of suspicion is required in case of delayed or recurrent surgical site infection to diagnose tuberculosis as a cause.

Keyword: Surgical site infection, tuberculosis, wound, granulomma.

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Introduction:

Tuberculosis remains a major global health problem ranks as the second leading cause of death[1]. The latest estimates 8.7 million new cases in 2011 and 1.4 million died from tuberculosis[1]. Geographically, the burden of tuberculosis is highest (26%) in India[1]. The country, Bangladesh ranks 6th among 22 highest burden countries in the world[2]. Postoperative surgical site infection is common in almost all countries of the world and it varies from patient to patient, hospital to hospital and depending upon various factors[3]. But surgical site infection due to tuberculosis is a rare entity, in most cases, is caused by reactivation of dormant tuberculosis, spread of the infection by either haematogenous route or direct inoculation from exterior or from a tuberculous abdominal lymph node or extension from underlying tubercular lesions[4,5].

Methodology:

This study included 18 patients (6 Male and 12 Female, aged 12 – 48 year) who had undergone surgery for various ailments between January 2009 to January 2013 at different hospitals in practicing area (Northern region of Bangladesh) of the authors. The patients developed delayed surgical site infections (2 weeks to 24 weeks after surgery) that were not responding to antibiotics and were sent for histopathological examinations of tissue from wound.

The patients had undergone Appendicectomy(n=5), Caesarean section(n=5), laparoscopic cholecystectomy (n=3), Open cholecystectomy(n=2), Excision of keloid(n=1), Haemorrhoidectomy(n=1), Umbilical sinus excision(n=1).

Tissues from wounds were collected with sterile biopsy forceps/haemostatic forceps and after chemical fixation with 10% neutral buffered formalin the specimen was sent for histopathological examination.

Pus/discharge from wounds was collected with the help of sterile cotton swabs and/or syringes and was sent immediately for culture and sensitivity test.

Culture for mycobacterium could not be done due to limitation of resources at our clinical setting.

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Results:

A total of 18 patients with delayed surgical site infections were included in this study. All patients had more or less similar presentations :

> appearance of erythema followed by breakdown of scar and suppuration,

> discharging sinuses,

> recurrent tiny stitch abscess formation,

in absence of systemic manifestations and no sign of improvement with traditional antibiotics and regular dressing.

All patients had no clinical symptoms of tuberculosis, no past history of tuberculosis and none had been contact with any patients of tuberculosis. So the diagnosis and initiation of treatment was delayed until confirmation by histopathology.

Among the 18 patients, 9 patients' wound tissues histopathologically showed granulomatous inflammation and epithelioid cells that consistent with tuberculosis. The remaining showed non-specific, chronic inflammation and foreign body granuloma.

Five of the 18 patients' wound swab revealed growth of staphylococci, 3 revealed gram negative E. coli and others showed no growth in aerobic and anaerobic traditional culture.

In routine blood tests, all patients revealed haematologically normal except 5 patients showed raised ESR, ranging from 20 – 44 mm in the 1st hour. Chest X-Rays were negative for all cases. Tuberculin test was not done in all cases. Culture for mycobacterium could not be done due to limitation of resources.

In this study statistical analysis was done with SPSS 16. Chi-Square showed significant association between histopathological report and incidence of tuberculosis (x^2=27.00, df=2, p<0.001) and strong correlation between histopathological report and incidence of tuberculosis (0.862, p<0.001). There is also significant association between onset of infection and incidence of tuberculosis (x^2=15, df=8, p<0.05).

Table-I

Summary of patients with tuberculous post-operative wound infection (Total 9 patients) :

Age in years	Sex	Preoperative diagnosis	Time interval	Presentation
20	Female	Appendicectomy	3 weeks	Scar abscess
22	Female	Caesarean section	2 weeks	Non-healing wound
35	Male	Excision of Keloid	24 weeks	Non-healing ulcer
48	Female	Laparoscopic Cholecystectomy	6 weeks	Port site abcess
25	Female	Caesarean section	12 weeks	Recurrent discharging sinus
35	Male	Laparoscopic Cholecystectomy	4 weeks	Port site abscess
35	Female	Appendicectomy	2 weeks	Recurrent discharging sinus
28	Female	Haemorrhoidectomy	12 weeks	Recurrent intra-anal sinus
12	Female	Excision of umbilical sinus	2 Weeks	Recurrent discharging sinus

Some pictures of Tubercular Wound

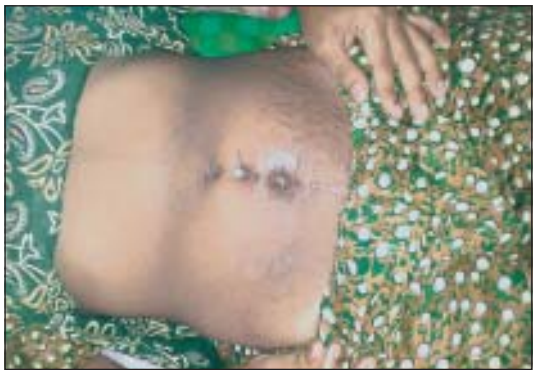

Fig.-1: *Post Caesarean Section Wound*

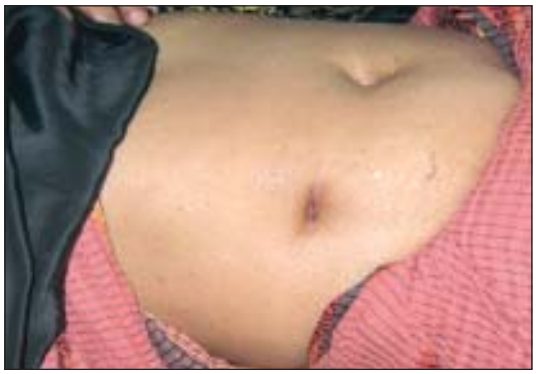

Fig.-2: *Post laparoscopic cholecystectomy port site wound*

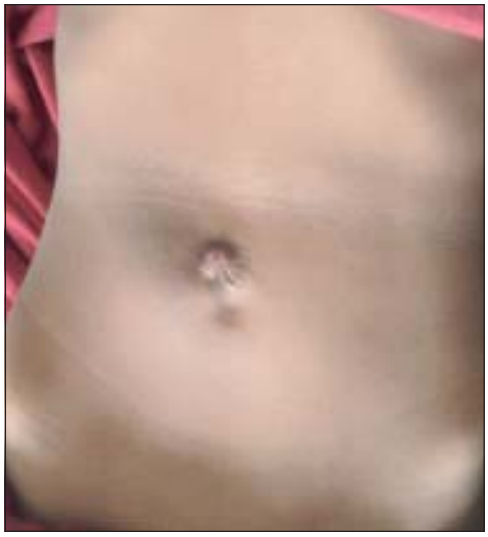

Fig.-3: *Umbilical Sinus wound*

Discussion:

In this study 9 patients were diagnosed tuberculous wound infection. Histopathologically all showed granulomata with epithelioid cells and among them only 4 showed variable areas of caseation necrosis, but others (5) showed significant supportive evidences like raised ESR and strongly positive Tuberculin Test. Patient had laparoscopic cholecystectomy and appendicectomy showed chronic cholecystitis and acute appendicitis in their operated specimen, histopathologically. Two patients had foreign body granuloma which were healed after removing of foreign body (suture materials) and then regular dressing. Others (7) showed non-specific inflammation which were completely healed by long term use of antibiotics, surgical debridement and regular dressing.

Histologic study was also the diagnostic tool in other studies[5]. Tuberculin test was not done in all cases. Culture for mycobacterium could not be done due to limitation of resources.

All tuberculous wound were responded well with standard anti-tubercular drugs and had no residual complication. The treatment was administered in collaboration with TB Clinics. All patients were under regular follow-up and complications free for 6 months.

Mycobacteria are important pathogens for post-surgical wound infections in many countries including India[7].

All post-operative wounds had initially healed after surgery except two (one caesarean wound and one appendicectomy wound), but latter became erythematous and gradually broke down to make discharging wound over a variable period of time. The wounds were painless and all patients with no systemic feature of tuberculosis. This non-healing wounds of confusing picture should always be ruled out by proper investigations, specially histopathology[7]. Begum HA reported 6 patients of post operative tuberculous wound infection, presenting mostly chronic discharging sinus (4 patients) and rest presented as non-healing wound[6]. Port site tuberculosis after laparoscopy are usually presented with port site abscess or persistent port site discharging sinus[8,9].

After the initial infection of primary tuberculosis in the primary sites, there is dissemination of tubercular bacilli to remote parts of the body[10]. The host's immune system becomes sensitized. In 90% of immunocompetent people, there are no clinical manifestations, but the infection remains for years, probably for life[11]. The individual who has such an infection may later develop clinical disease depending on the immune status.

Secondary tuberculosis is the pattern of disease that arises in such a previously sensitized host. It may follow shortly, but more commonly occurs decades after initial infection particularly when host resistance is weakened[12]. Due to this waning of protection, secondary tuberculosis may result from (a) exogenous reinfection, as occurs in geographical regions of high endemicity, or more commonly from (b) reactivation of a latent primary focus with haematogenous spread to the site of the secondary infection or (c) local reactivation at the secondary site[10].

Decreased immunity due to trauma may allow reactivation of latent bacteria at a distant focus, (which may be occult and undetectable on a chest X-ray) and result in subsequent seeding of the infection site[10]. Local reactivation can be precipitated by trauma or surgery, or any factor or insult that alters local tissue response. These again include injury, surgery, local vascular derangements, foreign body reactions or even chronic inflammation[10].

Conclusion:

Surgical site infection by tuberculosis may be more common than diagnosed. Tuberculosis must be considered in wounds that show delayed, non-healing or recurrent surgical site infection with non responding to antibiotics.

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A Screening Test for Iron Deficiency Anaemia and Thalassaemia Traits

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Summary:

Both iron deficiency and thalassaemia trait can present with hypochromic microcytic morphology. Naked eye single tube red cell osmotic fragility (NESTROF) is an inexpensive and simple test which can effectively differentiate iron deficiency anaemia from thalassaemia trait. Our study was an opportunity to observe the role of NESTROF in screening of thalassaemia trait among our study population. Initially NESTROF was carried out in 677 patients (N) population of four groups having both positive and negative NESTORF; for economical issue, auto-analyzer study and haemoglobin electrophoresis were done among only 100 randomly selected subjects, who were finally included in our study as final study population (n). In our study, NESTROF was 94.23% sensitive and its specificity was 92.08%. The predictive value of a positive test was 88.13% and predictive value of a negative test was 96.24%. Our study showed, NESTROF can effectively differentiate iron deficiency anaemia (IDA) from thalassaemia trait but, is not effective in co-existent IDA and thalassaemia.

Key Words: NESTROF, IDA, Thalassaemia

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Introduction:

Both Iron Deficiency Anaemia (IDA) and beta-thalassaemia trait (BTT) are the most frequent causes of microcytic hypochromic anaemia. Iron deficiency anaemia (IDA) may result from insufficient iron intake or menstrual loss, in woman of childbearing age or chronic blood loss in the gastrointestinal tract, in case of elderly subjects. Microcytic anaemia in case of thalassaemia results from impaired globin chain synthesis and decreased haemoglobinization.[1] Haemoglobinopathies are the common genetic disorders worldwide with estimated 1.5% of the world population being beta thalassaemia carriers. About 60,000 new carriers are born each year. Fifty percent of world thalassaemia minor are in Southeast Asia including Bangladesh.[2] a World Health Organization (WHO) report estimates that about 3.0% of populations are carriers of Beta thalassaemia and 4.0% are carriers of Hb-E in Bangladesh. World Health Organization (WHO) has recently highlighted the growing concern about anaemia, affecting an estimated 2000 million people, 50% of the cases caused by iron deficiency (WHO, 2004). [3,4] Iron deficiency is the most common single nutrient disorder in humans in both developing and developed countries. Iron-deficient erythropoiesis is characterized by the production of RBC with a decreased Hb concentration and high hypochromic cells percentage, while microcytes of beta thalassaemia are generally smaller, with low Hb content but more preserved Hb concentration. Hypochromia is the predominant peripheral blood feature in iron deficiency while in thalassaemia the degree of microcytosis relative to hypochromia is more striking.[5] NESTROFT (naked eye single tube red cell osmotic fragility test) has been used for population surveys, useful in screening for beta-thalassaemia and the common haemoglobinopathies as a reliable test. It is easy to perform, simple, inexpensive and does not require sophisticated equipment. It has a sensitivity ranging from 94 to 99 per cent. [6-8] The reliability, low operational cost and rapidity make the test suitable for population screening in the resource poor yet high disease prevalent setting. [6-9] Our study was an opportunity to observe the role of NESTROF in screening of thalassaemia trait among our study population.

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Materials and Methods:

This study was done in the Department of Haematology, BSMMU and in the Department of Pathology, Institute of Child Health and Shishu Hospital, Sher-E- Bangla Nagar, Dhaka from 1st January 2003 to 31st December, 2005. The study subject included randomly selected 677 patients (N), both male and female, aged from 12 to 60 years, who took haematology services at the above mentioned institutes. They were then divided into four different groups on the basis of results of complete blood count (CBC) by auto-analyzer, peripheral blood examination in order to identify the normal subjects from those with anaemia. Then serum ferritin (test based on ELISA) and agarose gel haemoglobin electrophoresis tests were done to determine the cause of anaemia among the patients having microcytic hypochromic anaemia. The normal subjects were labeled group –I : 392 subjects with normal haemoglobin, iron status and red cells indices and the rest of the patients were divided into three groups. Group - II: This group comprised of 200 patients who were obligate carrier of either beta-thalassaemia trait or hemoglobin E trait. Group - III: 60 cases of iron deficiency anaemia (IDA) and thalassaemia trait. Group - IV: 25 patients with iron deficiency anaemia (serum ferritin <12.0 ng/ml) alone. Finally, a total of 100 randomly selected subjects (n) were included in this study from the previous four groups along with positive and negative NESTROF.

Procedure of NESTROF: NESTROF was carried out in all 677 patients with the following procedure: 2.0 ml 0.36% buffered saline solution (pH-7.4) was taken in one tube and 2.0 ml-distilled water was taken in another tube. A drop of venous blood is added in both the tubes and they were left undisturbed for half an hour at room temperature. After half an hour both the tubes were shaken and then held against a white paper on which a thick black line was drawn. This line was also clearly visible through the contents containing distilled water. When the line was similarly visible through the contents of the tube filled with the buffered saline, then the test was considered negative; on the other hand, if the line not clearly visible, the test was considered positive. Moreover, any doubtful conditions were also considered positive.

For calculation, the number of true positive (TP), true negative (TN), false positive (FP) and false negative (FN) were determined. The sensitivity, specificity and predictive values were calculated as follows:

Sensitivity = (TP X 100) / (TP+ FN); Specificity = (TN X 100) / (TN+ FP),

Predictive value of a positive test = (TP X 100) / (TP+FP) and

Predictive value of a negative test = (TN X 100) / (TN+FN) [6,7]

Initially NESTROF was carried out in all 677 patients as N population, from this population four groups were separated having both positive and negative NESTROF results. However, for economical issue, auto-analyzer study and haemoglobin electrophoresis were done among only 100 randomly selected subjects, who were finally included in this study as final study population (n).

Results:

Among initial 677 patients (N), NESTROF was positive in 278 cases, of these 245 cases

(group-II and III) are obligate carriers of both Beta thalassaemia trait and Haemoglobin-E trait and they were true positive (TP) and 28 (group-I) did not have any abnormal haemoglobin and they were false positive (FP) (table I). 33 cases (normal subject- group I and IDA- group IV) were false positive (FP). The test was negative in 399 individuals, with 384 true negatives (TN) and 15 false negatives were (FN) (thalassaemia trait-group II and IDA and thalassaemia trait- group III).Finally, due to cost issue for auto-analyzer study and haemoglobin electrophoresis, a total of 100 randomly selected subjects were included in our study as final study population (n), from the previous four groups along with positive and negative NESTROF. Sensitivity and specificity of NESTROF was shown to be 94.23% and 92.08% respectively. Calculation also showed predictive value of a positive test was 88.13% and predictive value of a negative test was 96.24%.The result of NESTROF was evaluated with Hb%, Red Cell Indices (Red Cell Count, MCV, and MCH) (Table II). This result showed that low MCV & MCH with a relatively high Red Cell Count (as found in thalassaemia traits) was associated with positive NESTROF and low MCV, MCH associated with low Red cell Count (as found in iron deficiency anaemia) was associated with negative NESTROF. Results of estimation of HbA_2 and Haemoglobin-E in agarose gel electrophoresis among the 100 study subjects (n) (Table III) shows that in co-existent IDA and thalassaemia trait, there was a drop in Hb A2.

Table-I

Results of NESTROF (N= 677) in four groups

Groups	Final Study subjects (n=100)	NESTROF Positive	NESTROF negative	NESTROF (N= 677)
Group-I(Normal subjects)	38	28(7.14%)	364(92.86%)	392
Group-II(Beta thalassaemia traits or Hb E trait)	12	189(94.50%)	11(5.50%)	200
Group-III(both IDA & thalassaemia trait)	25	56(94.50%)	04(5.50%)	60
Group-IV(IDA)	25	05(20%)	20(80%)	25
Total number of cases	100	278(41.06%)	399(58.94%)	677

Table-II

NESTROF (N= 677) along with auto- analyzer haematological values of final study subjects (n=100)

Final Study subjects (n=100)	Hb (g/L) (Mean)	Red Cell Count (mean)	MCV (Mean)	MCH (Mean)	NESTROF (+)VE	ESTROF (-)VE
Normal (38)	12.0	4.8X 10^{12}//L	82 fl	30.4 pg	28	364
Beta trait(12)	10.5	4.9X 10^{12}//L	73 fl	23 pg	189	11
Hb-E trait(25)	11.2	5.10X 10^{12}//L	78 fl	24 pg	56	04
IDA(25)	7.8	3.6X 10^{12}//L	65 fl	68 pg	05	20

Table-III

Pattern of Hb Electrophoresis in the study subjects (n=100)

Interpretations	Haemoglobin pattern			
	Hb A	HbA_2	Hb F	HbE + HbA_2
Normal	96.60%	2.20%	1.20%	-
Beta-Thalassemia trait	94.10%	4.10%	1.80%	-
E trait	71.50%	-	1.20%	27.30%
Both IDA & thalassemia trait	96.60%	1.80%	1.60%	-

N.B: In Agarose Gel Haemoglobin Electrophoresis, HbE & HbA_2 appear in the same position and could not be isolated as a separate band. It is possible only if electrophoresis is performed on acid media.

Discussion:

In our study, sensitivity and specificity of NESTROF was shown to be 94.23% and 92.08% respectively; which was similar to that of Mehta et. al. and Kattamis et. al, where specificity 92.08% and sensitivity 94.23%.[6] We found the test effective in detecting almost 100% of subjects with Beta-thalassaemia trait, while it gives false positive results in nearly 10% of normal subjects.[6, 7] It is important to note that in beta-thalassaemia trait the concentration of haemoglobin A2 which is usually elevated, may be significantly reduced due to the coexistent IDA making the diagnosis extremely difficult which can be missed even in Hb-electrophoresis. This is of particular importance when a study is conducted in an area where iron deficiency is also prevalent like our country. Importance of the study of Peripheral Blood (PB) with red cell indices, serum ferritin and Hb electrophoresis are paramount for proper diagnosis of

coexisting iron deficiency anaemia (IDA) and thalassaemia trait (beta thalassaemia trait or haemoglobin-E trait). [12] For the diagnosis of iron deficiency anaemia clinical findings, presence of hypochromic microcytic blood picture and low serum ferritin levels (<10 ng/ml) are needed. Some patients may presents with chronic anaemia, sore tongues, angular stomatitis, cheliosis or koilonychias. So in our study the limitation was, to differentiate co-existent trait and IDA, as in coexisting IDA with thalassaemia trait the NESTROF test may not be effective, found in other Bangladeshi study. [13] In our study, the results of NESTROF were evaluated with Hb%, Red Cell Indices. Low MCV & MCH with a relatively high Red Cell Count found in thalassaemia traits was associated with positive NESTROF while low MCV, MCH with low Red Cell Count found in iron deficiency anaemia was associated with negative NESTROF in our study. Thus our study showed, NESTROF can effectively differentiate between thalassaemia trait and iron deficiency. This study also showed, NESTROF was easy to perform, less technical expertise and no initial capital outlay were required as like as other studies.[6-9,13,14]

Conclusion:

Our study showed NESTROF as a valuable screening tool differentiate thalassaemia trait and IDA. On the other hand, as in coexisting IDA with thalassaemia trait the NESTROF test may not be effective, so further study will be needed to see the response of oral iron therapy to identify true iron deficient patients. In areas with limited laboratory facilities and for field screening NESTROF can be used in diagnosing and counseling thalassaemia carriers, thus may help to prevent thalassaemia in our country.

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Conflict of Interest: None

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Role of Insulin Sensitizers in Raised Alanine Aminotransferase in Non-alcoholic Fatty Liver Disease in Glucose Intolerance Patients: A Short-Term Experience with Metformin Plus Pioglitazone Versus Metformin Alone

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Summary:

Objectives:To evaluate and compare the effectiveness of metformin plus pioglitazone versus metformin alone in treatment of raised alanine aminotransferase (ALT) in non-alcoholic fatty liver disease (NAFLD) in patients with newly detected diabetes mellitus (DM) and impaired glucose tolerance (IGT).

Materials and methods: In this open label clinical trial, newly detected DM and IGT patients with raised ALT and ultrasound proven NAFLD were treated with either metformin and pioglitazone combination (group 1) or metformin alone (group 2). They were followed up upto 6 months.

Results:Total number of patients was 49 (27 in group 1 and 22 in group 2) and there was male predominance in either group. Age was almost identical between two groups (46±9.3 and 45.4±5.7 years in group 1 and group 2 respectively). Significant reduction in values of fasting blood glucose (FBG), 2 hours post breakfast values (ABF), HbA1c, cholesterol (CHOL), triglycerides (TG) and ALT of the study subjects were achieved in either group after six months (Group 1: FBG 8.89±1.4 vs 6.37±0.5 mmol/l, ABF 13.2±2.07 vs 8.34±0.84 mmol/l, HbA1c 8.15±0.87 % vs6.7±0.40%, CHOL 205.26±30.74 vs 178.89±18.59 mg/dl, TG 226.15±50.06 vs 155.85±20.99 mg/dl, ALT 91.52±23.14 vs 45.74±12.63 mg/dl and in Group 2 : FBG 9.39±2.26 vs 6.98±1.20 mmol/l, ABF 13.38±2.93 vs 9.13±1.46 mmol/l, HbA1c 8.10±0.92 % vs7.03±0.71%, CHOL 206.55±29.9 vs 195±23.55 mg/dl, TG 235.59±46.22 vs 178.91±38.24 mg/dl, ALT 105.59±18.63 vs 66.36±16.02 mg/dl).In comparison between two groups, Group 1 had better metabolic control compared to their counterpart of Group 2 at the end of 6 months [Group 1 vs Group 2: FBG (p=0.024), ABF (p=0.022), CHOL (p = 0.010), TG (p =0.010)]. There was significant reduction in ALT as well (p = 0.000).

Conclusion:Combination of metformin and pioglitazone is more effective than metformin alone in reducing ALT in NAFLD in newly detected DM and IGT patients.

Key words: Alanine aminotransferase, diabetes mellitus, impaired glucose tolerance, non-alcoholic fatty liver disease.

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Introduction:

The epidemics of obesity, metabolic syndrome, type 2 diabetes mellitus (DM) and atherosclerosis are increasing worldwide.[1] Non-alcoholic fatty liver disease (NAFLD), long time unnoted entity, is becoming recognized as a condition possibly involved in the

pathogenesis of these diseases. Support for this hypothesis emerges from studies revealing that NAFLD precedes the manifestations of the metabolic derangements.[2,3] The spectrum of NAFLD may be from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH) which may be complicated to cirrhosis and even hepatocellular carcinoma.[4,5]

The term NAFLD is used to describe a condition of fat accumulation in liver in absence of excessive alcohol consumption (< 20 g/day) and other specific causes of hepatic steatosis. NAFLD affects some 10-24% of general population and the prevalence increases upto 6 foldin obese persons.[6] NAFLD is the cause of asymptomatic elevation of ALT in up to 90% of cases.[7] Regardless of body mass index (BMI), the presence of type 2 DM significantly increases the risk and severity of NAFLD.[4,5]Trunkal obesity is an important risk factor even in a patients with a normal BMI.[8] About half the patients with hyperlipidemia are found to have NAFLD on ultrasonography (USG).[9]

Most patients with NAFLD are asymptomatic at diagnosis. Common symptoms are fatigue, malaise, right upper quadrant pain or discomfort and sensation of fullness. Hepatomegaly is common.[10,11] Other findings relate to obesity and other features of metabolic syndrome. Mild to moderate increased serum levels of aspartate aminotransferese (AST), ALT or both are the most common and often the only laboratory abnormality. The ratio of AST: ALT is usually <1 and the ratio increases as fibrosis advances.[10] Hypertriglyceridemia increases the risk of NAFLD.[9]

Good metabolic control in DM or dyslipidaemia is not always effective in reversing NAFLD. Weight loss shows improvement on liver test results.[12-15] No medications have been proved to directly reduce or reverse liver damage independent of weight loss. Many drugs have been used with variable degree of improvements in liver function tests and hepatic histology.[16-21]

Emerging evidence confirms that NAFLD can be progressive and associated with significant morbidity and mortality. Despite efforts aimed at improving early detection and prevention, many patients are still seen at the advanced stages. ALT is the best and most reliable non-invasive method for screening NAFLD.

Over the last few years, clinical trials evaluated the use insulin sensitizers in treatment of NAFLD. Mixed results, heterogeneous therapeutic approaches and the small numbers of subjects have limited their applications as clinical guideline. In the current study, we have tried to evaluate the effectiveness of the combined insulin sensitizers which would act on different receptors at the tissue level.

Materials and Methods:

This open level clinical trial was carried out in the outpatient (OPD) wing of Department of Gastrointestinal, Hepatobiliary and Pancreatic Diseases (GHPD) at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh in the year 2010. Sixty newly detected DM and IGT patients, referred at GHPD-OPD for raised ALT and ultrasound proven NAFLD were enrolled in this study. Patients with chronic liver disease (CLD), positive HBsAg and anti-HCV and history of alcoholism were excluded from the study. All patients were on hypocaloric diet. Every alternate patients were prescribed either metformin 850 mg twice daily and pioglitazone 30 mg once daily (Group 1) or metformin 850 mg twice daily (Group 2) for six months. Total 49 patients (27 patients in group 1 and 22 in group 2) completed the trial. Patients were assessed clinically and by laboratory investigations at enrolment (visit 1), at 3rd (visit 2) and at 6th months (visit 3). Satistical analysis was done by using frequencies and percentages and by the applying paired sample test within the group and unpaired t test and chi-square test between groups and *p* value of <0.05 was considered significant. Ethical clearance was obtained from ethical review committee of BIRDEM before starting the trial and informed written consent was taken from all patients before enrolment.

Results:

Total number of patients was 49. Mean age was 45.80±8.54 years. Male were 65.3% and female were 34.7%. Baseline and anthropometric measurements of study population were shown in Table I. Thirteen (26.5%) patients were asymptomatic, 14 (28.6%) patients had a feeling of abdominal fullness, 10 (20.4%) patients complained about upper abdominal pain and 12 (24.5%) complained about both upper abdominal pain and fullness. Twenty seven (55.1%) patients were treated by metformin 850 mg twice and pioglitazone

30 mg once daily (Group 1) and 22 (44.9%) patients were treated by metformin 850 mg twice daily (Group 2).

Significant improvements were noted with treatment in metabolic control like fasting and post prandial blood glucose, HbA1c and lipid profile in both groups in 2nd and 3rd visits (Table II and III).

Values of ALT showed significant improvements in 2nd and 3rd visits (Table IV). The inter-group difference regarding ALT, FBG and TG were significant in every visit (Table V). Though the inter-group difference regarding ABF, total cholesterol and HbA1c was not significant at 1st visit, it became significant in subsequent visits (Table 5).

Table I

Baseline characteristics and anthropometric measurements of study population

Variables	Group 1 (n=27)	Group 2 (n=22)
Age (years)	46.0±9.3	45.4±5.7
Sex (male, female) (%)	74.1, 25.9	54.5, 45.5
DM, IGT (%)	92.6, 7.4	81.8, 18.2
Height (cm)	159.9±6.1	157.6±7.9
Weight (kg)	69.4±8.5	68.5±11.0
BMI (kg/m2)	27.1±2.2	27.4±3.2
Waist circumference (cm)	90.6±4.2	91.3±4.7
Hip (cm)	93.5±3.5	94.1±4.1

Table-II

Biochemical parameters of group 1 in three visits

Variables	Visit	mean±SD	Comparison between visits	P value
	1	8.89±1.44	V1-V2	<0.001
FBG (mmol/L)	2	7.04±0.79	V2-V3	<0.001
	3	6.37±0.50	V1-V3	<0.001
	1	13.20±2.07	V1-V2	<0.001
ABF (mmol/L)	2	9.48±0.99	V2-V3	<0.001
	3	8.38±0.84	V1-V3	<0.001
	1	8.15±0.87	V1-V2	<0.001
HbA1c (%)	2	7.20±0.47	V2-V3	<0.001
	3	6.70±0.40	V1-V3	<0.001
	1	205.26±30.74	V1-V2	<0.001
CHOL (mg/dl)	2	187.44±21.58	V2-V3	<0.001
	3	178.89±18.59	V1-V3	<0.001
	1	226.15±50.06	V1-V2	<0.001
TG (mg/dl)	2	177.26±26.62	V2-V3	0.004
	3	155.85±20.99	V1-V3	<0.001

Data were expressed as maen±SD. Mean values between the visits were compared by paired t-test.

Table-III

Biochemical parameters of group 2 in three visits

Variables	Visit	mean±SD	Comparison between visits	P value
	1	9.39±2.26	V1-V2	<0.001
FBG (mmol/L)	2	7.88±1.53	V2-V3	0.003
	3	6.98±1.20	V1-V3	<0.001
	1	13.39±2.93	V1-V2	<0.001
ABF (mmol/L)	2	9.90±1.76	V2-V3	<0.001
	3	9.13±1.46	V1-V3	<0.001
	1	8.10±0.92	V1-V2	<0.001
HbA1c (%)	2	7.34±0.76	V2-V3	0.003
	3	7.03±0.71	V1-V3	<0.001
	1	206.55±29.90	V1-V2	<0.001
CHOL (mg/dl)	2	191.14±26.12	V2-V3	0.291
	3	195.00±23.55	V1-V3	0.034
	1	235.59±46.22	V1-V2	<0.001
TG (mg/dl)	2	199.82±40.73	V2-V3	0.004
	3	178.91±38.24	V1-V3	<0.001

Data were expressed as maen±SD. Mean values between the visits were compared by paired t-test.

Table-IV

Serum ALT levels in three visits in two groups

Group	Visit	ALT (U/L)	Comparison between visits	P value
	1	91.52±23.14	V1-V2	<0.001
1	2	62.78±14.79	V2-V3	<0.001
	3	45.74±12.63	V1-V3	<0.001
	1	105.59±18.63	V1-V2	<0.001
2	2	81.77±16.29	V2-V3	<0.001
	3	66.36±16.02	V1-V3	<0.001

Data were expressed as mean±SD. Mean values between visits were compared by paired t-test.

Table-V

Significance of different biochemical parameters between two groups

Variables	Visit	Group	Mean±SD	P value
	1	12	8.87±1.449.39±2.26	0.338
FBG (mmol/L)	2	12	7.04±0.797.87±1.52	0.018
	3	12	6.37±0.556.98±1.20	0.024
	1	12	13.20±2.0713.38±2.93	0.805
ABF (mmol/L)	2	12	9.48±0.999.90±1.75	0.299
	3	12	8.34±0.849.13±1.46	0.022
	1	12	8.15±0.848.11±0.92	0.844
HbA1c (%)	2	12	7.21±0.477.34±0.76	0.459
	3	12	6.74±0.407.03±0.71	0.086
	1	12	205.26±30.74206.55±29.30	0.883
CHOL (mg/dl)	2	12	187.44±21.58191.14±26.12	0.590
	3	12	178.89±18.59195.00±23.55	0.010
	1	12	226.15±50.06235.59±46.22	0.500
TG (mg/dl)	2	12	177.26±26.62199.82±40.73	0.024
	3	12	155.85±20.99178.91±38.24	0.010
	1	12	91.52±23.14105.59±18.63	0.026
ALT (U/L)	2	12	62.78±15.7981.72±16.29	<0.001
	3	12	45.74±12.6366.36±16.02	<0.001

Data were expressed as mean±SD. Maen values of two groups were compared by unpaired t-test.

Discussion:

Treatment strategies for NAFLD are improving the insulin resistance by weight loss, exercise and pharmacotherapy with insulin sensitizers. In our study, we have tried to evaluate and compare the efficacy of metformin and pioglitazone combination versus metformin alone for the reduction of ALT in NAFLD.

Mean age of the study population was over 45 years. In a study 65.4% patients were in 40 – 59 years age group.[3]As previously noted, NAFLD is the hepatic manifestation of metabolic syndrome. Risk factors associated with NAFLD include central obesity, type2 DM, insulin resistance and dyslipidemia.[4,23] The values of mean BMI, waist circumference, and TG in our patients clearly indicate that insulin resistance was risk factor for developing NAFLD in our population as well. In a population based study,it was found that waist circumference was recognized as a simple parameter for estimation of liver fat accumulation. It was found that presence of NAFLD correlates significantly with BMI and waist hip ratio which support our findings.[6]

Over the period of 3 and 6 months follow up, both the treatment groups showed improvements in HbA1c, more in combination group which confirmed the well established issues of glucose lowering effect of metformin and pioglitazone and more powerful blood glucose lowering effect of combination of both the drugs as stated in American Diabetic Association (ADA) guideline 2012 and guideline of American College of Clinical Endocrinology (AACE) 2012.

A reduction in ALT is an acceptable end point for a proof of concept of exploratory trial in NAFLD. In our trial, serum ALT showed significant improvement at 3rd and 6th months in both groups. These finding confirmed the beneficial effect of insulin sensitizers in NAFLD as seen in other studies.[18-22]These studies evaluated either metformin or thiazolidinediones versus diet and lifestyle measures and no study

evaluated combination of insulin sensitizers. Our findings are in favor of combination of drugs.

Metformin is less expensive than most other treatment modalities of NAFLD. Most studies with prolonged use of metformin have shown no or little side effects and thus can be used safely for long period of time. For pioglitazone current recommendations are that the patients should be clinically monitored and it should not be used in those with advanced congestive cardiac failure (NYHA class III and IV).

Our study had some limitations. Limited numbers of patients were evaluated for a short time. Liver biopsy was not done and patients were not followed up with fibroscan or USG.

Conclusion:

In conclusion, it can be said that both metformin and combination of metformin and pioglitazone are effective in reducing ALT in NAFLD and combination is better. Not only that, the combination group had better results in improving lipid profile and glycaemic status. However, larger, multicenter studies can be done for better and more reliable results.

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A Study on Diagnostic Importance of Fiber Optic Laryngoscopy (FOL) in Patients with Upper Airway Disorders

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Summery:

Background: Upper airway symptoms are quite common. Many of these symptoms underlie serious upper airway pathologies which should be diagnosed at an early stage so that optimum treatment can be given. Often it seems to be difficult to diagnose upper air way pathology by conventional indirect laryngoscopy (I/L), especially when the lesion is at an early stage. In this situation fiber optic laryngoscopy (FOL) is very helpful.

Objective: To identify lesions in the larynx in patients with persistent upper airway disorders and to compare the diagnostic yield of FOL over I/L.

Method: This was a cross-sectional study conducted partly in department of ENT and Head & neck surgery, BIRDEM General Hospital and partly at the same department of BSMMU during the period of July to December 2012. 100 adult patients were taken having upper airway symptoms. Study subjects were evaluated by history, physical examinations, and ENT examinations. All patients underwent indirect laryngoscopy and FOL. Data were recorded and analyzed.

Results: Age of the respondents was between 18-72 years. The mean ± SD was 54 ±11.79 years. Common symptoms among the participants were hoarseness, sore throat, neck swelling, breathless ness, cough, odynophagia, earache etc. On I/L examinations 30% were vocal cord polyps, 14% v. cord edema, 17% v. cord growths, 11% v. cord nodules, 6 % v. cord palsy, 4% ulcerated lesions, 13 % poor vision and 5% were normal. On FOL examinations, 30% were vocal cord polyp, 18% v. cord edema, 21% v. cord growth, 14% v. cord nodule, 8 % v. cord palsy, 5% ulcerated lesion, 2% laryngeal web, 2 % were normal study and there were no poor vision. A comparison was made between the findings of I/L and FOL which showed that FOL is superior to I/L in diagnosing upper airway disorders as evidenced by findings of 2% lesions among 5% patients having normal I/L findings. Chi-square test was done between I/L and FOL findings which was statistically significant; (P value was .002) i.e. FOL procedure is valuable diagnostically in comparison to I/L.

Conclusion: In many occasions I/L findings are inconclusive in daily ENT practice. Moreover, in some cases there is poor vision to identify the lesion. Therefore, Routine FOL evaluation is valuable in patients with significant, chronic and progressive upper airway symptoms. It should always be considered in patients with persisting and progressive symptoms even though I/L appeared normal.

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Introduction:

Fiberoptic imaging was initially developed to visualize inaccessible regions of the body[1]. Current fiberoptic nasopharyngolaryngoscopes are lighted, are flexible with 2-way articulation, provide high resolutio photo and video capabilities, and can have a distal diameter as small as 2 mm[2].

Fiberoptic nasopharyngolaryngoscopy can allow visualization of the following structures[3]: nasal cavity, septum, middle meatal space and infundibulum, frontal recess, sphenoid, ethmoid recess, turbinates, posterior choanae, eustachian tube orifices, adenoid if any, nasopharynx, posterior surface of the uvula and palate, velopharyngeal valve, base of the tongue, pharyngeal and lingual tonsils, vallecula, part of pyriform spaces, epiglottis/ supraglottis, glottis and immediate subglottis with mobility or immobility of the vocal folds and arytenoids[4,5].

Fiberoptic nasopharyngolaryngoscopy is indicated when visualization of the nasopharyngolaryngeal anatomy is needed for diagnosis, treatment, or both[6]. In the nasal cavity, fiberoptic nasopharyngolaryngoscopy can

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visualize polyps, tumors, foreign bodies, or sources of epistaxis. In the nasopharynx, the scope can help identify suspected tumors or adenoidal hypertrophy[7]. In the oropharynx or hypopharynx, fiberoptic nasopharyngolaryngoscope may be used to evaluate foreign bodies and potential airway obstruction from such etiologies as neoplasm and also other pathologies like tonsillar hypertrophy, glossoptosis, or laryngomalacia[8]. In the vocal cords- polyps, nodules, SOL, and paralysis of its movement can also be identified with fiberoptic laryngoscopy[9].

Another application for nasopharyngolaryngoscopy is assessment of velopharyngeal insufficiency[10]. While the patient counts aloud or repeats a specific phrase, the nasopharyngolaryngoscope in the nasopharynx can be used to assess the pattern of velopharyngeal closure[11]. Fiberoptic endoscopic evaluation of swallowing (FEES) has emerged as a comparable alternative to video fluoroscopy and modified barium swallow in the evaluation of dysphagia and aspiration during swallowing[12]. Nasopharyngolaryngoscopy is considered a benign procedure with few contraindications and mild complications in experienced hands[13].

Upper airway disorders are very common. These are frequently encountered in daily ENT practices. These patients are commonly treated with antihistamines and antibiotics without proper evaluation of the upper airway. Although many patients are examined with indirect laryngoscopy, this is not always conclusive and visualization is poor[14]. Fiberoptic laryngoscopy is the procedure by which upper airway can be examined appropriately with adequate illumination and visualization. Findings can also be displayed for all with monitor. Therapeutic procedures can be done as well in selected cases[15].

In this study an attempt had been made to find out the laryngeal lesions in symptomatic patients with the help of FOL and to compare the diagnostic yields of FOL with that of I/L

Methods:

This was a cross-sectional analytic study conducted with 100 adult patients having upper airway symptoms to evaluate their airway and their socio-demographic characteristics and attributes associated with the symptoms. All study subjects were underwent indirect laryngoscopy (I/L) and Fiberoptic laryngoscopy (FOL) procedures (Pentax, G112031 Japan, FNL10RBS was used in BIRDEM & Model-FNL-15RP3, Sl # A110462, Pentax, Japan was used in BSMMU). The total period of study was from July 2012 to December 2012. The study was undertaken partly at the department of otolaryngology & Head-Neck Surgery, BIRDEM and at partly at the department of otolaryngology & Head-Neck Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU). Eligible subjects with persistent upper airway symptoms for more than three weeks who does not improved with conservative measures were included- Patients seen at ENT outpatient department (OPD) of BIRDEM & BSMMU, In patients of ENT department of BIRDEM & BSMMU, referred patients from different departments like Internal medicine, Endocrinology, Nephrology, Surgery and other departments of BIRDEM hospital - enrolled after informed consent. After ethical clearance, data were collected by face to face interview using a semistructured questionnaire and from procedures results review. Data were analyzed by SPSS software, cross tabulation, chi square test and independent sample tests.

Results:

In this study the respondents aged 18 -72 years were selected. The mean ± SD of age of the respondents was 54 ±11.79 years and 33.8% respondents were of 55 to 64 age group. Maximum and minimum age was 72 and 18 years where range was 53 years (Table- I).

Table-I

Age group distributions among the patients

Age group (in Years)	Frequency (n)	Percent (%)
18-28	17	17
29-38	14	14
39-48	12	12
49-58	22	22
59-68	16	16
69-72	19	19
Total	100	100

Almost three-fourth were male and one-fourth was female. Female patients were 22 (22.0 %) and rests were male 78 (78.0 %). Data was mostly collected at working hours which might be the reason for presence of high proportion of male in the sample unit. Regarding

educational status 65% were up to SSC, 18% HSC, 8% graduate and 9% were illiterate. On occupation, 62% were businessman, 22% were service holders, 14% housewives, and 2% were jobless. Common symptoms among the participants were hoarseness of voice, sore throat, neck swelling, breathless ness, cough, odynophagia, earache etc (Table- II).

Table-II

Symptoms among the patients (n=100)

Symptoms	Frequency (n)	Percent (%)
Hoarseness of voice	57	57
Breathlessness/stridor	5	5
Sore throat	4	4
Neck swelling	2	2
Difficulty in swallowing	13	13
Other (cough)	19	19
Total	100	100

On indirect laryngoscopic (I/L) examinations 30% were vocal cord polyp, 14% v. cord edema, 17% v. cord growth, 11% v. cord nodule, 6 % v. cord palsy, 4% ulcerated lesion, 13 % poor vision and 5% were normal study(Figure-1).

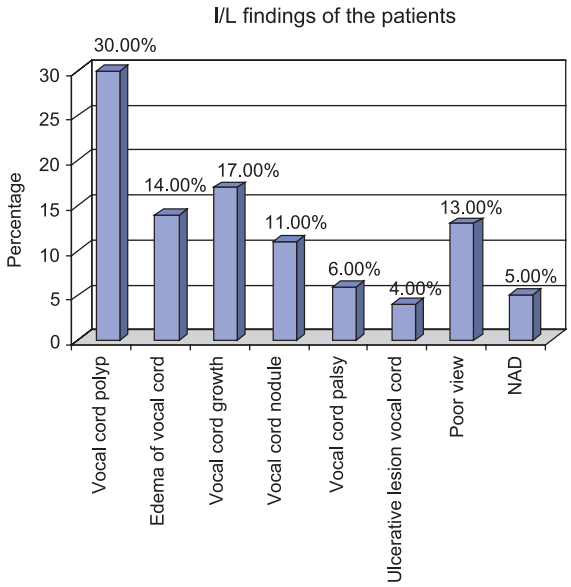

Fig.-1: *I/L findings of the patients (n=100)*

On direct laryngoscopy (FOL) examinations, 30% were vocal cord polyp, 18% v. cord edema, 21% v. cord growth, 14% v. cord nodule, 8 % v. cord palsy, 5% ulcerated lesion, 2% laryngeal web, 2 % were normal study and there were no poor vision(Figure-2).

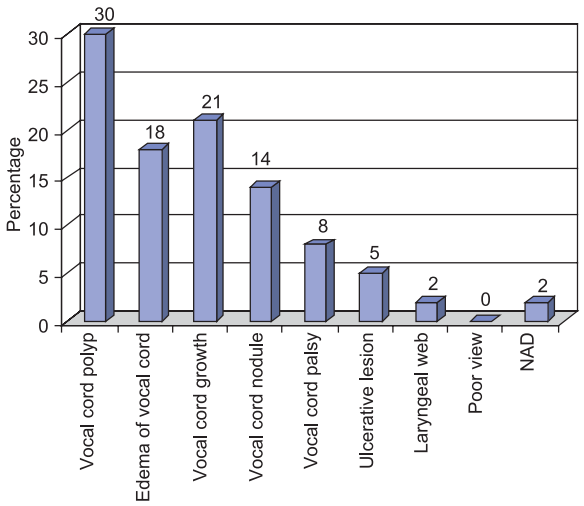

Fig.-2: *FOL findings of the patients (n=100)*

A comparison has also been made between findings of I/L and FOL in tabulated form to see the difference at a glance (Table-III).

Finally chi-square test was done between I/L and FOL findings which was statistically significant (Table- IV).

Table-III

Comparison between findings of IL and FOL (n=100)

Findings	I/L		FOL	
	n	%	n	%
V.cord polyp	30	30	30	30
oedema of v. cord	14	14	18	18
V. cord growth	17	17	21	21
V. cord nodule	11	11	14	14
V. cord palsy	6	6	8	8
Ulcerative lesion	4	4	5	5
Laryngeal web	0	0	2	2
Poor view	13	13	0	0
NAD	5	5	2	2
Total	100	100	100	100

Table-IV

Chi-Square test of I/L and FOL findings (n=100)

Procedure	lesion	no lesion	total	X^2	df	p value
I/L	82(82.0%)	18(18.0%)	100(100.0%)			
				9.964	1	0.002
FOL	98(98.0%)	02(2.0%)	100(100.0%)			

Note: On I/L examination lesion found in 82.0% cases. On the other hand On FOL examination lesion was found in 98.0% cases. Statistically these differences were found significant.

Discussion:

Upper airway disorders are the common ENT disorders encountered in general practice. Malignancy is an important cause of upper airway symptom[16]. However, other common causes of these symptoms are v. cord nodule, v. cord polyp, v. cord edema, chronic laryngitis etc. In some instances, over use of voice or voice abuse contribute to the development of these symptoms. The consumption of tobacco, alcohol, betel leaf, drugs etc can also lead to development of these symptoms in the absence of significant pathology [17].

Upper air way lesions may remain silent initially; may be evident only when the patient is symptomatic. Studies regarding endoscopic evaluation of upper airway diseases are few. Therefore it is difficult to conclude which factors predict the laryngoscopic outcome in upper airway symptomatic patients.

A prospective study-"Benign vocal cord lesions - a study of 25 cases" was carried out in the department of Otolaryngology and Head-Neck Surgery of Sir Salimullah Medical College & Mitford Hospital, Dhaka[18]. The study revealed- Vocal cord polyp-12(48%), Vocal cord nodule- 05 (20%), Vocal cord papilloma-1(04%) and Multiple papillomatoseses 07(28%) [18].

In one study- a comparative study among direct, indirect and fiber optic laryngoscopy to evaluate v. cord paralysis after thyroid surgery revealed that FOL is the best method for evaluating the upper airway disorders [19].

In our study the respondents aged 18-72 years were selected. The mean ± SD of age of the respondents was 54 ±11.79 years. Among the study subjects majority were in 49 to 58 years age group (22.0%) followed by 69 years & above age group (19.0%).

So majority being within 49 to 58 years age group suggests a more occurrence of upper airway lesions in this age group. But there may be other factors underlying this as well.

About three-fourth were male and one-fourth was female. Female 22(22.0 %) and rests were male 78 (78.0 %). This also indicates an increased occurrence of upper air way diseases in male than female. Smoking and exposure to other noxious agents, overuse of voice etc. are more common in male which might be predisposing factors for male preponderance. Moreover, data was mostly collected at working hours which might also be a reason for presence of high proportion of male in the sample unit.

Regarding educational status 65% were at and below SSC, 18% HSC, 8% graduate and 9% were illiterate. It has been seen that, the more educated patients are more health conscious & presents early, thus disease is detected at an early stage. Many cancer patients can be treated with a curative intend if they presents at an early stage of the disease.

Common symptoms among the participants were hoarseness, sore throat, neck swelling, breathless ness, cough, odynophagia, earache etc. Majority patients were presented with hoarseness (57%), among them majority patients were diagnosed as benign disease, i.e. vocal cord polyp, nodule & edema.

On occupation, 62% were businessman, 22% were service holders, 14% housewives, and 2% were jobless. Vocal cord nodule was seen more in patients who were housewife & had small children. Among the service holders, patients who are teachers of primary school had presented with vocal cord edema- may be due to over use of voice. Another thing is that, majority of the study population are businessman in occupation. So

there may be some occupational exposure relating to the disease occurrences.

On indirect laryngoscopic (I/L) examinations 30% were vocal cord polyp, 14% v. cord edema, 17% v. cord growth, 11% v. cord nodule, 6 % v. cord palsy, 4% ulcerated lesion, 13 % poor vision and 5% were normal study.

On direct laryngoscopy (FOL) examinations, 30% were vocal cord polyp, 18% v. cord edema, 21% v. cord growth, 14% v. cord nodule, 8 % v. cord palsy, 5% ulcerated lesion, 2% laryngeal web, 2 % were normal study and there were no poor vision. This 2% symptomatic patients having normal upper airway on laryngoscopic examination may be due to an allergic, functional or a lower respiratory disorders.

A comparison has also been done between findings of I/L and FOL in tabulated form to see the difference at a glance. This showed that fiber optic laryngoscopic examination is superior to indirect laryngoscopy in diagnosing upper airway disorders which is evidenced by findings of 2% lesions among 5% patients having normal I/L findings.

Finally chi-square test was done between I/L and FOL findings which was statistically significant; (P value was .002) i.e. this study revealed that FOL procedure is valuable diagnostically in comparison to I/L.

Although optimum care had been tried in every steps of this study, still some limitations existed:

The study was conducted in a selected institution. So the study population might not represent the whole community. Probability sampling technique could not be employed to recruit the study unit; they were selected purposively due to time constraints. As a result, there might be some selection bias. In spite of maximum effort by the researcher due to time and resource limitation sample size was small; a larger sample size would have given a better result.

Conclusion:

In this study, an evaluation was made over the study population having upper airway symptoms. The evaluation was done with I/L and FOL procedures over the study population. A comparison was also made between the findings of I/L and FOL. The aim was to see the diagnostic yield of FOL over I/L. In our study, majority of the study population had lesions on I/L. Some participants had poor vision and some had normal upper airway on I/L. Study showed that many of the study subjects having poor vision and normal I/L findings had lesions on FOL. Some new lesions (e.g. web) were also detected on FOL which were not detectable on I/L. Moreover, significant lesions (e.g. malignancy) were detected on FOL than I/L. Therefore, Routine FOL evaluation is valuable in patients with significant, chronic and progressive upper airway symptoms. It should always be considered in patients with persisting and progressive symptoms even though I/L appeared normal. Further research is expected to shed light on the role of FOL, in particular to investigate whether this modality improves outcomes.

Recommendation

- Every chronic, progressive or persistent upper airway symptoms should be evaluated carefully with FOL when I/L finding is inconclusive or even normal.
- Primary care physicians should be informed that only drug treatment or I/L examination is not sufficient for persistent or progressive upper airway symptoms; rather the patient should be referred for FOL.
- Further in depth research should be conducted to clarify the importance of FOL in patients with upper airway disorders.

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Thyroid Status of Infertile Women Attending at Infertility Outdoor in BSMMU

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Summary:

Aim: To evaluate the thyroid status in infertile women.

Materials and methods: A cross sectional study was conducted in the department of Infertility of Bangabandhu Shaekh Mujib Medical University from January 2012 to December 2012. A total 400 patients of infertility were studied. The thyroid function status of the subjects were assessed and analyzed.

Results: Of the 400 women enrolled for the study, 221(55%) patients with primary infertility and 179 (45%) patients were with secondary subfertility. The mean age of the responders were 22.3±4.6 years, the mean duration of marriage were 4.5±1.2 years and mean BMI were 23.2±3.1 kg/m^2.Among the 400 patients 70.50% that is 293 patients were euthyroid, TSH level was increased in 23% or in 92 subjects. Depending upon the TSH levels, hypothyroid infertile women were further subdivided into subclinical hypothyroidism where TSH 4–6 mIU/L with normal FT4 (9-24 pmol/L) and clinical hypothyroidism where TSH > 6 mIU/L with raised FT4 level. It was found that 66 (71.74%) of hypothyroid infertile women were with subclinical and remaining 26 (28.26%) were with clinical hypothyroidism.Hyperthyroidism that is low TSH level (<.5 mIU/L) found in 15(3.75%) subjects and visible goiter was present in only 2 patients. In 96 hypothyroid infertile females, the mean TSH levels were 7.34 ± 2.13 mIU/L, and mean FT4 level was 17.34±3.23pmol/L. The mean PRL levels were 52.46 ±11.17 ng/ml.

Conclusion: Thyroid dysfunction is an important factors for infertility. Early diagnosis and timely intervention can reduce the burden of infertility due to thyroid dysfunction.

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Introduction:

Infertility is defined as a failure to achieve pregnancy during 1 year of frequent, unprotected intercourse[1]. In the general population, it is estimated that 84% of females would conceive within 1 year of regular unprotected sexual intercourse. This rises cumulatively to 93% after 3 years [2-3.]

The relation of infertility and thyroid disorder is not yet clear. Undiagnosed and untreated thyroid disease can be a cause for infertility as well as sub-fertility. Thyroid hormones are essential for normal growth, sexual development and reproductive function. Thyroid dysfunction can affect fertility in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin (PRL) levels, and sex hormone imbalances. Therefore, normal thyroid function is necessary for fertility, pregnancy, and to sustain a healthy pregnancy, even in the earliest days after conception.[4-5]

Thyroid glands produce hormones that regulate metabolism and important organ functions like reproduction and mental health[4]. However, it is true that thyroid problem can sometimes be an impediment to getting pregnant for anovulation and menstrual irregularities with no eggs to fertilize, conception becomes impossible[6]. In addition, some women experience a short luteal phase- The luteal phase is the time frame between ovulation and onset of menstruation. Luteal phase needs to be of sufficient duration (13-15 days) to nurture fertilized egg.[7] Luteal phase defect has been diagnosed in 3-20% who in infertile patients.[8]

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Hypothyroidism may also increase circulating active estrogen and interfere with ovulation. This increased bioactive estrogen may be due to decreased metabolism of estrogen in the liver or decrease level of protein that binds it in the circulation, like sex hormone binding globulin (SHBG) in adequate amount binds to hormone and reduces free fraction of estrogen. This persistent elevation of bioactive estrogen disrupts the midcycle preovulatory LH and FSH surges as required for ovulation[9]. Since thyroid hormones are involved in the gonadotropin induced estradiol and progesterone secretion by human granulosa cells, hypothyroidism would interfere with ovarian function and fertility.[10] Hyperprolactinemia resulting from longstanding primary hypothyroidism has been implicated in ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion when mildly elevated to oligomenorrhea or amenorrhea when circulating prolactin levels are high.[11]

Thyroid evaluation should be done in any woman who wants to get pregnant with family history of thyroid problem or irregular menstrual cycle or had more than two miscarriages or is unable to conceive after 1 year of unprotected intercourse. The comprehensive thyroid evaluation should include T_3, T_4, thyroid stimulating hormone (TSH), and thyroid autoimmune testing such as thyroid peroxidase (TPO) antibodies, thyroglobin/ antithyroglobin antibodies, and thyroid stimulating immunoglobulin (TSI). Thyroid autoimmune testing may be included in the basic fertility workup because the presence of thyroid antibodies doubles the risk of recurrent miscarriages in women with otherwise normal thyroid function.[12–14]

Thyroid dysfunction can be easily detected by assessing TSH levels in the blood. A slight increase in TSH levels with normal T_3 and T_4 indicates subclinical hypothyroidism whereas high TSH levels accompanied by low T_3 and T_4 levels indicate clinical hypothyroidism.[15] Subclinical hypothyroidism is more common. It can cause anovulation directly or by causing elevation in PRL. Many infertile women with hypothyroidism had associated hyperprolactinemia due to increased production of thyrotropin releasing hormone (TRH) in ovulatory dysfunction.[16,17]

So, awareness of the thyroid status in the infertile couple is crucial, because of its significant, frequent and often reversible or preventable effect on infertility. Many aspects of the role of thyroid disorders in infertility need further research.With this background, the present study has been contemplated to investigate the prevalence and etiology of different thyroid disorders in infertile patients attending at infertility outdoor BSMMU.

AIM

To evaluate the thyroid status in infertile women.

Materials and Methods:

The cross sectional study was conducted on 400 women (age group 20–40 years) on their first visit to Infertility outdoor of Gynecology and Obstetrics Department of BSMMU from January 2012 to December 2012. The study was approved by the Institutional Ethical Committee and was conducted after taking informed, written consent of the participants. Subjects were selected purposively according to the availability of the patients. Sample size was determined from "Tables of minimum sample size"

Inclusion criteria:

- Age 20-40 years
- Duration of marriage >1 year

Exclusion criteria:

- Infertile women having pelvic pathology, like- Fibroid Uterus, tubular blockage, pelvic inflammatory disease, endometriosis on diagnostic laparoscopy or hysteroscopy and with genital TB (PCR-positive); with liver, renal or cardiac diseases
- Patients having systemic diseases, (Diabetes Mellitus, Hypertension, Renal disease, Liver disease, Cardiac disease) those already on treatment for thyroid disorders or hyperprolactinemia
- Male factor abnormalities also were excluded from the study.

Routine investigations such as random blood sugar (RBS), hemogram, urine routine examination, and ultrasound were done. TSH and PRL were measured by the electrochemiluminesence method as per the instruction manual for Elecsys, 2010 (Roche, USA). Normal TSH and PRL levels were 0.27–4.5 ìIU/ml and 1.9–25 ng/ml, respectively and FT4 (9-24 pmol/L), as per kit supplier's instruction. Therefore, hypothyroidism was considered at TSH levels of > 4.5 ìIU/ml and hyperprolactinemia at PRL levels of >25 ng/ml.

Statistical analysis of results was carried out using percentages.

Results:

Of the 400 women enrolled for the study, 221(55%) patients with primary infertility and 179(45%) patients were with secondary subfertility.76[19.29] The mean age of the responders were 22.3±4.6 years, the mean duration of marriage were 4.5±1.2 years and mean BMI were 23.2±3.1 kg/m^2

Among the 400 patients 70.50% that is 293 patients were Euthyroid, TSH level was increased in 23% or in 92 subjects. Depending upon the TSH levels, hypothyroid infertile women were further subdivided into subclinical hypothyroidism where TSH 4–6 mIU/L with normal FT4 (9-24 pmol/L) and clinical hypothyroidism where TSH > 6 mIU/L with raised FT4 level. It was found that 66 (71.74%) of hypothyroid infertile women were with subclinical and remaining 26 (28.26%) were with clinical hypothyroidism. Hyperthyroidism that is low TSH level (<.5 mIU/L) found in 15(3.75%) subjects and visible goiter was present in only 2 patients.

In 96 hypothyroid infertile females, the mean TSH levels were 7.34 ± 2.13 mIU/L, and mean FT4 level was 17.34±3.23pmol/L. The mean PRL levels were 52.46 ±11.17 ng/ml.

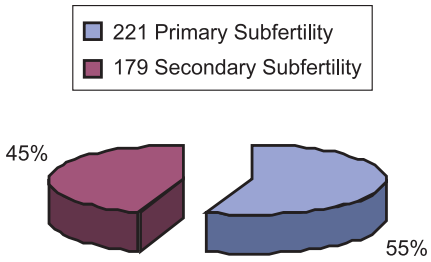

Fig.-1: *Distribution of the subjects according to the type of infertility (n=400)*

Table-I

Socio-demographic variables in study subjects (n=400)

Variables	Study subjects (n = 400)	Range
Age (Years)	22.3±4.6	18.6-28.6
BMI (kg/m^2)	23.2±3.1	20.2-30.1
Mean duration of infertility (years)	4.5±1.2	3.1-5.8

Table-II

Distributions of study subjects according to thyroid function (n=400)

Types of thyroid status	Number	Percentage (%)
Euthyroid	293	73.25
Hyperthyroid	15	3.75
Subclinical hypothyroid	66	16.50
Clinical hypothyroid	26	6.50

Table-III

Comparison of Biochemical examination between groups (n=400)

Hormons	Mean level	Range
Serum FT_4 (micromole/L)	17.34±3.23	13.69-22.44
Serum TSH (mIU/L)	7.34 ± 2.13	2.73-9.54
Serum PRL(ng/ml)	52.46±31.17	20.11-70.60

Discussion:

Prevalence of hypothyroidism in the reproductive age group is 2–4% and has been shown to be the cause of infertility and habitual abortion.[18] Thyroid dysfunction is a common cause of infertility which can be easily managed by correcting the appropriate levels of thyroid hormones.[19,20] Thyroid hormones have profound effects on reproduction and pregnancy. Thyroid dysfunction is implicated in a broad spectrum of reproductive disorders, ranging from abnormal sexual development to menstrual irregularities and infertility.[21] Hypothyroidism is associated with increased production of TRH, which stimulates pituitary to secrete TSH and PRL. Hyperprolactinemia adversely affects fertility potential by impairing GnRH pulsatility and thereby ovarian function.[20]

The current cross sectional study of 400 infertile women showed 221(55%) patients with primary infertility and 179(45%) patients were with secondary subfertility. The mean age of the responders were 22.3±4.6 years, the mean duration of marriage were 4.5±1.2 years. Nambiar et al. and Mbah et al. found the mean age of the subjects were 25.19 (±4.17) years which are higher than the current study[22-23]. In this study, data reflecting early marriage prevalent in Bangladesh. The higher age of the above mentioned authors may be due to increased

life expectancy, geographical and racial influences may have significant impacts.

In the present study the mean BMI were 23.2±3.1 kg/m^2.Mbah et al.[23] found the statistically significant differences in body weight as found between the hypothyroid and non-hypothyroid pregnant women[15]. The relationship of thyroid function with BMI also described by Glinoer et al. and Vermiglio, Presti and Argentina[24-25].

An elevated TSH indicates primary hypothyroidism, and serum-free T4 levels will help to categorize this as either overt or subclinical hypothyroidism. Among the 400 patients 73.25% that is 282 patients were Euthyroid, TSH level was increased in 23% or in 92 subjects. Depending upon the TSH levels, hypothyroid infertile women were further subdivided into subclinical hypothyroidism where TSH 4–6 mIU/L with normal FT4 (9-24 pmol/L) and clinical hypothyroidism where TSH > 6 mIU/L with raised FT4 level. It was found that 66 (16.50%) of hypothyroid infertile women were with subclinical and remaining 26 (6.50%) were with clinical hypothyroidism. These findings are very close to the study done by Janssen *et al* .[26]

The prevalence of hypothyroidism in women of reproductive age (20-40 years) varies between 2% to 4%.[18] Relatively higher crude prevalence rate of hypothyroidism (8%) in the infertile women found in our study could be due to special referral pattern of the patients who were referred to the hospital based on suspicion of thyroid abnormalities.

Hyperprolactinemia was found in 20.75% cases, which is higher than in USA. The prevalence of hyperprolactinemia was higher in Iraq (60%) and even in Hyderabad, India, it is higher (41%) as compared to the present study. Hyperprolactinemia may result from stress, and the variable prevalence may be due to the different stress levels in different areas.[13,17]

Hyperthyroidism was found in 3.75% of the infertile patients in the present study. Joshi *et al* [27] evaluated 53 hyperthyroid patients and found 5.8% of them to be infertile. In this study goiter was present in only two patients.

Therefore, the normal TSH levels are the pre-requisite requirements for fertilization. For these reasons, TSH and prolactin are commonly-ordered clinical tests in evaluating infertile women. The decision to initiate thyroid replacement therapy in subclinical hypothyroidism at early stage may be justified in infertile women. Our data also indicate that variations in TSH levels in the narrower range or borderline cases, i.e. 4–5, 5–6, and >6.0 ìIU/ml, should not be ignored in infertile women which are otherwise asymptomatic for clinical hypothyroidism. This group of infertile women, if only carefully diagnosed and treated for hypothyroidism, can benefit a lot rather than going for unnecessary battery of hormone assays and costly invasive procedures. For better management of infertility cause, we should plan further studies with the large sample size and long-term follow-up which are necessary to validate the variation in TSH and PRL levels.

It may be concluded that thyroid dysfunction could initiate, maintain or worsen the infertility status and thereby correcting thyroid state, infertility could be managed in a better way. This hypothesis seems to hold true even now but it lacks appropriate evidence based systematic analysis to establish the necessity of routine screening of all the infertility patients for thyroid function and thyroid-specific autoantibodies even without clinical evidence of overt thyroid disorders because patients with anti-TPO and anti Tg autoantibodies are much likely to develop thyroid dysfunction later in the later life.

Conclusion:

The present study was done to see the thyroid status of infertility women. In the light of the findings of the present study and discussion thereof, it is found that thyroid disorder are very commonly found in women who are suffering from infertility, and the most common thyroid disorder is sub clinical hypothyroidism. So, it is recommended to undertake further study with larger sample size to find whether Thyroxin therapy in sub clinical hypothyroid improves fertility status. It is also recommended to see whether those having sub clinical hypothyroidism associated with thyroid peroxidase antibody are more prone to become infertile and overt hypothyroidism.

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The Role of Sentinel Lymph Node Biopsy in the Management of Breast Cancer

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Summary:

The sentinel lymph node (SLN) is defined as the first node(s) receiving lymphatic drainage from a primary tumour. A promising alternative to axillary lymph node dissection (ALND) is sentinel lymph node biopsy. SLN biopsy has been introduced as a technique to identify axillary lymph node most likely to contain tumour cells metastasizing from a primary carcinoma of breast. Several methods of identifying the SLN exists, including the use of radioactive tracer, lymphazurin dye or combination of the two via intraparenchymal and/or intradermal, peritumoral or periaerolar injection sites. Intraoperative evaluation of SLNs are done by performing FS(Frozen Section) on all the lymph nodes after serially sectioning them at 3-4mm intervals; at least 2 levels are cut of all the sentinel lymph nodes. In addition, touch preparation cytology(TP) smear may also be made for evaluation. The limitations of SLNB is that a proportion of patients who have metastasis limited to the SLN can be predicted when there is a combination of tumour size <1.0cm, the absence of lymphovascular invasion and micrometastatic disease (<0.2cm) in SLN. However for patients with large breast cancer, the role of SLNB is controversial. Early studies of SLNB in large breast cancer patients demonstrated a high (8-18%) false negative rate, with the accuracy worsening with the increasing size. Excision of SLNs have an extremely low morbidity and a high degree of staging accuracy. A tumour-free SLN virtually excludes lymphatic involvement of the entire regional lymphatic basin. More than 50 observational studies of SLNB validated by a back up ALND demonstrate that SLNB is feasible, accurate and suitable for virtually all patients with operable clinically node negative disease. Sentinel lymph node biopsy not only provide prognostic information, but also aims to guide adjuvant therapy without the untoward side effects of complete axillary dissection.

Key words: Sentinal lymph node, Management, Breast Cancer.

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Introduction:

Breast cancer is the leading cause of death in women with over 3,00,000 deaths annually world wide[1]. Axillary nodes status is the best single predictor of disease outcome in patient with early stage breast cancer. It has been shown that the presence of axillary node metastasis reduces the patient's survival by 28-40%[2] and the likelihood of treatment failure increases with the increase number of positive axillary nodes[3]. Furthermore the removal of axillary nodes also improves local and regional control, which leads to better over all survival. Axillary lymph node dissection (ALND) has been the only reliable method for determining lymph node status[4]. However the clinical importance of axillary control and the extent of axillary surgery remain controversial issues. Previous studies on sentinel lymph node biopsy (SLNB) validated by a back up axillary lymph node dissection (ALND) confirm that SLND is both feasible and accurate, reliably detecting axillary metastasis in 97% of all patients and 93% of node positive cases[5].

The surgical management of invasive breast cancer has included complete removal of the tumour, with documentation of negative margins by either mastectomy or breast conserving surgery and synchronous complete axillary lymph node dissection (ALND). However the complication rate of ALND are reported to be 20-55%. This complications include lymphedema, sensory nerve damage, haemorrage and post operative seroma formation as well as need for general anaesthesia[6]. In invasive breast carcinoma, axillary lymph node metastasis is seen in only 40% patients undergoing ALND[7], and is even less in early breast cancer; therefore ALND is not needed in the

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majority of the patients. Since ALND is also associated with significant morbidity. A promising alternative to ALND is sentinel node (SLN) biopsy for axillary staging of invasive breast cancer. Sentinel lymph node mapping is a minimally invasive procedure and is very effective and accurate method of evaluating the regional lymph nodes in breast cancer patients. It is noteworthy that a pathologically negative sentinel lymph node predicted the absence of metastasis. The reminder of regional lymph node basin with about a 98% degree of certainty[8]. The sentinel lymph node is defined as the first node(S) receiving lymphatic drainage from a primary tumour. It is therefore the node most likely to contain metastatic breast carcinoma. A tumour-free SLN virtually excludes lymphatic involvement of the entire regional lymphatic basin. Sentinel lymph node biopsy (SLNB) not only provides prognostic information but also aims to guide adjuvant therapy without the untoward side effects of complete axillary dissection. More than 50 observational studies of SLNB validated by a back up ALND demonstrate that SLNB is feasible, accurate and suitable for virtually all patients with operable, clinically node negative disease.

Historical perspective:

The concept of sentinel node was first described by Cabanas R in 1977 in the context of penile carcinoma[9]. In 1992 Morton and his colleagues reported a blue dye technique for lymphatic mapping and sentinel node biopsy in clinically node negative melanoma patients[10] and later by Van der veen and colleagues with lympho scintigraphy to select melanoma patients for regional lymph node dissection[11]. In the decade since the pioneering reports of Krag et al and Giuliano et al, SLNB has become a new standard of care for axillary lymph node staging in patients with breast carcinoma[12]. Lymphatic mapping and SLNB are clearly changing the paradigm for the treatment of breast cancer.

Sentinel lymph node biopsy technique:

Sentinel lymph node biopsy is simple technique which uses subdermal or peritumoral injection of vital blue dye or radio-labelled colloid or both substances together to identify the first lymph node draining the primary tumour. Several methods of identifying the SLN exists, including the use of radioactive tracers, lymphazurin dye or combination of the two via intraparenchymal and /or intradermal, peritumoral or periaerolar injection sites. In 1998 O'Hea et al[13] reported their initial experience at Memorial Sloan-Kettering cancer centre that the blue dye and radioisotope were the complementary technique in SLN mapping biopsy in breast cancer patients, and that the overall success of this procedure was maximized when the two are used together(93%) as compared to when used alone(75 & 88% respectively) in SLND mapping in the breast cancer patients. With increasing experience of the breast surgical oncologists with this procedure over the last decade. SLNB is usually straight forward and a simple operation which has become standard of care for surgical management of breast cancer. Before the surgical resection of breast tumour(lumpectomy or mastectomy) blue dye and redioactive tracer is injected into the breast in a peritumoral, intradermal or periaerolar manner. Isotope counts are taken using a hand held-gamma probe for supraclavicular, infraclavicular, parasternal and axillary areas. More than a 95% of the time a hot spot is found in the ipsilateral axilla. An axillary incision is made the surgeon identifying all blue and /or hot nodes as well as palpable nodes. These are removed until the axillary background counts fall below a threshold value: defined as the background count; most authors report a median of two SLN per patient[14]. A success of 90-95% in finding the SLN and no more than 5-10% false negative results would seem reasonable targets for validation trials[15]. Results of identifying SLN using different technique are shown in Table-1. Intraparenchymal injection was the first technique described and is the most widely accepted. Recent data suggest that the intradermal technique is highly accurate and may increase the SLN identification rate. SLN localization was successful in 97% of cases with intradermal radioisotope injection and in 78% of those with intraparenchymal injection, a statistically significant difference[16]. Knox and Ley compare the intraparenchymal Vs intradermal injection of radioisotope for identification of SLN in breast cancer patients and reported that intradermal technique may increase SLN identification and is easy to use and has acceptable false negative rate (2%)[17]. The greater ease of SLN identification rate with intradermal injection may be due to the rich lymphatic network of skin overlying the breast as well as reduction in shine effect. Krag et al conducted multicenter validation study using radioactive tracer technique. The overall rate of identification of

hot spots was 93% with an accuracy of 97%, specificity 100% and sensitivity 89%[18].

Intra-operative evaluation of sentinel lymph nodes: Careful intraoperative palpation of the axilla is an essential component of SLN biopsy. Apart from the fact that the detection rate is approximately 80-90% in the largest series, the key problems are false negative and intraoperative examination of sentinel node. Routine frozen section (FS) examination appears to miss up to 30% of metastasis in sentinel nodes [19]. However the value of routine intraoperative SLN frozen section is controversial. If positive, FS has the obvious advantage of allowing an immediate axillary dissection and thereby avoiding the reoperation. On the other hand FS is costly, time consuming and subject to false negative results. Brogi et al in 2005 demonstrated that FS, touch preparation(TP) and cytological smear (CS) are equivalent for the intraoperative assessment of SLN in breast cancer (comparable sensitivities were 59%, 57%, 59% respectively)[20]. Each method was more sensitive in detecting macrometastasis (>2mm tumour deposite, 96%, 93%, 93%) than micrometastasis (< 2mm, 27%, 27%, 30% respectively). The added benefit of combining methods is small and the failure of intraoperative assessment is largely due to an inability to detect micrometastatic disease. A study by Krogerus et al[21] compared the widely used method of intraoperative evaluation of SLN which is a modification of the method introduced by Veronesi et al[22] including bisecting the lymph node in its long axis and examining serial sections to their own novel method. Krogerus's method included sectioning the lymph node into thin slices (1-1.5mm thick) perpendicular to the long axis and arranged on a prefrozen tissue-Tak, frozen section from two level were then examined. With this method, they found more and smaller metastatis compared to the widely used method and also the technique was less time consuming. Recently intraoperative evaluation of SLN includes performing FS (Frozen section) on all the lymph nodes after serially sectioning them at 3-4mm intervals; at least 2 levels are cut of all the sentinel lymph nodes. In addition touch preparation cytology (TP) smear may also be made for evaluation. However there exists a personal bias among pathologists in examining the cytology smears especially pathologists who are not practicising cytopathologist. TP is an additional and complementary method to FS in the intraoperative evaluation of SLN. The FS includes examining all lymph nodes bisecting them if they are more than 0.5cm in thickness and cutting at least two levels of each section. The sentinel node can be examined intra-operatively by frozen section or imprint cytology, both of which have a high specificity[23]. Axillary node clearance can subsequently be performed if intra-operative examination of the node is positive for malignancy; thus avoiding the need for a second surgical procedure.

The introduction of SLNB has allowed focus examination of tumour biology within the sentinel node. The clinical role of immunohistochemistry (IHC) and polymerase chain reaction (PCR) in detecting micrometastatic disease remains however at an investigational stage[24].

Pathologic evaluation of sentinel lymph nodes on permanent sections (Role of serial sectioning (SS) and immunohistochemistry (IHC)): while SLNB has clearly established its status and has become the new standard of care in axillary staging of breast cancer, there seems to be little consistency in the pathologic procedures used by different laboratories in their evaluation. Lymph nodes were marked as sentinel or non-sentinel. A preliminary frozen section was performed on the sentinel and non-SLNs at the Mayo clinic. If the SLN was negative for tumour, the lymph node was formalin fixed and paraffin embedded and at least four additional levels were examined. Two levels were stained with standard haematoxyline and eosin (H&E) and an additional level stained with cytokeratin antibody, together with negative control. The SLNs removed at the university of Pennsylvania were formalin fixed, paraffin embedded and evaluated with H&E and immunohistochemistry. All non-SLNs were evaluated with standard H&E sections. In all cases, the size of the SLN was measured using an occulometer. A micrometastasis was defined as a tumour deposit of <2.0mm. A metastasis >2.0 mm was considered to be a macrometastasis. If multiple tumour deposits were present in the SLN, the sum of the tumour deposits was used to classify the metastasis as micro –or macrometastasis. In cases in which there was more than one SLN positive for tumour, the patient was grouped according to the largest size of metastasis. Primary tumour or re-excision specimens were evaluated by routine histology. Various studies have shown that

SLNB with examination of multiple serial sections(SS) and immunohistochemistry(IHC) greatly improves the sensitivity for identifying nodal metastatis especially micrometastasis (<0.2cm). It has been suggested that these more comprehensive methods of pathologic examination will find axillary lymph node metastasis in 7-42% of patients with breast carcinoma initially diagnosed as lymph node negative and that missed metastasis may be prognostically significant[25]. Vialo et al recommended sectioning the SLN entirely at close intervals[26].

As shown in Table-2, increasing the sectioning interval from 50 micrometer to 290 micrometer may miss as many as 17.7% of micrometastatic SLN.

A study by Intra et al showed that examination of SLN by serial sectioning and IHC increases the detection rate of metastasis from, 9-33% in infiltrating carcinoma[27]. A recent study at MD Anderson Cancer Centre by Chagper et al reported that 18% of initially node negative by H&E, sentinel nodes were converted to positive by additional examination of SS and performing IHC[28]. This is supported by other studies in which addition of IHC using cytokeratin antibodies AEI/3 and Pan CK increased the sensitivity of SLNB and converted about 10% of otherwise lymph node negative patient to lymph node positive[29]. Giuliano reported that 42.3% of SLN negative by H&E were positive by use of anti-cytokeratin antibodies, similar rates were reported by Reintgen and Krag et al[30].

Micrometastasis:

Lymph node metastasis in patient with breast carcinoma represent a broad spectrum of pathology findings ranging from gross disease, to H&E detected macrometastasis >2mm, to H&E and/or IHC detected micrometastasis <0.2mm, to single tumour cells found only by IHC. These gradations certainly reflect spectrum of prognostic significant[31]. At one extreme, in 2000, Rosser[32] and Carter et al[33] suggested that the micrometastasis are not biologic metastasis at all but rather the benign transport of breast epithelium by preoperative manipulation of breast and are devoid of clinical significance.

Veronesi et al[34] data showed that the sentinel lymph node involved by microfoci (<0.2mm) of cancer cells are associated with a considerable rate of metastatic involvement in the remaining axillary lymph nodes. They believe that the presence of microfoci in the SLN is an indication to perform a total ALND. The Memorial Sloan-Kettering Cancer Center has developed a nomogram to provide an accurate risk estimate using pathological characteristics of primary tumour such as tumour size, grade, presence of lymphovascular invasion, multifocality and estrogen receptor status together with SLN characteristics including size of metastasis, number of sentinel node positive and method of detection which may help in predicting non-sentinel node status after SLNB[35]. This nomogram has been validated by study from MD Anderson Cancer Center[36].

Factors affecting SLN Status:

SLNB has false negative rate of 0% to 1.4% reported in many studies. As a result many medical centres are now using SLNB without a completion ALND in patients who have negative SLN. Bass et al[37] described the lymphatic mapping experience at the H.Lee Moffitt Cancer centre and Research Institute from 1994-1999 in 1, 147 breast cancer patients and reported 0.83% false negative rate of SLN. The risk of false negative results is low and may be further reduced if multicentric and multifocal tumours are excluded. Memorial Sloan-Kettering Cancer Center in 2000[38] identified histological features of SLN positive cancers that allowed for the prediction of non-SLN metastasis at shown in Table-3. According to their study the most accurate prediction of non SLN metastasis arose from the combination of three variables significant in univariate analysis: tumour size, lymphovascular invasion, and size of SLN metastasis. The proportion of patients who have metastasis limited to the SLN can be predicted when there is a combination of tumour size <1.0cm, the absence of lymphovascular invasion (LVI), and micrometastatic disease (<0.2cm) in SLN. It has been shown by other studies too that the tumour size is directly related to the probability of axillary lymph node involvement[39]. For patients with large breast cancer, the role of SLNB is controversial. Early studies of SLNB in large breast cancer patients demonstrated a high (8-18%) false negative rate, with the accuracy worsening with the increasing size. Hill AD et al reported that the accuracy of SLNB appeared to diminish with the increasing size[40]. The accuracy was 100% with T1a,b and decreased to 82% in T2,T3. This inaccuracy might be caused by alternate lymphatic drainage pathways, or by the increased prevalence of axillary metastatis in patient with large tumour. The tumour size and the size of SLN metastasis alone, as reported by other investigators may not be the only predictors of further residual disease in the axilla. The amount of disease harbored by all the SLN as a whole, reflected by the number of positive SLN and the ratio of positive SLN to total SLN(s), should also be considered as an

indication of the amount of further disease that may be present in the rest of axillary basin. The presence of more than one positive SLN and /or a ratio of positive SLN(s) to total SLN(s) greater than 0.5 should alert the clinician to a significant possibility of further disease in axillary basin in patients with a positive SLN[41].

Role of SLNB in patients undergoing Neoadjuvant chemotherapy:

The increasing use of neoadjuvant chemotherapy (CT) in patients with breast cancer has added to the challenge of axillary staging in these patients. It has been reported that SLNB performed prior to neoadjuvant CT eliminates any chemotherapeutic effects on the technical aspects of lymphatic mapping such as sclerosing of lymphatics in response to chemotherapy in the lymph nodes. Obtaining accurate axillary basin information prior to initiation of neoadjuvant chemotherapy may have therapeutic as well as prognostic implications. Jones et al recommended SLNB before neoadjuvant CT in clinically node negative patients at presentation[42]. Their sentinel node identification rates were significantly better when mapping is performed before neoadjuvant CT compared to after completion of CT (100% Vs 80.6%); failure to map correlated with clinically positive nodal disease at presentation and residual disease at ALND. Among patients who mapped successfully after CT, the false negative rate was found to be high (11%).

The role of SLNB in prophylactic mastectomy (PM):

Indications for prophylactic mastectomy range from lobular carcinoma-in situ (LCIS) to a genetic test showing BRCA 1 or 2 mutation, cosmesis and cancer phobia. Occult cancer has been found in upto 5% of PM cases. Dupont EL et al consequently considered the potential expansion of the use of SLN biopsy in these cases and reported that the non-specific technique of peri-aerolar injection of mapping agents appears to be accurate and sensitive for the identification of sentinel lymph node of patients under going PM[43]. The lymph node mapping may eliminate the need for axillary dissection if the local disease is detected in the breast following prophylactic mastectomy.

Role of SLNB in clinically positive axillary nodes:

By current guidelines, clinically positive axillary nodes are a contraindication of SLNB; but clinical examination is falsely positive in a considerable proportion of patients with either moderately or highly suspicious findings and is by itself insufficient justification for axillary lymph node dissection. Its overall accuracy in various studies varies from 63-68%.

Follow up and survival analysis:

The follow up of patients after SLNB as for breast cancer patients in general, is for life. The rate of isolated axillary relapse after a negative SLNB is comparable to that after a conventional ALND 1% or less[44]. The long-term sequel of SLNB remains to be defined, especially the incidence of axillary recurrence. Previous studies also showed quiet infrequent(0% to 2.1% at follow up of 40-180 months) local recurrence after ALND. Given the low rate of local recurrence after ALND; many studies reported comparably good results in patients with a negative SLNB and no ALND with axillary local recurrence ranging from 0% to 1.4% at 14 to 46 months of follow up[45].

Although SLNB has recently been incorporated into TNM classification, the optimal histopathological work up of SLNs is currently not standardized. Validation trial done in 2005 on survival analysis following SLNB demonstrated its accuracy in staging early breast cancer. It was reported that patients with a positive SLNB result had a significant lower, five year disease free survival rate than patients with a negative SLNB result. This correlated well with established stage II & III survival information. In conclusion, SLNB is a successful method of staging breast cancer and should be part of the standard of care in this disease.

In summary, SLNB has become the standard of care in the surgical management of a large subset of breast cancer patients. With increasing experience of surgeons and by developing standard protocols by pathologists for handling and processing of these lymph nodes the false negative rates have gone down, sensitivity of identifying micrometastasis has improved greatly, which has made this procedure in the treatment of choice.

Table-I

Sentinel Lymph Node Biopsy Using Different Technqiques Weiser et al[3]

Method	SLN found (%)	Sensitivity	Accuracy
Isotope	92	93	97
Blue dye	78	91	97
Isotope+blue dye	89	97	99

Table-II

Relation of Sectioning Interval with Missed SLN Micrometastasis[23]

Sectioning interval(mm)	Missed micro-metastasis(%)	No. with non sentinel lymph node metastasis
110	5.3	1
170	8.8	0
230	12.4	2
290	17.7	3

Table-III

Correlation of Primary Tumor Size, Lympho-vascular Invasion (LVI) and SLN Meastasis Size with Non SLN Metastasis[3]

Number of Predictive Factors Present Tumor Size: <1.0cm, LVI negative, SLN metastases <0.2 cm	Sentinel Lymph Node Only Positive (% cases)
3	100
2	74
1	66
0	43

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Self-monitoring of Blood Glucose (SMBG): Cornerstone of Diabetes Management- Bangladesh Perspective: A Recommendation

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Summary:

SMBG is a crucial factor in diabetes management. It offers a quick check of glycemic status, helps to identify hypoglycemia and hyperglycemia. In addition SMBG assists in clinical decision making and as such it complements HbA1c. But due to many reasons SMBG is not practiced properly and adequately. In recent years several international guidelines higllighted the importance of SMBG for diabetes management. Very few diabetic patients in Bangladesh actually perform SMBG regularly at home. The awareness of the benefits of SMBG is also low. There is no uniformity in SMBG practice among the patients as there is no local guideline to help the physicians in determining the optimum SMBG frequency for their patients. So a working guideline on SMBG is the call of the day. This article is an attempt in that direction. Exploring international guidelines and evaluating their applicability in local context a number of recommendations have been proposed.

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Background

As one of the most common chronic diseases, diabetes mellitus (DM) has wide-ranging effects involving millions of people all over the world[1]. It is a major global public health problem that negatively impacts health status of the patients that is rapidly getting worse. After cancer and heart disease, Diabetes is the third leading cause of death[2]. Apart from individual suffering, diabetes also incurs huge health expenditure both for the patients and the society. Being a lifelong disease, it requires continuous monitoring and strict adherence to physician recommended treatment. In 2006, the General Assembly of the United Nations unanimously adopted a resolution (61/225) which recog-nizes that diabetes is a global pandemic posing a serious threat to global health, acknowledging it to be a chronic, debilitating, and costly disease associated with major complications[3]. Diabetic patients needs to modify their lifestyle for a better prognosis and must be involved in self-management of their disease.

Currently there are 382 million people suffering from diabetes worldwide, which is approximately 8.3% of the total adult population[4]. International Diabetes Federation predicts that by 2035 the number of people with diabetes will rise to 592 million, this equates to approximately three new cases every 10 seconds, or almost 10 million per year[4].Among all the cases of diabetes, about 10% are type 1 while the rest are type 2 DM[4]. Eighty percent of the people with diabetes are currently living in middle and low income countries, where the epidemic is rising at an alarming rate. About 175 million people with diabetes remain undiagnosed, progressing silently to macro vascular and micro vascular complications[4]. Around 5 million people in 2013 died of diabetes or related complications, that is one people in every six seconds.In South-East Asia the disease is growing fast, accounting for one-fifth of total cases worldwide[4]. People with diabetes in India, Bangladesh, and Sri Lanka make up 98.8% of the Region's total diabetes population. In 2013 there were 72.1 million cases of diabetes; by 2035 it is set to reach 123 million, a staggering 71% increase[4].

Bangladesh is a United Nations-designated least developedcountry (LDC) with a disproportionately high diabetes population[5.] Among all people living with diabetes in the 48 LDCs, more than one-third live in Bangladesh[5]. The national prevalence of diabetes is 5.52%with more than 12% of the adult population affected bydiabetes or Prediabetes[6]. Almost 50% of the population with diabetes is undiagnosed[6]. Among those with diabetes,only 1 in 3 people is treated, and roughly 1 in 4 achieves treatment targets[7].

The principal target of diabetes management is to bring down hyperglycemia to a level designated by international guideline. Numerous clinical studies showed reduction in diabetic complications as a result of improved blood glucose control[8]. Achievement and

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maintenance of glycemic goal helps to prevent or slow the progression to different complications of DM. All the existing diabetes management guidelines, e.g .of IDF, ADA, CDA, AACE emphasize on control of blood glucose, albeit there is a slight difference in their approaches to attainment of target glycemic level. Better implementation of these approaches is essential for the patients to understand and accomplish the desired glycemic target set out by these guidelines.

Health professionals working with diabetes and scientific societies concerned with evaluation of management strategies overwhelmingly agree that self-monitoring of blood glucose (SMBG) adds valuable information and complements the use of glycosylated hemoglobin (HbA_{1c})[9]. HbA_{1c} is an index of long term glycemic control and a useful predictor of microvascular, macrovascular and neurological complications of DM[10]. However, because HbA_{1c} is based on time-averaged result and does not provide real time feedback, it has limitations. In contrast, SMBG can distinguish between fasting, pre-prandial, and postprandial hyperglycemia; detect glycemic excursions; identify and monitor resolution of hypoglycemia; and provide immediate feedback to patients about the effect of food choices, activity, and medication on glycemic control. SMBG can also help to determine the effectiveness of the oral antidiabetic agents permitting better adjustment of the doses of these drugs than is possible with HbA_{1c}alone[11]. So SMBG is an indispensable component of diabetes management. Technology has made SMBG very easy and simple to perform. Educational and supportive programs with the use of SMBG based on principles of self-management have been advocated by clinicians and educators alike[12]. But this approach is often underutilized because of the nature of the procedure which may be perceived as distressing by many patients.

In type 1 diabetes and insulin treated type 2 diabetes, the utility of SMBG is irrefutable. However the frequency of SMBG in non-insulin treated type 2 diabetes is less intense[13, 14], although it has been demonstrated that SMBG may be associated with a healthier lifestyle and/or better disease management[15]. Regular and frequent SMBG also reduces HbA1c in T1DM and T2DM patients who are oninsulin therapy and improves control in T2DM patients receiving oral antidiabetic drugs. A number of international guidelines have been published specifically on SMBG, including IDF and ADA guidelines. Many countries, like Canada, Australia, India have all developed their own recommendations on SMBG on the basis these guidelines. As the timing and frequency of SMBG vary among them, a consensus statement on SMBG has also been advanced. However, there is still no uniformity in prescribing SMBG among physicians dealing with diabetes.

In Bangladesh the scenario is worse. There is no large scale population based study to assess the practice of SMBG. A study (DIABCARE) conducted in various branches of Diabetic Association revealed that the proportion of patients practicing home blood glucose monitoring was low at 31 (21.1%) [7]. Majority of patients 109 (77.9%) prefer blood glucose monitoring test done at the doctor's office only[16], even though World d Health Organization (WHO) strongly suggests that patients should continue blood glucose monitoring at home, keep the records and bring that to their physicians during consultation[13]. The condition of the rest of the country is most likely to be similar. The reason for the low utilization of SMBG cannot be exactly pinpointed. But it can be safely assumed that lack of awareness and motivation are important factors for such a poor SMBG practice. Many diabetic patients in Bangladesh are also uncomfortable with the idea of performing SMBG multiple times daily and may find it somewhat problematic to keep track of SMBG results in order to inform the physician about their blood glucose values in the subsequent visit. Patient reluctance also makes the some physician unwilling to prescribe

SMBG, based on the belief that their patients may not follow their advice.So there is a deficiency from the perspective of both the physician and the patients that lead to lack of proper SMBG practice as suggested by global recommendations.

Therefore a strong thrust is necessary to the direction of SMBG to make both physicians and patients aware of the importance of proper SMBG practice. There are several international recommendations but all of these may not be applicable for Bangladesh considering cultural and social differences. So it is imperative to adapt the global strategy in the local setting by appropriate modification of the published guidelines. A set of recommendations regarding SMBGin Bangladesh

must also reflect the fact that substantial disparity exist between actual and recommended frequency of SMBG testing[17]. A local SMBG guideline needs to incorporate these issues, bridge the gap between global and local practice of SMBG, addresses the barriers to SMBG testing and identify the most convenient frequency and timing of glucose monitoring for Diabetic patients.

Rationale for a local guideline on SMBG

Institutional measurement of blood glucose (fasting or post prandial), along with assessment of HbA_{1c} has been commonly used as the convenient means of evaluating glycemic control in patients with diabetes. However, clinic-based measurements of blood glucose may not offer an accurate picture of the glycemic pattern for a particular patient, since the settings under which the test is conducted are quite different from those prevailing at the patients home. Also, most of these tests are done in the morning hours, leaving clinicians none the wiser as to what happens to the glucose levels after the other two main meals of the day (lunch and dinner) [23]. Understanding the glycemic variability is crucial for the physicians in order to design treatment protocol for individual patients. Formal assessment of glycemic variability requires sophisticated methods like continuous glucose monitoring (CGM) which is not available in our country and may be difficult to implement in our existing management practice. A more practical solution is regular SMBG should give the clinician a general idea of the swings in blood glucose level in a particular patient. A number of observational studies support this claim[23-25].Therefore, incorporation of SMBG into the self-management regimen with an effective educational intervention can minimize the risk of complications in diabetic patients. Consequently, most diabetologists today recommend SMBG as part of the diabetes treatment plan to the majority of their patients.

There is clear evidence concerning the value of SMBG in diabetic patients treated with insulin[18-19]. However, in people with type 2 diabetes who are not taking insulin, the evidence is equivocal[20].McAndrew and colleagues[21]conducted a systematic review of relevant studies on the impact of SMBG on A1C levels in people with type 2 diabetes from 1990 to 2006 and found that evidence from the cross-sectional and longitudinal studies was inconclusive. On the contrary, a meta-analysis by Poolsup and colleagues[22] assessing the expediency of SMBG in individuals with type 2 diabetes demonstrated that SMBG was effective in reducing A1C levels in non-insulin-treated type 2 diabetes. Nevertheless, a global consensus conference on SMBG has found that this method is the best way for people with diabetes, as well as healthcare professionals (including diabetes educators), to assess the ongoing efficacy of all aspects of the diabetes management regimen, including, but not limited to, medication and patient behavior[23].

In Bangladesh physicians themselves usually play the role of diabetes educators for their patients. A national guideline on SMBG succinctly delineating role and practice of SMBG will immensely assist them in their desire to achieve improved quality of life for individual diabetic patients. Several clinical practice guideline committees around the world have made recommendations regarding SMBG. Although IDF has prepared and disseminated a global version of SMBG recommendations, many countries develop their own SMBG strategy applicable to their situation because the ground situation may be less than ideal to implement global guideline, so it needs to be modified. The same is true for Bangladesh where reality demands adaptation of the international standards of SMBG practice to conform prevalentstate of affairs. Based on the IDF, ADA recommendations and the statement of global consensus conference on SMBG, we in Bangladesh can develop our own guideline that will define the place of SMBG in diabetes care and its use within the existing health care infrastructure, in context of the social setting of our country. This will go a long way to greatly improve the health of diabetic patients from their current level, ensuring a better prognosis and longer complication free period.

So a national SMBG guideline in line with global standard is the need of the day. It is a prerequisite for management of diabetes, regardless of whether the patients use insulin or not, although the regularity and scheduling of SMBG is not identical for these two groups. A national agreement on SMBG practice will guide the physicians in preparing a management plan for their patients and to organize educational programs for them. Such a guideline is strongly linked to a patient-centric approach of care, the cornerstone of diabetes management.This will work to raise the current standard

of care in Bangladesh and guarantee that patients receive the treatment according to their clinical requirement.

International Guidelines: Summary

In general, these guidelines unanimously acknowledge the benefit of SMBG in individuals with type 1 diabetes using insulin. However, the guideline committees all noted that further study is needed in cases of type 2 diabetes patients on oral antidiabetic agents. Available literature provides no clear guidance due to differences in study designs, populations and interventions.

International Diabetes Federation (IDF)[24] recommended that SMBG should also be considered as part of ongoing diabetes self-management education to assist people with diabetes to better understand their disease and provide a means to actively and effectively participate in its control and treatment modifying behavioral and pharmacologic interventions as needed. SMBG should be used when individuals with diabetes and/or their healthcare providers have the knowledge, skills and willingness to incorporate SMBG and therapy adjustment into their care plan in order to attain agreed treatment goals. SMBG protocols (intensity and frequency) should be individualized to address each individual's specific educational/ behavioral/clinical requirements (identify/prevent/manage acute hyper- and hypoglycemia) and provider requirements for data on glycemic patterns and monitor impact of therapeutic decision making. The purpose(s) for performing SMBG should be agreed between the person with diabetes and the healthcare provider. These agreed upon purposes/ goals and actual review of SMBG data should be documented. An easy procedure for patients to regularly check on their glucose meter performance should be a requirement for SMBG use.

Various other guidelines are suggested by ADA[25] (American Diabetes Association), AACE[26] (American Association of Clinical Endocrinologists), NICE[27] (National Institute for Health and Clinical Excellence, UK), Canadian Diabetes Association[28], Australian Diabetes Association[29] for their own people.

In addition there is a global consensus statement on SMBG[30]. According to it SMBG is recommended 3-4 times daily

for patients at or above target receiving multiple daily insulin injections or using an insulin pump, more than 2 times daily for patients above target using insulin or oral agents or insulin plus oral agents, 2 times daily for patients at target managed with once daily insulin alone or oral agents alone. 1-2 times daily for patients at target managed with oral agents plus once daily insulin. Recommended frequencies should be varied for individual patients especially those not at glycaemic target or in the setting of other special clinical circumstances.

Recommendations:

Pre- and postprandial glucose targets of the patient should be selected by healthcare provider. Individuals with diabetes should attempt to achieve and maintain target blood glucose levels. Also Individuals with diabetes (and/or their care-givers) and their healthcare providers should cultivate the knowledge, skills and willingness to incorporate SMBG monitoring and analyzing data to identify patterns of glycemic excursions, assessing any influential factors, and implementing appropriate action(s);performing ongoing SMBG to assess the impact of any therapeutic changes made. SMBG should be considered at the time of diagnosis as well as part of ongoing self- management education to enhance the understanding of diabetes as part of individuals' education and to facilitate timely treatment initiation and titration optimization. The purpose(s) of performing SMBG and using SMBG data should be agreed between the person with dia-betes and the healthcare provider. Furthermore, with the availability of SMBG and glycated protein testing, routine laboratory blood glucose testing by health care providers should no longer be used to assess glycemic control except to supplement information obtained from other testing methods and to test the accuracy of SMBG. Comparisons between results from patient self-testing of blood glucose in the clinic and simultaneous laboratory testing are useful to assess the accuracy of patient results. An ongoing educational enterprise should be designed to reinforce the knowledge of SMBG use and test result interpretation by healthcare professionals. SMBG should also be integrated in the existing educational setup. Finally, urine glucose testing is not a replacement of SMBG and is restricted to those rare situations when there is no access to SMBG devices for testing.

Regarding frequency of SMBG, for patients receiving ≥3 insulin injections every day (MDI), 2-3 times daily

with full glucose profile on holiday i.e.Friday. Additionally they should check blood glucose prior to exercise, when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving. The frequency of testing may be increased on the basis of decision of the physician.For patients receiving only 1-2 insulin injections every day/ only oral antidiabetic medications/combination of both, SMBG should be performed 1-2 times daily (Appendix B).The frequency of testing may be increased on the basis of physician's discretion.Pregnant women with insulin-treated diabetes should check their blood glucose at least 3 times daily, pre meal SMBG on alternate days and 3 post meals in the intervening days.Diabetic patients treated with only lifestyle modification, SMBG should be conducted at least weekly.SMBG practices (intensity and frequency) should be adapted to each individual's specific edu¬cational/behavioural/clinical requirements (to identify/ prevent/manage acute hyper- and hypoglycaemia) and provider requirements for data on glycaemic patterns and to monitor impact of therapeutic decision making.Patients 'should preserve accounts of home blood glucose test results and convey these to the physician in the next visit.

Regarding testing procedure SMBG use requires an easy procedure for patients to regularly monitor the performance and accuracy of their glucose meter. Plasma calibrated meters provides more accurate results compared to non-plasma calibrated meters. Meters that provide average glucose profile along with pre and post prandial values are better.

Conclusion:

Diabetes is a significant and growing worldwide concern with potentially devastating consequences[4].Optimal management of glycaemia can reduce the risk of development and progression diabetic complications. Profiling of blood glucose through self-monitoring at various times of the day is therefore essential to get an overall picture of glycemic status of the individual. When used properly, SMBG provides a wealth of information regarding the blood sugar profile of the patient and helps in improving glycemic control by reducing hyperglycemic peaks and hypoglycemic troughs and by minimizing glycemic variability.

SMBG should always be considered as complementary to measurement of glycated hemoglobin. Each provides different information which is essential for designing better patient care. The optimal regimen for SMBG has to be individualized for the particular patient and is a function of many variables including personal preference and affordability. To derive maximal benefit from SMBG, the patient and clinician should work in tandem to analyze the information obtained and take action based on the information.

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Prolonged Fever in Adult Still's Disease – A Case Report and Review of Literature

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Summary:

Prolonged high fever is a common clinical problem and sometimes the diagnosis is difficult, management can be a challenge to the clinicians. Adult onset Still's Disease is a rare systemic inflammatory disorder of unknown etiology that is responsible for a significant proportion of cases of fever of unknown origin and can also have serious musculoskeletal sequelae. The disease presents as a diagnostic and therapeutic challenge to the clinicians and clinical guidelines are lacking. The emergence of classification criteria, discovery of better serological markers and the application of new biological agents may all provide the clinicians with significant tools for the diagnosis and management of this complex disorder.

Key words: Adult Still's Disease (ASD), Adult-onset Still's Disease (AOSD), arthritis, ferritin

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Introduction:

In 1897, George Still described a special form of arthritis in children, what is today called Still's disease. In Still's original description, he attempted to distinguish a form of chronic joint disease in children from rheumatoid arthritis in adults. The distinct features included pyrexia, splenomegaly and enlargement of lymph nodes. Still's did not describe the presence of rash, an important feature in the diagnosis of Still's disease today. The similar illnesses were found in adults and reported by many clinicians, some of which as undiagnosed fever or pyrexia of unknown origin. The first use of the term "adult Still's disease" was by Eric Bywaters, the eminent English Rheumatologist in 1966.[1]

Adult Still's disease (ASD) or adult-onset Still's disease (AOSD) is a rare, immune-mediated, multisystem inflammatory disorder of unknown etiology characterized by daily high spiking fever, evanescent rash and arthritis, frequently accompanied by sore throat, lymphadenopathy, splenomegaly and neutrophillic leucocytosis. It is frequently underdiagnosed and remains one of the main reasons for hospital admissions due to pyrexia of unknown origin.[2] The disease commonly affects young individuals between 16 and 35 years of age and male and female are affected equally.[3] The clinical picture is variable with mild to life threating courses. The disease is self-limiting, intermittently active or chronic.[4] Diagnosis is clinical and may be lengthy because it requires exclusion of infectious diseases, neoplasms including lymphoma and leukaemias, and autoimmune diseases. High serum ferritin levels associated with a low fraction of its glycosylated component are useful diagnostic and disease activity markers.[5]

Case Report:

A 22 - year old married female , short stature, housewife, low socioeconomic status, mother of a one year child, from a rural area of Bangladesh, was admitted into our female medical ward with history of high intermittent fever with chills and rigor, polyarthralgia, sore throat, bodyache and weight loss for 3 months. The fever was high spiking, 103 degree F or above, rose rapidly in the evening and then subsided to or near normal by several hours or the next morning (Fig.-1a). In some days, two fever spikes were noticed. Her sore throat was described as a severe, constant burning pain in the area around pharynx, more prominent during febrile period. Physical examination showed an emaciated (weight-29 kg), toxic girl with moderate anemia, no skin rashes, swollen and tender both wrists, left ankle joint, cervical

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Fig.-1: *Photograph of the Patient*

lymphadenopathy , mildly enlarged non-tender liver and splenomegaly.Cardiovascular and respiratory system examination revealed normal findings. Deep cervical lymph nodes in the left anterior triangle of the neck were palpable, 3 in number, size 1 – 2 cm in diameter, soft in consistency, non tender, freely mobile and not fixed to underlying structures or overlying skin. During her long febrile period, she was treated with phenoxymethylpenicillin, levofloxacin, doxycycline, cefixime, antimalarial drugs before hospital admission without any benefits. Her laboratory investigations were as follows : Complete blood count & peripheral blood film - Hb 9.3 gm/dl , ESR 106 mm/1st hour , RBC-3.81million/cumm, MCV-74fl, MCH- 24pg , WBC-30,000/cumm (Neutrophil - 87% , L -11%, M - 2% E - 0%) , Platelet – 487,000/cumm , Malaria parasite - not found ; Widal Test - T O – 1:80, T H – 1:80, A O – 1:40, A H-1:40, B O- 1:40, B H- 1:40, and after 2 weeks, no rising titre ; blood culture twice yielded no growth of any bacteria, ASO Titre - 107 IU/ml , S. Creatinine - 0.85 mg/dl , Random blood sugar - 6.2 mmol/L; Urinalysis - normal ; Urine Culture repeatedly - no growth. X-ray chest, ECG and transthoracic echocardiography showed normal findings. Abdominal ultrasound revealed normal findings except mild hepatosplenomegaly. Following hospital admission, she was treated empirically with quinine and then ceftriaxon without any improvement. As the patient was not recovering, she was further investigated, some investigations were repeated and the results were as follows : Complete blood count - Hb 8.6gm/dl , ESR 108 mm/1st hour , WBC -26,000/cumm (N -82%, L-16%, M - 01%, E - 01%) ; R A Test – negative, ANA - negative , Anti CCP - negative , CRP - 76 mg/L , VDRL – nonreactive, Tuberculin Test - 05 mm, S. Ferritin - 2400 ng/ml(highly elevated), S Bilirubin-0.4 mg/dl , S. ALT- 26U/L, Urinalysis – normal , S. Fibrinogen- 394 mg/dl , X-ray chest and paranasal sinuses - normal. Serum protein and haemoglobin electrophoresis, bone marrow aspiration was under plan and waiting. Infectious and neoplastic causes of her illnesses were tried to be ruled out by a thorough clinical and laboratory reports evaluation.

Literatures were reviewed and a diagnosis of Adult onset Still's Disease(AOSD) was made considering Yamaguchi criteria.[6] Tablet prednisolone(1mg/kg/day) and methotrexate(7.5mg weekly) orally were started. Her condition was dramatically improved. She became afebrile (Fig.-1b), appetite and general condition improved.

Subsequent investigations after 6 weeks showed the following : CBC Hb-10.2g/dl, WBC-14000/cumm(N-70%, L-25%,M-4%, E- 1%) , ESR-15mm in 1st hour, CRP- 6 mg/L .

Follow up visit after 6 month : Healthy smiling girl with mildly tender both wrists with slightly restricted

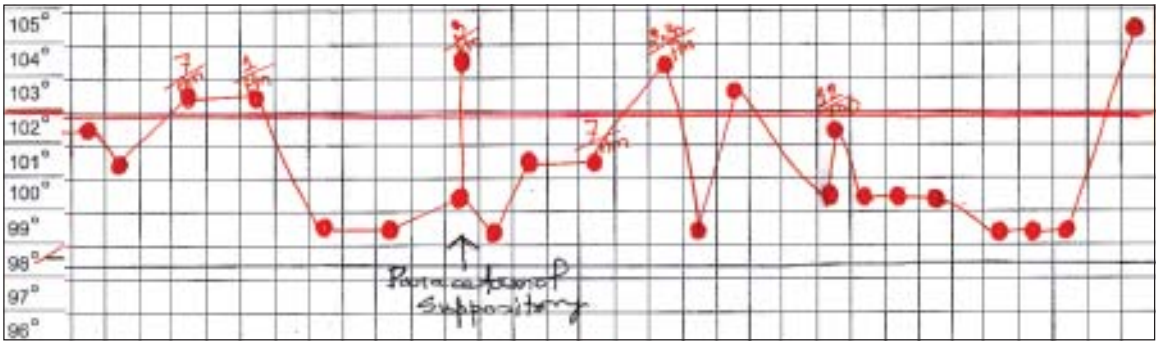

Fig.-2(a): *Daily high spiking fever recorded (some part) in this patient.*

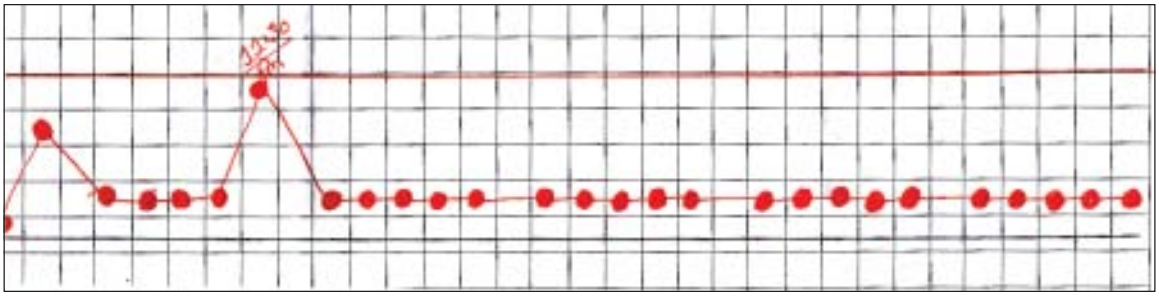

Fig.-2(b): *The fever subsided after the start of corticosteroid treatment.*

movements; regularly taking methotrxtate 7.5mg weekly orally and laboratory investigations as Hb 11.1g/dl, ESR 20 mm in1st hour, CRP 6 mg/L , S. Ferritin - 11.5ng/ml.

Follow up visit after 2 years : Reasonably good health but mild tenderness involving both wrists on passive movement, no fever and no other symptoms, CBC- Hb-12.7g/dl, WBC- 13660/cumm (N-70%, L- 24%, M-06%), ESR- 10mm in 1st hour, CRP – 3mg/L, ANA-Negative, S. Ferritin- 18.2ng/L.

Discussion:

Data on diagnosis and treatment of Adult Still's Disease are limited in medical literature and consists of mainly case reports, small series and some retrospective studies; current knowledge is largely descriptive. Diagnosis is clinical and requires exclusion of infectious, neoplastic and connective tissue diseases. Laboratory tests are nonspecific and show increased immunological response.[3,7,8] There is a speculation that the disease has features of nonnecrotising immune complex vasculitis.[1] The disease occurs throughout the world, typically affects 16- 35 years old and presents with fever, arthralgia, and sore throat, and skin rash. The fever is typically high and spiking, usually quotidian and occasionally double quotidian. The spike occurs in the late afternoon or evening. The duration of fever is typically brief, and the temperature falls rapidly.[3, 9]

The majority of the patients with AOSD have arthralgia and arthritis, with incidences ranging from 64% to 100%. Joints affected most frequently are the knees, wrists, ankles, although involvement of elbow, shoulder and small joints of hands are also described. Usually, several joints are involved at the same time. Often, patients have morning stiffness of joints that lasts for several hours.[3, 10]

The rash is perhaps the most helpful feature in the diagnosis of Still's disease, especially when present in association with high fever and arthralgia. It is predominantly a truncal rash but can spread to the arms and legs including the palms and soles, but usually does not involve the face. The typical eruption is a salmon-pink macular or maculopapular rash beginning as small macules that may coalesce; the rash usually is not pruritic, evanescent and may be missed. Patients may not notice it.[1,11-13] We did not notice any skin rash in this patient, probably because of black complexion.

Diagnosis of Adult Still's Disease

There is no single diagnostic test for Adult Still's disease and the diagnosis is clinical and not based on serology. Response to empirical corticosteroid therapy generally helps in diagnosis.[11] Laboratory investigations reveals high WBC count with neutrophilic leukocytosis , raised ESR, high CRP, very high ferritin, high level of AST, ALT and Fibrinogen reflecting systemic inflammation. Rheumatoid factor (RF) and antinuclear antibody (ANA) are classically negative.[3,14]

Recently, serum ferritin and glycosylated ferritin have received a lot of attention as diagnostic and disease activity marker. The glycosylated fraction of ferritin is a more specific marker of AOSD than ferritin itself. In this patient, glycosylated ferritin was not estimated due to unavailability. In healthy subjects, 50-80% of ferritin is glycosylated; in inflammatory diseases, 20 – 50% of ferritin is glycosylated and in AOSD, less than 20% is glycosylated.[3,15] Cytokines, such as interleukin(IL)-1, IL-6, interferon(IFN)-gamma, and tumor necrosis factor-alpha, are elevated in patients with AOSD.[16]

At least 7 sets of classification criteria have been devised; of which Yamaguchi, Cush and Fautrel criteria are important. However, the Yamaguchi criteria have

the highest sensitivity. Diagnosis requires at least 5 criteria, with at least 2 of these being major diagnostic criteria.[3]

Major criteria

- Fever of at least 39 degree centigrade for at least one week
- Arthralgia or arthritis for at least two weeks
- Nonpruritic salmon colored rash (usually over trunk or extremities while febrile)
- Leukocytosis (10000/microL or greater), with granulocyte predominance

Minor criteria

- Sore throat
- Lymphadenopathy
- Hepatomegaly or splenomegaly
- Abnormal liver function tests
- Negative tests for antinuclear antibody and rheumatoid factor

Exclusion criteria

- Infection
- Malignancies
- Other rheumatic diseases

The reported case had almost all the features of Yamaguchi criteria. Skin rash was not obvious, probably because of black complexion. So, a diagnosis of Adult onset Still's Disease was made.

Treatment of AOSD includes NSAID, corticosteroids, immunosuppressive drugs and biological agents. Immunosuppressants including methotrexate, gold, azathioprine, cyclosporine, leflunomide, tcrolimus, and cyclophosphamide; along with intravenous immunoglobin are tried. Biological agents or anticytokines (e.g. anti-TNF-alpha, anti-IL-1, anti-IL-6) have been successfully used in refractory cases.[2, 16-18] We treated the patient with NSAID, corticosteroids and methotrexate with satisfactory response.

The clinical course of AOSD can be divided into three main patterns with different prognosis : self-limited or monophasic, intermittent or polycyclic systemic and chronic articular pattern. The reported case seems to be chronic articular pattern. AOSD, though not common, can be from milder form of disease to a life threatening condition.[19-21]

Macrophage-activation syndrome (MAS) is a severe, potentially life threatening complication, associated with Adult-onset Still's disease. The hallmark clinical and laboratory features include high fever, hepatosplenomegaly, lymphadenopathy, pancytopenia, liver dysfunction, disseminated intravascular coagulation, hypofibrinogenamia, hyperferritinaemia and hypertriglyceridaemia. The condition is triggered by a viral infection or a medication. Despite marked systemic inflammation, ESR is depressed because of low fibrinogen level.[22, 23, 24] Occasionally, AOSD may be complicated by thrombotic thorombocytopenic purpura and haemolytic uraemic syndrome.[25]

Conclusion:

Adult onset Still's disease (AOSD) is a rare systemic inflammatory disorder of unknown etiology and pathogenesis, usually presenting with high spiking fever accompanied by systemic manifestations. It is hypothesized that it may be a reactive syndrome where various infectious agents may act as disease triggers in a genetically predisposed host. The suggested etiologies, clinical manifestations and prognoses are diverse. There is no single diagnostic test for AOSD; rather, the diagnosis is based on a set of criteria, the most important of which are indeed clinical. Treatment aims at both minimizing inflammation and halting disease progression. Non-steroidal anti-inflammatory drugs (NSAID), glucocorticoids and disease modifying antirheumatic drugs (DMARD) are used. Novel therapeutic approaches, such as anti-tumor necrosis factor blockade and stem cell transplantation, monoclonal antibodies, may be effective.

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Angiomyxoma Presenting as an Unusual Vaginal Mass

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Summary:

Angiomyxoma is a rare tumour which arises from pelvis. A case of an Angiomyxoma of vagina in a 35year old lady is reported. The patient was presented with a mass about 7×8 cm coming down through introitus and urinary discomfort. Mass was dissected out and Histopathological examination revealed angiomyxoma. Though it is a rare tumour it is clinically misdiagnosed with vaginal polyp, vaginal cyst or inversion of uterus.

(J Banagladesh Coll Phys Surg 2014; 32: 229-230)

Introduction:

Angiomyxoma is a rare slow growing and soft and benign tumour that predominantly affects in the perineum of women in reproductive age.[1]It can be mistaken both clinically and microscopically for several other conditions. Here we report a rare case of aggressive anxiomyxomawhich was present in Faridpur Medical College Hospital,Faridpur, Bangladesh.

Case Report:

A 35 years old lady presented in Gynaecology outpatient department with the complaints of a mass in introitusand something coming down per vagina for 5-6 months. She also noticed burning sensation and difficulty in passing urine for last few days. Patient was dumb, separated from husband and poor lady. The mass was gradually increasing in size and attain a big size within six months with a pressure sensation in introitus. When she developed unbearable complication her relatives brought her in hospital. She had one child, age about 17years. On examination there was a mass about 7×8×8 cmprotruding through introitus, which was soft and irregular consistency but with a shiny smooth surface. It was neither uterus, nor a polyp and could not reducible,but it was pushed into introitus manually. USGshows a small myoma in uterus and a growth of about 7×8 cm, but the origin of mass could not mentioned. As there was urinary complication Intravenous urography was done. It shows filling defect in urinary bladder due to pressure effect of the mass. As it was not certain about the origin of the mass, at first laparotomy and total abdominal hysterectomy was done. While opening the vault a fairly big mass could palpated seems to originate from vagina. Then the mass was removed per vaginal route by giving incision on anterior vaginal wall. It was non capsulated, solid nodular lobulated yellow-bluish lipoma like structure. Histopathological report revealed the mass as anxiomyxoma.

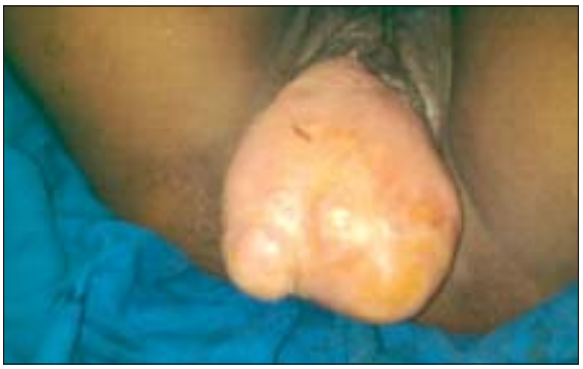

Fig.-1: *Unusual mass protruding through introitus.(Printed with permission)*

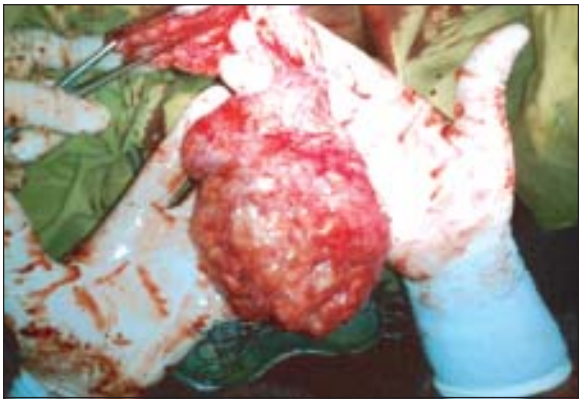

Fig.-2: *Mass during dissection*

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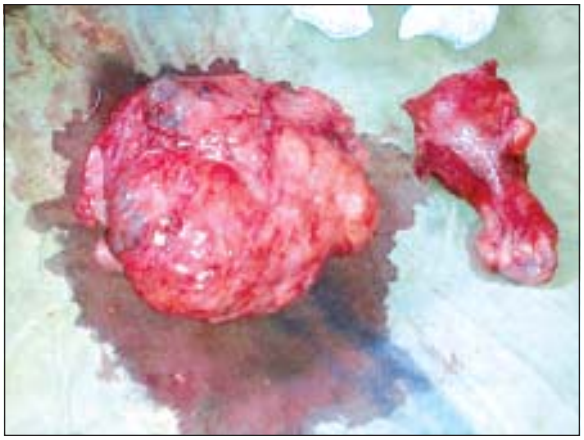

Fig.-3: *Massand the uterus after hysterectomy*

Discussion:

Anxiomyxoma is an uncommon tumour which predominantly grows in pelvic and perineal region in female[2]. The age distribution is wide and peak incidence is at 31-35years. Male to female ratio is 6:1[1]. These large sized tumours areslow growing and painless. The presenting features are nonspecific. It may present as a palpable mass or heaviness and discomfort in lowerabdomen or vulva[3]. It may be clinically misdiagnosed as inguinal hernia or a bartholin cyst, cervical polyp, vaginal polyp, myxoma, lipoma, vulval mass, Gartner's duct cyst or vaginal prolapsed.[4]. The term "aggressive anxiomyxoma" was designated to the neoplasm to emphasize the neoplastic nature of the blood vessels and its tendency to be locally aggressive and recur after treatment. Recurrence rates up to 70% have been reported. So long term follow-up of the patient is necessary.[5].

The patient had difficulty in urination which is a common symptom in urinary tract infection. When a female patient come with such symptom a detailed history and examination is necessary. A simple pelvic examination may reveal the cause ofdysuria in some case.Physical examination including specular examination of the vagina and urethra may reveal causes of dysuria that are not related to urinary tract infections [6].

Because of its propensity to occur in female patients during reproductive years, it is possible that aggressive angiomyxoma is a hormonally responsive neoplasm.[7].Surgical excision is the treatment of choice in most of the times.In some cases removal of the tumour is difficult due to local infiltration and adjuvant therapy may be used. Treatment options include use of hormonal manipulation, such as tamoxifen, raloxifen or GnRH analogs, radiotherapy and arterial embolisation.[6].

It often recurs and there is no correlation between the size of the tumors and the chance of recurrence.The tumor has widely been known that have no potential to metastasize. But some recent reports arecontrary to this knowledge.[8]

Conclusion:

Anxiomyxoma is a benign mesenchymal tumor occurring in young females of reproductive age. The patient may present with alump or urinary symptom which should be carefully evaluated. Medical history, physical examination and finally histopathological examination can help the diagnosis of the condition.

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Systemic Lupus Erythematosus Simulating Kikuchi Fujimoto's Disease: A Case Report

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Summary:

Kikuchi Fujimoto's disease (KFD) is a rare, immune-mediated, self-limiting disorder with unique histopathological features. KFD is usually seen in young Asian females; however, cases have been reported throughout the world and in all ethnicities. It has been recognized that there is a rare association between Systemic Lupus Erythematosus (SLE) and KFD via sporadic case reports. The exact pathophysiological relationship between these two diseases is still unclear. We report a case of a young Asian female who presented with persistent fever followed by development of lymphadenopathy and was diagnosed as Kikuchi Fujimoto's disease based on lymph node biopsy. Although an SLE workup was done and she initially did not meet the American Rheumatology Association (ARA) diagnostic criteria for lupus.The lymph node biopsy did not show typical features of SLE. At last criteria of SLE became obvious with time and case was diagnosed as SLE.

Key words: Kikuchi-Fujimoto, Lymphadenopathy, Pyrexia, SLE.

(J Banagladesh Coll Phys Surg 2014; 32: 231-234)

Introduction:

To the clinician, systemic lupus erythematosus is important as because it is potentially fatal disease that is easily confused with many other disorders. Pathogenic antibodies are produced against the components of the cell nucleus. The abnormal immune response results in target tissue injury, and the ensuing inflammatory reaction deranges various organ functions. Nearly every organ system may be involved in the disease course. It may present initially with non-specific symptoms or atypical manifestations, so the diagnosis may present a considerable challenge at the early stages[1-3].On the other hand, Kikuchi Fujimoto's disease (KFD) is a rare, immune-mediated, typically self-limiting disease first described in Japan in 1972 [4, 5]. Clinically, patients present with persistent fever and lymphadenopathy which may be painful; cervical lymph nodes are most commonly involved. Other symptoms such as fatigue, night sweats, nausea and vomiting, weight loss, arthralgia, and a variety of cutaneous lesions are also reported[6, 7]. Laboratory findings are nonspecific including elevated erythrocyte sedimentation rate (ESR), neutropenia, lymphocytosis, mildly elevated transaminase, and elevated lactate dehydrogenase (LDH) [6-8].Diagnosis is made via lymph node biopsy with a histopathological finding characterized by a histiocytic necrotizing lymphadenitis without granulocytic infiltrate[6]. The association of KFD and SLE is described in some studies [9, 10]. It is also speculated that KFD may be one of the manifestations of SLE[10]. Here we are presenting a case where we got dilemma initially between kikuchi's disease and SLE.

Case Report:

A 23 years female medical student of Dhaka Medical College, presented with high grade continued fever for 6 days .There was no focal symptom except mild headache and anorexia. On query, she did not give any history of travel to any malaria endemic zone, contact with tuberculosis patient and exposure to any medication. On general examination her temperature 102°F, pulse 114/minute, blood pressure 80/60 mm of Hg and mild anemia was present. On systemic examination there was nothing significant. She was admitted to Dhaka Medical College Hospital with

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suspicion of possible viral fever. Some investigations were sent immediately. Patient was admitted to hospital with advice to take plenty of fluid intake and Tab.Paracetamol 500 mg three times daily.

On next day, her investigations reports were S. ALT- 45 U/L, S. AST- 90 U/L. Complete blood count reveals hemoglobin- 10gm/dl, total count of white blood cell- $10.6\times10^3/mm^3$, ESR 100 mm in 1st hour, N- 74%, L-21%, E-0.4%. Dengue NS1 antigen was also negative. Other investigations were within normal limit.

On 4th day of her admission, there was no sign of remission of fever. Meticulous physical examination was done and there was nothing significant. Empirically Inj. Ceftriaxon 2 gm twice daily was started. Spiking fever and constitutional symptoms persisted. On 10th day, we started Inj. Meropenem 1 gm three times daily keeping Ceftriaxon 2 gm twice daily continued. On 11th day of her admission, detailed examination done again. This time few palpable lymph nodes were present in the anterior and posterior cervical chain, left supra clavicle region and also bilateral inguinal region. Lymph nodes were discrete, tender, free from underlying and overlying structure and largest one was 1.5×1.5 centimeter in left anterior cervical chain. We started a third antibiotic with Moxifloxacin 400 mg through intravenous route daily as her fever was not responding to previous regime. Some investigations were sent from day 9 to day11.

Reports of investigations were as follows, Hb- 7.9 gm/dl, total count- $3.4610^3/mm^3$, N-84%, L-15%, M-0.6%, platelet count- $14610^3/mm^3$, ESR-100 mm in 1st hour, CRP-23.7 mg/L and peripheral blood film revealed normocytic normochromic anemia with moderate rolouex formation. Blood for malarial parasite and triple antigen were negative. Urine R/M/E and C/S were also normal. Mantoux test result after 72 hours was 4mm. Ultrasonography of whole abdomen revealed mild hepatomegaly, cholelithiasis, enlarged ovaries but no ascites and pleural effusion. FNAC of left supraclavicular lymph node revealed focal aggregation of epithelioid cells. Background shows neutrophil,lymphocyte. No malignancy seen. Features suggestive of granulomatous inflammation (Fig-1). ANA (Indirect immunofluresence on He-2 ell) showed strongly positive, pattern- Speckled variety. Serum ferritin was 5689.09 µgm/L.

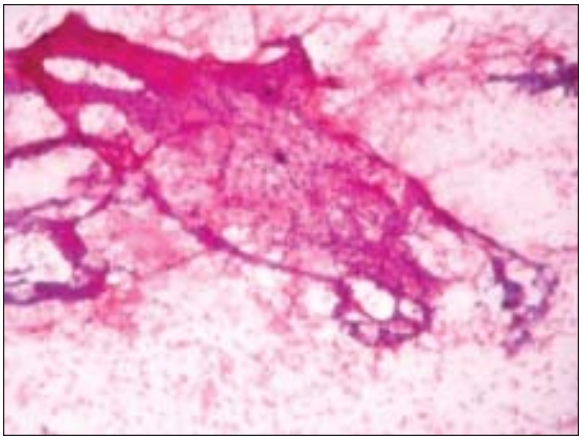

Fig.-1: *FNAC of Lymph Node showing granulomatous inflammation.*

We started category one anti TB regimen on the background of fever, lymphadenopathy, high TB prevalence in this subcontinent and finding of lymph node FNAC. We stopped Ceftriaxon. Still fever didn't respond and on the very next day fever was 106°F. On 14th day of her admission, CT scan of whole abdomen revealed mild hepatomegaly, cholelithasis, bilateral mild pleural effusion, bilateral basal consolidation and no ascites, (Fig-2). On next day, test result of RA was negative but anti ds DNA antibody was positive with titre of 129.5U/mL.

On 16th day of her admission, Coomb's test result was negative. Biopsy of left cervical lymph node revealed acute necrotizing lymphadenopathy (Kikuchi's disease). Later on we reviewed the slide and it showed massive

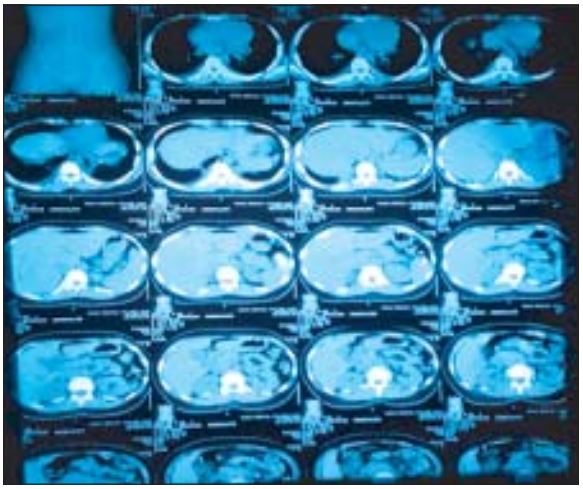

Fig.-2: *CT showing bilateral pleural effusion, Hepatomegaly, basal consolidation*

apoptosis with accumulation of histiocytes, polymorphs were absent. No haematoxylin body was seen. No granuloma or malignancy was seen either. Diagnosis of histopathology report was necrotizing lymphadenopathy and differntial diagnosis was SLE lymph adenitis. (Fig-3) Complement C3, C4 and repeat urine R/M/E was normal. Repeat complete blood count showed, Hb- 8.4 gm/dl, total count of WBC- $410^3/mm^3$, N-70%, L-20%, M-8%, E-2%, platelet count- $22010^3/mm^3$ and ESR-100 mm in 1st hour . Serum lactate dehydrogenase was 426U/L.

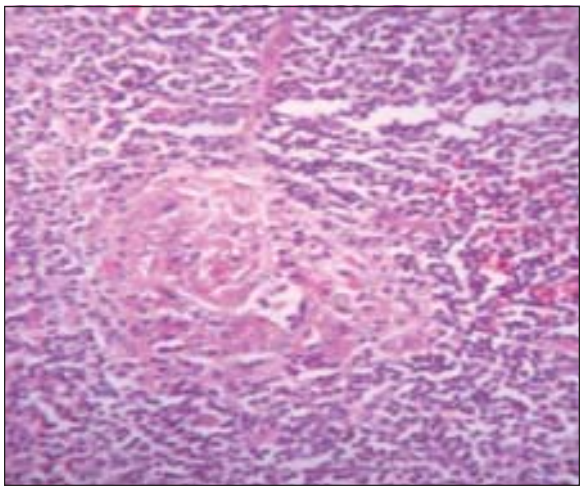

Fig-3: *LN biopsy showing apoptotic necrosis.*

Systemic steroid 1mg/kg body weight with supportive treatment was started on day 20 and within 48 hours complete remission of fever occurred. Tapering of steroid was started after 2 weeks of commencement. Patient responded quickly. We discharged the patient with advised to follow up regularly. Follow up visit at 3rd and 6th week revealed marked clinical improvement. January 2014, she developed typical butterfly rashes on the face over the cheek, nasal bridge, sparing the nasolabial fold that are fixed, erythematous, some are flat, some are raised that are aggravated on exposure to sunlight. Also erythematous rash present over the chin. Steroid was adjusted and patient responded partially with treatment. With above regimen, we added Tab.Hydroxycholoroquine 200 mg twice daily. Then dose was adjusted accordingly. Now patient is on systemic steroid (7.5 mg) in every alternate day and hydroxychloroquine (100mg), 12 hourly. With this treatment her rashes almost disappear and she performs her daily activity normally.

Discussion:

KFD is a rare but recognized cause of pyrexia and lymphadenopathy of an unknown origin. Based on a study done by Kucukardali et al. in 2007, 330 cases of KFD were reported in the Medline database; among those, 77% were females with a mean age of 25, and 70% of patients were under age of 30. Asia had the most reported cases followed by Europe and America. The most common symptoms were persistent fever (35%) and lymphadenopathy (100%). High sedimentation rate (40%), leucopenia (43%), anaemia (23%) is also observed in a majority of patients, and positive ANA has also been reported in KFD patients[6]. On the other hand SLE also present with pyrexia of unknown origin and lymphadenopathy. In our case, empirical antibiotic was given as a presumptive undetermined infection. Clinically, tuberculous lymphadenitis always remains a major differential diagnosis, especially in developing countries like Bangladesh. So subsequently, when we got granulomatous inflammation on FNAC of left supraclavicular lymph node, we started empirical anti TB therapy although the cytology revealed no caseous necrosis.

Histologically, SLE and KFD can be very challenging to differentiate and at times impossible. In KFD, histopathological findings include varying degrees of necrosis, histiocytic proliferation with activated T lymphocytes, small lymphocytes and plasma cells without granulomatous inflammation with absent neutrophils and eosinophils[11] . Adjacent vessels may be thrombosed. In contrast to KFD, SLE lymphadenitis demonstrates hematoxylin bodies (aggregates of degenerated nuclear debris), Azzopardi phenomenon (degenerated nuclear material aggregated in the walls of blood vessels), abundant plasma cells, prominent reactive follicular hyper-plasia, sparse cytotoxic T cells and capsular and pericapsular inflammation[11,12]. In our patient's biopsy specimens, massive apoptosis with accumulation of histiocyte, absence of polymorphs, granulomas and malignancy or hematoxylin bodies support the diagnosis of KFD rather than SLE. But these striking features might not be identified in every case of SLE associated lymphadenitis, however, and the diagnosis cannot always be ruled out on histological grounds alone[13]. Imamura and coworkers[14] hypothesized that KFD might reflect a self limited SLE-like autoimmune condition induced by virus infected

transformed lymphocytes. Yet the results of serologic studies testing antinuclear antibodies, rheumatoid factor, and other immunologic parameters consistently have been negative in these patients [15].

The clinical and immunological features required for diagnosis of SLE are well documented and specific. Our case fulfilled four out of the eleven ARA criteria, compatible with the diagnosis of SLE having two episodes of lymphopenia (<1500/mm³), highly positive ANA, anti ds DNA antibody and bilateral pleural effusion. Though there was bilateral basal consolidation on CT chest, it can be explained with SLE as a feature of bronchopneumonia.

Conclusion: Although the incidence of Kikuchi-Fujimoto disease is rare, this disorder must be considered among the differential diagnosis when a young female patient present with fever and cervical lymphadenopathy. Clinically Kikuchi's disease may mimic systemic lupus erythomatosus. Therefore a careful histopathological examination and concomitant immunological investigations are necessary in arriving at diagnosis.

Acknowledgement:
Conflicts of Interest: None declared

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Correction of Skeletal Discrepancy and Facial Aesthetics by Combination of Orthodontic Management and Orthognathic Surgery

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Summary:

Clinical management of non-growing adult patients with dentofacial deformity could be provided with better outcome when approach in-combined with orthodontic and orthognathic surgery than that of single approach alone. This study describes a case of a 26years old Bangladeshi female presented with bimaxillary protrusion treated with the combination of orthodontic and orthognathic surgery.

(J Banagladesh Coll Phys Surg 2014; 32: 235-240)

Introduction:

A bimaxillary protrusion is a condition in which the maxillary and the mandibular incisor teeth protrude severely so that the lips cannot be closed together. The condition is usually considered as an Angle Class I malocclusion,[1] and the anterior teeth are well aligned. However, it sometimes shows either mild crowding or spacing or mild vertical discrepancies ranging from an open bite to a deep bite.[2] The majority of patients who suffer from this condition seek treatment more for the enhancement of facial esthetics than for dental esthetics and function.[3] Facial esthetic problems related to bimaxillary protrusion include extreme protrusion of the anterior teeth, lip incompetence, and strain with hypermentalis action on closure, thick looking lips with an everted vermilion border, and a toothy appearance due to an apparent chin deficiency.[2] This convex profile is found predominantly in Africans and Asian adults including the Chinese, the Japanese and in Caucasians.[4]

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Orthodontic management of bimaxillary protrusion cases usually involving additional anchorage control using trans-palatal bar, reverse pull headgear, and more recently mini-implant.[5,6] However treatment time duration of more than years requires depending upon the severity of malocclusion.[7] So in present case it was planned for a combination of orthodontic and orthongathic surgery to get a more predictable outcome within a short time duration. Pre-surgical orthodontics and postsurgical orthodontic management and orthognathic surgery with extraction of all permanent first premolar, a maxillary anterior segmental osteotomy and a mandibular anterior subapical osteotomy was planned for. Individual orthodontic management or orthognathic surgical management to correct skeletal discrepancy and to improve facial aesthetic has been reported in the literature.[8] However combination of multidisciplinary involvement to manage such case in Bangladesh previously was not revealed in literature review. Therefore the aim of this case study is to reveal the treatment outcome of a combined orthodontic and surgical management of a Bangladeshi female with skeletal discrepancy.

Report of the Case:

A 26 years old unmarried female from Narsingdi reported to a private dental practice office in Dhaka with complain of ill-facial appearance due to unattractive smile by over exposure of gum and teeth while laughing (Figure 1 A,B). Her parents were also seeking short duration treatment as they need to settle their daughter's marriage as she already became over age for settlement (according to their opinion). Her past medical, dental and developmental history did not revealed any trauma or temporo-mandibular joint

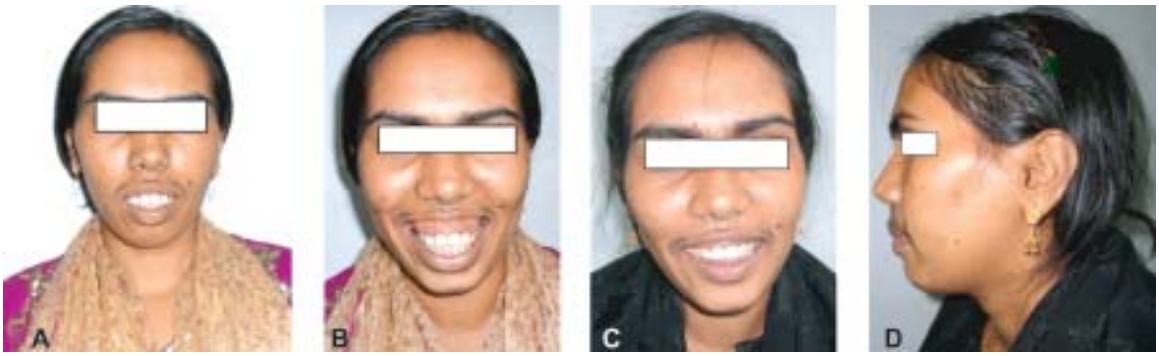

Fig.-1: *Extra oral photograph demonstrate patients pretreatment anterior lip seal in resting conditions (A), lip, teeth and gingival position during smile (B); post treatment lip & teeth position (C) and post-treatment improved facial profile(D).*

disorder, no evidence of abnormal development due to hormonal influence, no protruding tongue thrusting, no abnormal swallowing pattern, no remarkable history of improper oral habits like thumb sucking, nail or pencil biting. However, her enlarge palatine tonsil, with relevant a mouth breathing pattern were noted which could be a contributory factor for developing protruded maxillary and mandibular anterior alveolar process.

On extra-oral facial form and lateral face profile examination, convex facial profile with protruding lips, exposure of upper teeth and gingiva noticed in resting condition. Smile analysis shows excessive exposure of upper and lower gingiva and teeth, beyond the lower border of upper lip and upper border of the lower lip causing the distortion of smile arc which ultimately resulting ill facial appearance during smiling and laughing (Figure 1 A,B). Intra-oral examinations reveal carious both upper second molar teeth, badly broken lower left second molar(37), third molar(38) and right second molar(47) teeth (Figure 2 A,C,F,G,I) with

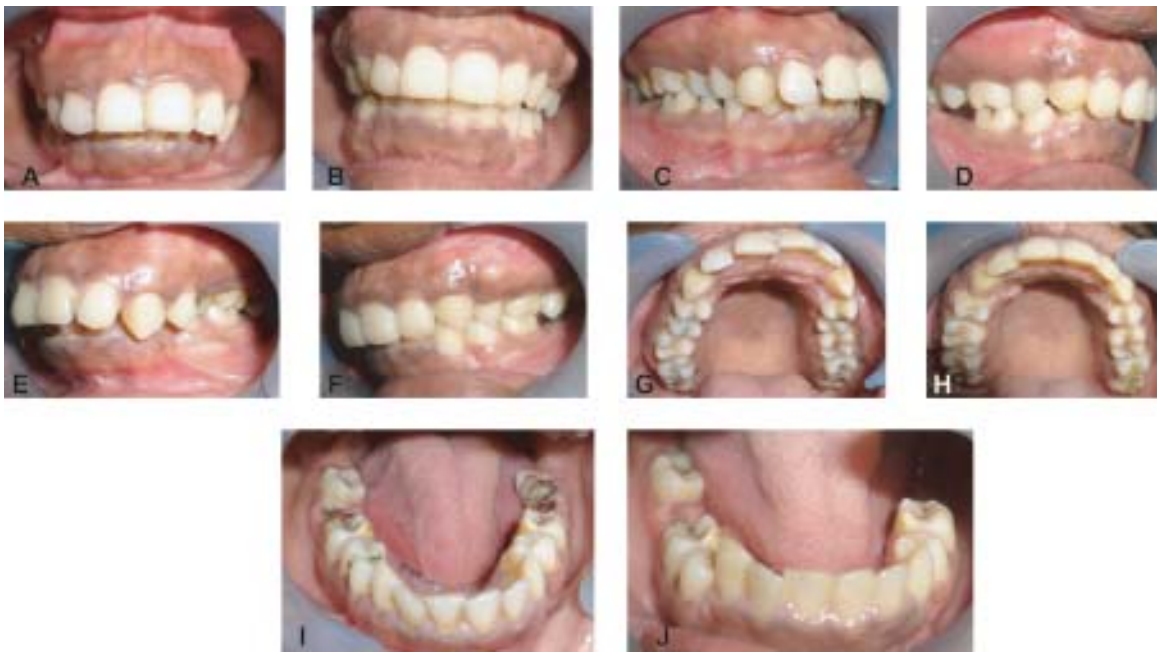

Fig.-2: *Patients intra oral photograph shows pre treatment front view (A), right lateral view(C), left lateral view(E), upper occlusal view(G),lower occlusal view (I) and post treatment front view (B), right lateral view(D), left lateral view(F), upper occlusal view(H),lower occlusal view (J).*

moderate gingivitis despite of patients reporting regular teeth brushing. This significantly explains the possible consequence of oral breathing habits resulting dry mouth with increasing carious tendency. Routine radiographic examinations with panoramic radiograph did not shows any periapical lesions on broken teeth (37, 38, 47) or caries extended to pulp chamber (17, 27) requiring endodontic treatment (Figure 5 A). On dental cast analysis it reveals that patient having a class I molar and canine relationship with increasing overjet 5.5 mm and overbite 3.0mm. Lateral cephalometric radiograph analysis shows increase SNA and SNB resulting from increase ANB which concluded a bimaxillary proclination case (Table 1). Orthodontic treatment planning with extracting all first premolar teeth and using orthodontic mini-implant (to prevent anchorage loss) were prescribed. However patient's parents were seeking alternate method of management as this conventional treatment might require almost two years to manage this case and as they were in a hurry to arrange a marriage settlement of their daughter.

Finally a combination of orthodontic treatment and orthognathic surgery were prescribed and accepted by the patient and her parents. Initial pre-surgical orthodontic treatment was done to correct the rotated teeth, crown root angulations of the teeth, space closure, and reduce the overjet and deep overbite. A standard edgewise technique bracket of 0.022×0.025 slot sized was used, where the final finishing wire was 0.021×0.025 stainless steel with proper torque control on upper anterior teeth. Extraction of all four first premolar with a segmental osteotomy cut on upper and lower anterior segment to retrocline the anterior segment and then fixed with the remaining jaw bone with miniplate and screw were planed. Therefore after completing the initial pre-surgical orthodontic treatment patient's dental cast was recorded and articulated on a dental articulator to evaluate the present pre-surgical jaw relationship. Then a mock surgery was performed on the articulated model and a bight wafer made of auto cured acrylic resign was constructed on that mock surgery model that will guide the maxillofacial surgeon to evaluate the post surgical jaw relationship during surgical procedure (Figure 3 A,B).

Patient's orthognathic surgery was performed in the department of oral and maxillofacial surgery of Shaheed Suhrawardy Medical College Hospital, Dhaka. With proper aseptic caution, under general anesthesia a

Table-I

Cephalometric Parameter changes by treatment approach.

Cephalometric Parameter	Pre treatment	Post treatment
SNA	85°	82°
SNB	80°	78°
ANB	5°	3°
FMA	27°	27°
Interincisal Angle	118°	124°
U1 to S-N plane	94°	102°
L1 to mandibular plane	5°	2°

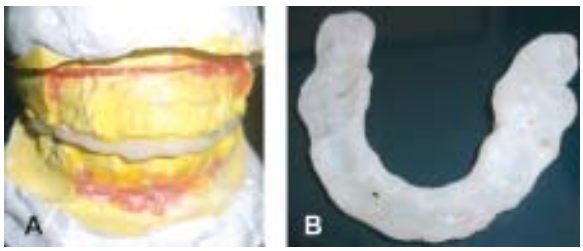

Fig.-3: *Construction of acrylic made interocclusal wafer splint on the articulated model with mock surgery (A), which is ready to use (B).*

vertical incision on the long axis of the distal margin of upper first premolar (14 & 24) was made on the right and left vestibule of the mouth extending from the gingival papilla to the functional depth of the vestibule. Then both premolars were extracted and vertical cut on the bone were given using tungsten carbide drill bits then bone segment were removed by using drill bits in a vertical area of the extraction site (Figure 4 A). With an aid of muco-peri-osteal elevator, retracting the mucoperiosteum from the overlying bone, a through and through tunneling were made connecting the both incision line. Then a horizontal osteotomy cut were made through the tunnel, protecting the root apex of all anterior teeth. Then the upper anterior segment were made immobilized with an aid of osteotom placed transpalatally from the vertical cuts going through downwards and forwards and with placing finger on the palatal mucosa to prevent laceration. Then reposition of anterior maxillary segment was done and the occlusal relationship was checked with the acrylic made interocclusal wafer splint (Figure 4 B). After extracting both lower first premolar, circumvestibular incision was made on the lower anterior vestibule of the mouth extending horizontally from the root apex of both lower canines. Care was taken to locate and protect the both mental nerve. On both side of the mandible a vertical cut was made from the alveolar crest to the level of canine root apex through and through the both cortices. Then both the vertical cuts were connected by the horizontal subapical osteotomy made about 5 mm below the teeth apices (Figure 4 C). The segment was mobilized by using an osteotome and bony interferences were removed to place the teeth into the prefabricated occlusal splint. Both the maxillary and mandibular anterior segments were stabilized by using miniplate fixation (Figure 4 D).

Post surgical intermaxillary fixation to maintain the vertical position of the teeth and increase intercuspal interdigitation elastic with bracket hook and arch wire were used. After 6 weeks of post surgery arch wire were changed and final finishing tooth movement were done with a 0.018×0.22 NiTi wire and 0.021×0.22 NiTi wire successively. Patient was advised to use light elastic full time, including while eating for the first 4 weeks after surgery; full time except for eating for another 4 weeks; and just at night for a three week period. After 3 months of post surgical treatment patient braces were removed and removable hawleys retainer on both jaws was given to use. An improved occlusion relation (Figure 1D,C and 2 B,D,F,H,J) was achieved with a favorable skeletal change as mentioned in Table 1.

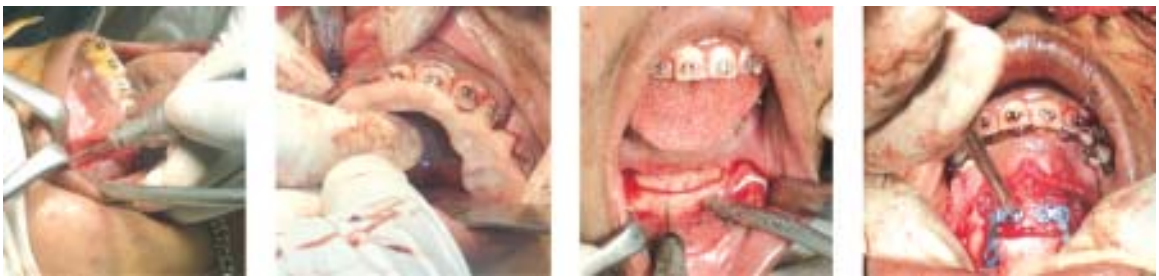

Fig.-4: *Intra oral photograph shows steps of orthognathic surgical technique vertical cut on right maxillary vestibule (A), occlusal relation checking with acrylic wafer after finishing of segmental osteotomy on maxilla(B), subapical anterior mandibular cut on mandible (C), and fixation of mobile segment with miniplate screw (D).*

Fig.-5: *Photograph of oral panoramic radiograph(OPG) shows pre treatment occlusion (A), post surgical occlusion (C) when there is braces to continue post orthodontic treatment, and final finishing occlusion (C) after removal of orthodontic braces.*

Fig.-6: *Cephalometric evaluation of post treatment occlusion and skeletal relationship by frontal cephalometric radiograph (A), lateral cephalometric radiograph (B), and tracing of lateral cephalometric post treatment radiograph (C).*

After removal of the dental braces patient's was also advised for prosthesis teeth replacement on lower posterior edentulous space. Threading of her facial hair over her upper lip and removal of mole on her left check with leaser therapy was also advised to improve external facial appearances. Repeated phone contact was made with patient and her parents, to ensure them the prosthetic teeth replacement and beautification of her facial skin to improve outlook, however she and her parents were too satisfied with their existing treatment outcome to make any further delay for her marriage settlement. So, no further collection of photographic records with occlusion having proper teeth prosthesis and a photogenic face with exotic look women appearances were not possible to present. Though patient reported to be healthy and having a happily married life till date.

Discussion:

Achieving an acceptable pleasant full smile and proportionate facial structure depends on the combination of underlying hard tissue skeleton, overlying soft tissue outline and proper presentation of the existing tooth tissue.[9] Achievement of the optimal esthetics of this case depends on several favorable factors of the conditions of the patient, they include: (i) Neutral skeletal base relationship with only anterior maxillary and mandibular prognathism. (ii) Adult with limited potential of growth. (iii) Convex facial profile. If there would severe skeletal discrepancy, with potential growth that would hamper the post treatment stability.[7] To obtain the long-term stability of the corrected occlusion and skeletal relationship, patients have to resolve the respiratory problems and avoiding thrusting their tongue anteriorly (if they have) all the time.[9]

Individual orthodontic treatment with longtime duration or only orthognathic surgery cannot manage such case. Age of the patients could not be a decelerating factor to manage a complicated cases by orthodontic treatment approach.[10] However only surgical correction cannot achieve good post surgical occlusion without aid of orthodontic treatment.[8] Multidisciplinary management approach have already been reported to achieve a good post-treatment outcome.[11] In our reported case pre and post treatment cephalometric evaluations show that both reduction of SNA and SNB angle improves the facial aesthetics (Table 1). The clinician should carefully differentiate between maxillary anterior posterior excess and mandibular anterior posterior deficiency, as maxillary anterior posterior deficiency or excess can occur in combinations of mandibular deficiency or excess. McNamara reported only 10% of a group of 277 patients with class I malocclusions had true maxillary anteroposterior excess.[12] Therefore careful diagnosis is required before formulating a treatment plan. The surgical techniques for repositioning the anterior maxilla have been introduced by Wassmund.[13] Later on most practical approach was introduced by Wunderer. [14] In our present case, post treatment

reduction of SNA, SNB, ANB with the increase inter-incisal angle and static FMA angle clearly explain the improvement of skeletal change in the anterior maxillary and mandibular region of the bimaxillary proclination cases without altering the deep cranial base. Moreover angular change of lower incisor (L1) and upper incisor (U1) position in relation to the cranial base and mandibular plane improve the smile largely. Another reason to chive favorable outcome as this was a case with non growing patients. Care must be taken to handle the case with any remnant growth or where late mandibular growth might occur.

Conclusion:

Combine effort with a multidisciplinary approach to manage cases of dentofacial deformity could be provide better treatment outcome. However care should be taken with cautious diagnosis and treatment planning.

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A Young Male Presenting with Polyuria and Unilateral Exophthalmos

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(J Banagladesh Coll Phys Surg 2014; 32: 241-243)

A 16-year-old boy from Nilphamari, Bangladesh presented with the complaints of gradual swelling of the left eye with protrusion over 1 year, increased thirst with polyuria for 2 months, and weight loss of around 5 kg over the same duration. The eye swelling was insidious in onset, limited to the left eye, associated with some redness but no lacrimation or fever and headache. He complained of excessive thirst, having to take up to 16 litres of water per day, which was associated with polyuria, including nocturia. He also developed two bony swellings on the left side of his skull which was associated with mild tenderness on palpation. He gave no history of bony pain, breathlessness, polyphagia or features of hyperthyroidism. On examination, there was non-tender proptosis of the left eye, but devoid of lid retraction, lidlag or ophthalmoplegia (Fig-1). All cranial nerves examination including funduscopy revealed no abnormality. He was haemodynamically stable and not dehydrated.

Investigations revealed normal haemogram, urea, creatinine and electrolytes, and normal blood glucose levels, effectively ruling out diabetes mellitus. ESR 70mm/ 1st hour. Thyroid profile was normal. Xray skull showed lytic lesions in frontal and parietal bones (Fig- 2)

CT scan of orbit showed a minimal enhancing soft tissue density mass lesion measuring 2x1cm in left orbit with minimal surrounding bony erosion suggestive of Histiocytosis X (Fig- 3) . MRI of the brain was unremarkable.

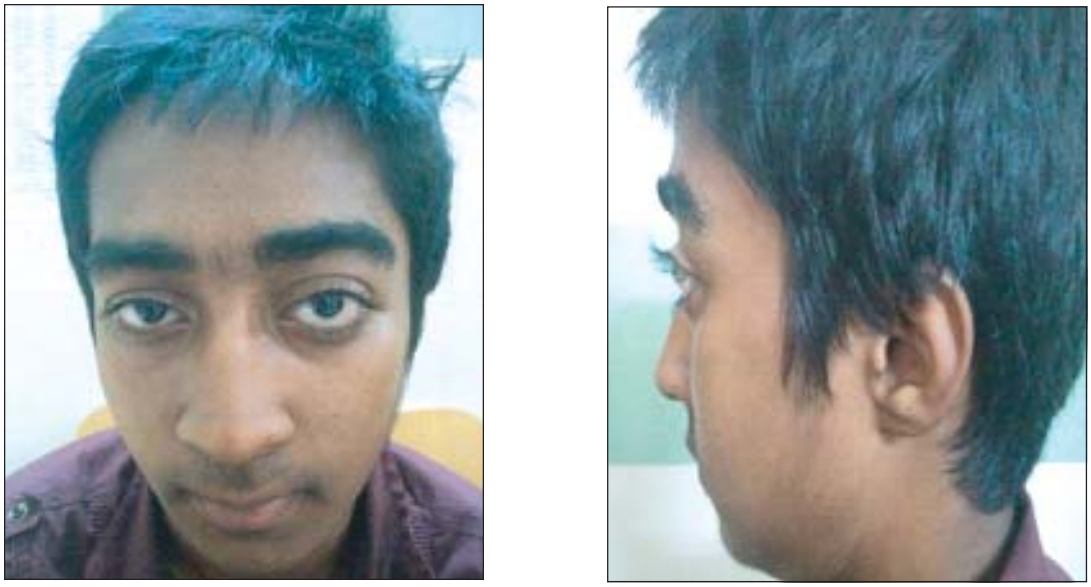

Fig-1: *Photograph showing Left sided exophthalmos front view and profile view.*

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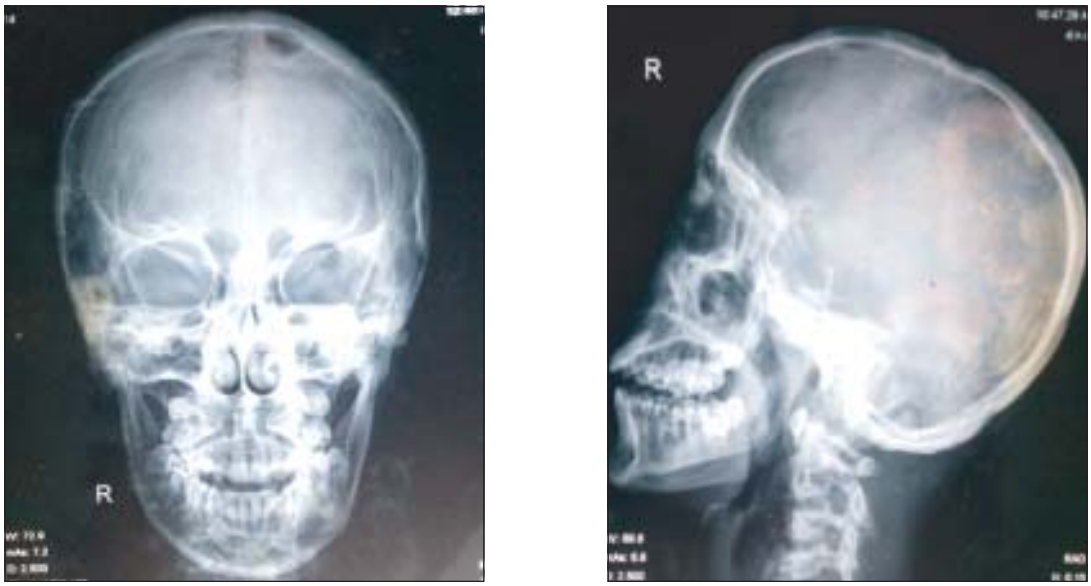

Fi-2: *X ray skull showing lytic skull lesions of frontal and parietal bones.*

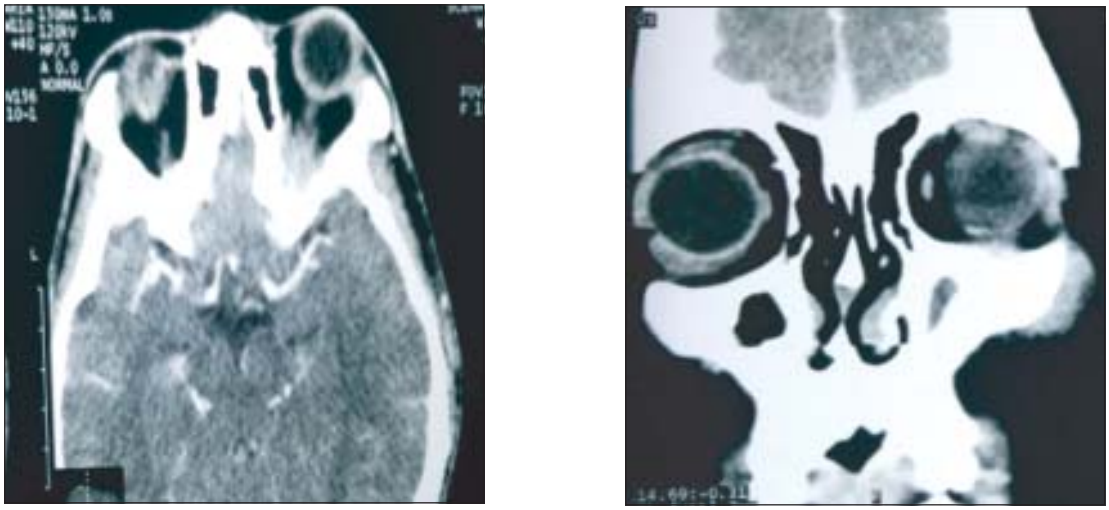

Fig-3: *CT scan of the orbit showing soft tissue mass in left orbit.*

Urine osmolality: 32mosm/kg. Serum osmolality: 285mosm/kg. Subsequent water deprivation test revealed the following : dehydration phase commenced at 7.30am. 2 hours later, urine osmolality:84mosm/kg; 4 hours later, urine osmolality: 140mosm/kg; test was terminated at 5 hours as patient developed intolerablethirst and 1.5kg weight loss. At the end of the test urine osmolality had increased to 184mosm/kg; serum osmolality: 275mosm/kg. 2 puffs of DDAVP was given and serum osmolality measured 1hr 30minutes later had increased to 346mosm/kg, suggestive of Central Diabetes Insipidus (CDI).

Bone marrow biopsy revealed features suggestive of reactive normal marrow. Skin biopsy showed dermis revealing perivascular infiltrate of chronic inflammatory cells. Bone biopsy was suggestive of histiocytosis X.

He was commenced on 2 puffs DDAVP spray in each nostril at night, which resulted in a significant reduction of water intake as well as urine output which reduced to

4-5L/day. At 3 month follow up, the patient was well on same dose, with improved constitutional symptoms and no nocturia, as well as reduced exophthalmos due to spontaneous regression of the orbital lesion.

Discussion:

Hand Schüller Christian (HSC) disease is one of the three components included in Langerhans cell histiocytosis, the other two being eosinophilic granuloma and Letterer-Siwe disease. The classical triad of HSC disease – exophthalmos, diabetes insipidus, and calvarial lytic lesions – is seen only in one-third of patients.[1,2]Also known as Multifocal HistiocytosisX syndrome, HSC is the chronic form of disseminated Histiocytosis X in which the skeletal system and soft tisues may be involved.It usually affects young children,more commonly seen in boys, with male:female ratio of approximately 2: 1.[2]

The most common site for solitary bone lesion is skull followed by long bones extremities, pelvis, ribs, scapula and spine. They are characterized in radiographs by single or multiple, round or oval lytic defects involving the medullary cavity.[2,3]

Central diabetes insipidus (CDI) is associated in 15-25% cases of Histiocytosis X, about half of whom manifest CDI early in the disease.[3,4] CDI may be associated with pituitary stalk thickening on imaging, although not present in all cases.75% of cases with CDI go on to disease free survival but require hormonal replacement.[3]

Unilateral or bilateral ocular and peri-orbital involvement resulting in exophthalmos, as well as scalp disease has also been reported.[4]

LCH is usually a self-limiting disease. In the absence of organ dysfunction, patients with either localized or multifocal LCH have an excellent prognosis.[5]

Treatment of Histiocytosis X may involve chemotherapy, radiotherapy or curettage surgery of the skull lesions. However as our patient showed spontaneous regression of the orbital lesion at follow up, he was continued on DDAVP spray, and no further intervention, as studies have shown that spontaneously regressing lesions need not be resected.[6]

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LETTER TO THE EDITOR

(J Banagladesh Coll Phys Surg 2014; 32: 244-245)

To

Editor-in-Chief

Journal of Bangladesh College of Physicians and Surgeons.

Sir,

I would like to thank you for publishing the article ' Maternal Outcome of Prolonged Pregnancy'. I have gone through it and found the content nice. I would like to share some of my observations and comments.

Post-term or prolonged pregnancy is defined as one that exceeds 294 days (42 weeks) from the first day of the last normal menstrual period[1,]. Because population studies indicate that in healthy women with otherwise uncomplicated pregnancies perinatal mortality and morbidity is increased beyond 42 weeks gestation[1,2] .There is risk of meconium aspiration, birth injury , hypoxia and stillbirth. There is also maternal concern about delay past expected date of delivery[3].

Pregnancy cannot be said to be prolonged without accurate dating. There is considerable variation in the way that the expected date of delivery is determined. It is known that the LMP even when recalled with confidence, can result in considerable dating error[4]. Using scan dates will result in fewer pregnancies being considered post-term[5]. An early USG (<14weeks) for dating is recommended for all women. This will reduce the number of women assumed 'post-term'. If an early ultrasound (<14weeks) is available the estimated date of delivery (EDD) should be calculated from ultrasound, ignoring the last known menstrual period (LMP). If ultrasound performed > 14weeks gestation the EDD should be calculated from LMP(if known) unless ultrasound differs more than one week. In women with oligomenorrhea, lactational amenorrhea or oral contraceptive withdrawal bleeding where a calculation cannot be based on the menstrual history, the first ultrasound prediction becomes the EDD[1].

Active induction does not appear to increase the caesarean section rate.Rather it is suggested that induction of labour(IOL) for prolonged pregnancy results in a reduction in caesarean section rate[6,7].It is now common practice to offer induction of labour to all women at 7 days past the due date[2]. Women should be informed that most women will go into labour spontaneously by 42 weeks. At the 38 week antenatal visit, all women should be offered information about the risks associated with pregnancies that last longer than 42 weeks, and their options. The information should cover the advantages and disadvantages of membrane sweeping[1,8]. Membrane sweeping makes spontaneous labour more likely, and so reduces the need for formal induction of labour to prevent prolonged pregnancy and not associated with an increase in maternal or neonatal infection or major adverse events. As it requires a vaginal examination, women may experience discomfort during the procedure with vaginal bleeding and contractions that do not lead to labour during the 24hours following the procedure.

At a visit close to 41 weeks gestation, for a women in whom an IOL is planned for around 42 weeks twice weekly fetal surveillance(AFI & CTG) should be done. Women with uncomplicated pregnancies should usually be offered induction of labour between 41+0 and 42+0 weeks to avoid the risks of prolonged pregnancy. The exact timing should take into account the woman's preferences and local circumstances. If a woman chooses not to have induction of labour, her decision should be respected. Healthcare professionals should discuss the woman's care with her from then on. From 42 weeks, women who decline induction of labour should be offered increased antenatal monitoring consisting of at least twice-weekly cardiotocography and ultrasound estimation of maximum amniotic pool depth[1,8].

Overall I think the article is updated, informative. Iwould like to thank the authersfor their hard work.

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Dhaka Medical College

Author's Reply

To

Editor-in-chief

Journal of Bangladesh College of Physicians and Surgeons.

Sir,

We thank Prof. Fardousi Islam and Asst. Prof. Nazneen Begum for their valuable comments on the original article. We agree to their opinion regarding estimation of EDD by USG before 14 weeks and by calculating LMP after 14 weeks. As all of our studies cases has come after 14 weeks, we estimated EDD by calculating LMP.

Though in patients having menstrual disturbances, lactation amenorrhoea or OCP withdrawal bleeding EDD can be calculated by USG, we excluded these patients for getting results with better accuracy.

We are agree to their opinion for induction of labour to all women at 7 days past the due date.

Dr. Parul Akhter, Asst. Prof. (Gynae & Obs.) Sir Salimullah Medical College and Mitford Hospital, Dhaka.

Dr. Masuda Sultana, Junior Consultant (Gynae), UHC, Meghna, Comilla.

Dr. Mahbuba Hoque, Junior Consultant (Gynae), Sadar Hospital, Narsingdi.

Dr. Sharmin Sultata, Gynae outdoor, 200 Beded Hospital, Narayangonj.

Dr Mst. Rahima Khatun, Junior Consultant (Gynae), Sadar Hospital, Satkhira.

Dr. Seema Rani Dabee, Junior Consultant (Gynae), 20 Beded Hospital, Aminbazar, Savar, Dhaka.

COLLEGE NEWS

(J Banagladesh Coll Phys Surg 2014; 32: 246-250)

College news Examinations news: Results of FCPS Part-I, Part-II and MCPS examination held in July are given bellow:

4874 candidates appeared in FCPS Part-I, examinatin held in July, 2014 of which 658 candidates came out successful.

Subject wise results are as follows:

Result of FCPS Part-I Examination (July, 2014)

SL. No.	Subject	July-14		
		Total Candidate	**Total Passed**	**Percentage %**
1.	Anaesthesiology	105	6	5.71
2.	Biochemistry	3	0	0.00
3.	Dental Surgery	214	20	9.35
4.	Dermatology & Venereology	64	1	1.56
5.	Family Medicine	1	0	0.00
6.	Haematology	15	3	20.00
7.	Histopathology	23	4	17.39
8.	Medicine	1615	300	18.58
9.	Microbiology	16	1	6.25
10.	Obst. & Gynae	1084	85	7.84
11.	Ophthalmology	104	12	11.54
12.	Otolaryngology	136	9	6.62
13.	Paediatrics	481	44	9.15
14.	Physical Medicine & Rehabilitation	28	8	28.57
15.	Psychiatry	18	1	5.56
16.	Radiology & Imaging	49	4	8.16
17.	Radiotherapy	39	6	15.38
18.	Surgery	879	154	17.52
19.	Transfusion Medicine	0		
	Total	**4874**	**658**	**13.50**

The following candidates satisfied the Board of Examiners and are declared to have passed the FCPS - II Examinations held in July, 2014 subject to confirmation by the council of Bangladesh College of Physicians and Surgeons

Roll No.	Name	From where graduated	Subject
024-8909	Md. Zahidul Hasan	Khulna Medical College, Khulna	Neonatology
024-8910	Ismat Jahan	Sir Salimullah Medical College, Dhaka	Neonatology
024-8913	Md. Habibul Hasan	Rajshahi Medical College, Rajshahi	Orthopaedic Surgery
024-8918	Most. Afroza Nazneen	Rajshahi Medical College, Rajshahi	Plastic and Reconstructive Surgery
024-8920	Mohammed Shahabuddin Khaled	Comilla Medical College, Comilla	Plastic and Reconstructive Surgery
024-8921	Mohammad Kamruzzaman	Rajshahi Medical College, Rajshahi	Plastic and Reconstructive Surgery
024-8922	Md. Golam Rabbani	Dhaka Medical College, Dhaka	Rheumatology
024-8923	Khondaker Arafuzzaman	Khulna Medical College, Khulna	Urology
024-8927	Md. Nazmul Islam	Comilla Medical College, Comilla	Urology
085-7002	Samar Chandra Saha	Dhaka Medical College, Dhaka	Anaesthesiology

Roll No.	Name	From where graduated	Subject
085-7007	Farhanaz Zainab	Chittagong Medical College, Chittagong	Anaesthesiology
085-7008	Abdullah Masum	Khulna Medical College, Khulna	Anaesthesiology
085-7009	Sharmin Mahbub	Sir Salimullah Medical College, Dhaka	Anaesthesiology
085-7012	Md. Kutub Uddin Khan	Sher-E-Bangla Medical College, Barisal	Anaesthesiology
085-7022	Sarker Mahbub Ahmed	University of Science & Technology Chittagong (USTC)	Dermatology and Venereology
085-7028	Md. Rezaul Islam	Dhaka Medical College, Dhaka	Dermatology and Venereology
085-7029	Anjana Chakraborty	Dhaka Medical College, Dhaka	Dermatology and Venereology
085-7038	Ayesha Akter	Comilla Medical College, Comilla	Dermatology and Venereology
085-7039	Imranul Hasan Murad	Chittagong Medical College, Chittagong	Dermatology and Venereology
085-7048	Rozina Afroz	Sir Salimullah Medical College, Dhaka	Dermatology and Venereology
085-7055	Shahela Nazneen	Sir Salimullah Medical College, Dhaka	Haematology
085-7106	Md. Kalim Ullah	Sir Salimullah Medical College, Dhaka	Medicine
085-7197	Muhammad Mostafizur Rahman	Rangpur Medical College, Rangpur	Medicine
085-7220	Razaul Karim	MAG Osmani Medical College, Sylhet	Medicine
085-7226	Nusrat Jahan	Dhaka Medical College, Dhaka	Medicine
085-7246	Sharmin Ahmed	Rangpur Medical College, Rangpur	Medicine
085-7248	Tufayel Ahmed Chowdhury	Faridpur Medical College, Faridpur	Medicine
085-7257	Tarek Shams	Chittagong Medical College, Chittagong	Medicine
085-7261	Muhammad Shahidullah	MAG Osmani Medical College, Sylhet	Medicine
085-7266	Abu Shahid Mohammad Rezaul Karim	Dhaka Medical College, Dhaka	Medicine
085-7269	Debasish Kumar Ghosh	Dhaka Medical College, Dhaka	Medicine
085-7275	Chandra Shekhar Bala	Khulna Medical College, Khulna	Medicine
085-7311	Mohammad Majharul Haque	Dhaka Medical College, Dhaka	Medicine
085-7323	Md. Mahfuj-Ul-Anwar	Rajshahi Medical College, Rajshahi	Medicine
085-7327	Md. Uzzwal Mallik	Sher-E-Bangla Medical College, Barisal	Medicine
085-7328	Subrata Podder	Dhaka Medical College, Dhaka	Medicine
085-7331	Rafiqul Hasan	Dhaka Medical College, Dhaka	Medicine
085-7371	Sk. Abdullah Al Mamun	Rajshahi Medical College, Rajshahi	Medicine
085-7389	Richmond Ronald Gomes	Dhaka Medical College, Dhaka	Medicine
085-7442	Md. Tauhidul Islam	Mymensingh Medical College, Mymensingh	Medicine
085-7444	Hossain Muhammad Mustafijur Rahman	Dhaka Medical College, Dhaka	Medicine
085-7454	Syed Mohammad Shaifuddin	Sir Salimullah Medical College, Dhaka	Medicine
085-7474	Abu Saif Mohammad Lutful Kabir	Chittagong Medical College, Chittagong	Medicine
085-7503	K. M. Ahasan Ahmed	Sir Salimullah Medical College, Dhaka	Medicine
085-7535	A.K.M. Shafiqul Islam	Dhaka Medical College, Dhaka	Medicine
085-7636	Suchitra Saha	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7641	Rupasree Biswas	MAG Osmani Medical College, Sylhet	Obst and Gynae
085-7661	Farhana Rahman	Mymensingh Medical College, Mymensingh	Obst and Gynae
085-7670	Mst. Sultana Naznin	Rangpur Medical College, Rangpur	Obst and Gynae
085-7680	Rahima Khatun	MAG Osmani Medical College, Sylhet	Obst and Gynae
085-7699	Foujia Sharmin	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7709	Zohra Liza	Chittagong Medical College, Chittagong	Obst and Gynae
085-7727	Nasrin Hasan	Jahurul Islam Medical College, Bajitpur	Obst and Gynae
085-7739	Fahmida Monir	Chittagong Medical College, Chittagong	Obst and Gynae
085-7745	Asma Rahman	Dhaka Medical College, Dhaka	Obst and Gynae
085-7770	Merina Jahan	Sher-E-Bangla Medical College, Barisal	Obst and Gynae
085-7779	Minara Sikder	Faridpur Medical College, Faridpur	Obst and Gynae
085-7796	Moumita Tripura Mumu	Dhaka Medical College, Dhaka	Obst and Gynae
085-7801	Shahana Ahmed	Rajshahi Medical College, Rajshahi	Obst and Gynae
085-7809	Rogina Amin	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7822	Sadia Mahfiza Khanam	Mymensingh Medical College, Mymensingh	Obst and Gynae
085-7825	Rabeya Begum Sumee	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7829	Naima Sharmin Hoque	Comilla Medical College, Comilla	Obst and Gynae

Roll No.	Name	From where graduated	Subject
085-7857	Kamrun Nahar Rani	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7869	Anonya Talukder	Mymensingh Medical College, Mymensingh	Obst and Gynae
085-7883	Mst. Shumsun Nahar	Shaheed Ziaur Rahman Medical College, Bogra	Obst and Gynae
085-7884	Raihana Shawgat	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7887	Sumia Ahmed Tazri	Dhaka Medical College, Dhaka	Obst and Gynae
085-7897	Gopa Kundu	Dhaka Medical College, Dhaka	Obst and Gynae
085-7910	Sarmin Ferdous	Mymensingh Medical College, Mymensingh	Obst and Gynae
085-7924	Farhana Jahan	Dhaka Medical College, Dhaka	Obst and Gynae
085-7925	Husne Har Hasi	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7932	Sharmin Hossain	Shaheed Suhrawardy Medical College, Dhaka	Obst and Gynae
085-7942	Faria Rashid	Armed Forces Medical College, Dhaka	Obst and Gynae
085-7945	Moshammat Fatima Akter	MAG Osmani Medical College, Sylhet	Obst and Gynae
085-7949	Sonali Rani Mustofi	Rangpur Medical College, Rangpur	Obst and Gynae
085-7952	Sayeeda Pervin	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7957	Sabrina Kadir	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-7958	Sumaiya Akter	Comilla Medical College, Comilla	Obst and Gynae
085-7996	Farhana Shabnam	Dhaka Medical College, Dhaka	Obst and Gynae
085-8003	Sharmin Abbasi	Ibrahim Medical College, Dhaka	Obst and Gynae
085-8030	Zakia Sultana	Rangpur Medical College, Rangpur	Obst and Gynae
085-8040	Tanzina Jahan	Chittagong Medical College, Chittagong	Obst and Gynae
085-8044	Jannatul Ferdous	Rajshahi Medical College, Rajshahi	Obst and Gynae
085-8053	Esmat Jahan	Dhaka Medical College, Dhaka	Obst and Gynae
085-8070	Mujtahid Mohammad Hossain	MAG Osmani Medical College, Sylhet	Ophthalmology
085-8075	Mahmooda Rahman	Fatima Jinnah Medical College, Lahore, Pakistan.	Ophthalmology
085-8082	Sidratul Muntaha Naznin	Rajshahi Medical College, Rajshahi	Ophthalmology
085-8087	Shah Md. Rajibul Islam	Chittagong Medical College, Chittagong	Ophthalmology
085-8093	Farzana Ali	Khulna Medical College, Khulna	Ophthalmology
085-8104	Munshi Ahmed Hossain	Rajshahi Medical College, Rajshahi	Oral and Maxillofacial Surgery
085-8107	Hasan Tareq Bin Noor	Pioneer Dental College, Dhaka	Oral and Maxillofacial Surgery
085-8109	Md. Shahjahan Ali	Dhaka Dental College, Dhaka	Oral and Maxillofacial Surgery
085-8111	A. T. M. Tarifuzzaman Rubel	Dhaka Dental College, Dhaka	Oral and Maxillofacial Surgery
085-8113	Sajid Hasan	Pioneer Dental College, Dhaka	Oral and Maxillofacial Surgery
085-8125	Nabila Anwar	City Dental College, Dhaka	Orthodontics and Dentofacial Orthopaedics
085-8139	Sheikh Masud	Dinajpur Medical College, Dinajpur	Otolaryngology
085-8145	Md. Khorsed Alam	Rangpur Medical College, Rangpur	Otolaryngology
085-8148	Md. Mahmudul Hasan Khan	Dhaka Medical College, Dhaka	Otolaryngology
085-8195	A N M Shahidul Islam Bhuiyan	Chittagong Medical College, Chittagong	Paediatrics
085-8216	Sorroare Hosen	Mymensingh Medical College, Mymensingh	Paediatrics
085-8230	Mohammad Ala Uddin	MAG Osmani Medical College, Sylhet	Paediatrics
085-8242	Md. Ashiqur Rahman	Dhaka Medical College, Dhaka	Paediatrics
085-8248	Tahmina Jahan Chowdhury	Rangpur Medical College, Rangpur	Paediatrics
085-8249	Md Mahmudul Hasan	Dhaka Medical College, Dhaka	Paediatrics
085-8259	Amrita Lal Halder	Sher-E-Bangla Medical College, Barisal	Paediatrics
085-8266	Noor-A-Sabah Liza	Sir Salimullah Medical College, Dhaka	Paediatrics
085-8289	Sumitra Mazumder	Mymensingh Medical College, Mymensingh	Paediatrics
085-8324	Mushtab Shira Mousumi	Dhaka Medical College, Dhaka	Paediatrics
085-8350	Fahmida Islam	Chittagong Medical College, Chittagong	Paediatrics
085-8355	Tarannum Khondaker	Z.H. Sikder Women's Medical College, Dhaka	Paediatrics
085-8358	Dipa Saha	Armed Forces Medical College, Dhaka	Paediatrics
085-8362	Rozina Akhter	Z.H. Sikder Women's Medical College, Dhaka	Paediatrics
085-8377	Sanjida Pervin	Rangpur Medical College, Rangpur	Physical Medicine & Rehabilitation
085-8381	Naima Siddiquee	Sir Salimullah Medical College, Dhaka	Physical Medicine & Rehabilitation
085-8382	Moinuddin Hossain Khan	MAG Osmani Medical College, Sylhet	Physical Medicine & Rehabilitation
085-8383	Mohammad Moin Uddin	Chittagong Medical College, Chittagong	Physical Medicine & Rehabilitation

Roll No.	Name	From where graduated	Subject
085-8385	Towhid Tofail	Sapporo Dental College, Dhaka	Prosthodontics
085-8388	Aeysha Suddika	Sapporo Dental College, Dhaka	Prosthodontics
085-8390	Mohammad Farid Uddin Ahmed	Sher-E-Bangla Medical College, Barisal	Psychiatry
085-8391	Nasim Jahan	Z.H. Sikder Women's Medical College, Dhaka	Psychiatry
085-8392	Md. Masud Rana Sarker	Chittagong Medical College, Chittagong	Psychiatry
085-8401	Mohammed Mominul Hoque Sarker	Sher-E-Bangla Medical College, Barisal	Radiology & Imaging
085-8445	Mohammad Khaleduzzaman Khan	Sher-E-Bangla Medical College, Barisal	Surgery
085-8452	Abu Sayed Mollah	Faridpur Medical College, Faridpur	Surgery
085-8486	Muhammad Mofazzal Hossain	Mymensingh Medical College, Mymensingh	Surgery
085-8516	Md Kabirul Hassan	Dhaka Medical College, Dhaka	Surgery
085-8518	Md Kamruzzaman	Khulna Medical College, Khulna	Surgery
085-8531	Mohammad Jasim Uddin	Comilla Medical College, Comilla	Surgery
085-8544	Mayin Uddin Mahmud	Chittagong Medical College, Chittagong	Surgery
085-8554	Mohammad Haroon Or-Rashid	Dhaka Medical College, Dhaka	Surgery
085-8563	Mohammad Saiful Malek	Mymensingh Medical College, Mymensingh	Surgery
085-8565	Mahbub Hasan	Dhaka Medical College, Dhaka	Surgery
085-8567	Md Nazrul Islam	MAG Osmani Medical College, Sylhet	Surgery
085-8580	Md. Naheduzzaman	Dinajpur Medical College, Dinajpur	Surgery
085-8581	Mohammad Sajjad Hossain	Chittagong Medical College, Chittagong	Surgery
085-8585	Prodip Kumar Karmakar	Rangpur Medical College, Rangpur	Surgery
085-8587	Mohammad Abdul Quadir	Chittagong Medical College, Chittagong	Surgery
085-8588	Md. Showkat Ali	Sir Salimullah Medical College, Dhaka	Surgery
085-8591	Kazi Nasid Naznin	Chittagong Medical College, Chittagong	Surgery
085-8608	Ali Nafisa	Rajshahi Medical College, Rajshahi	Surgery
085-8616	Tapan Kumar Mondal	Sher-E-Bangla Medical College, Barisal	Surgery
085-8617	Md. Abdur Rahim	Sher-E-Bangla Medical College, Barisal	Surgery
085-8622	Muhammad Faridul Haque	Sher-E-Bangla Medical College, Barisal	Surgery
085-8626	Mohammad Ashfaqur Rahman	Mymensingh Medical College, Mymensingh	Surgery
085-8633	Md. Ariful Alam Suman	Rangpur Medical College, Rangpur	Surgery
085-8637	Sheikh Mohammad Zakirullah Rasha	Bangladesh Medical College, Dhaka	Surgery
085-8647	Muhammad Harun-Ar-Rashid	Sir Salimullah Medical College, Dhaka	Surgery
085-8654	Mohammad Alamgir	Comilla Medical College, Comilla	Surgery
085-8659	Kazi Israt Jahan	MAG Osmani Medical College, Sylhet	Surgery
085-8669	Sayera Banu Sheuly	Rajshahi Medical College, Rajshahi	Surgery
085-8671	Nadia Farzana Islam	Chittagong Medical College, Chittagong	Surgery
085-8679	Mohammed Akhter Hasib Dewan	Rajshahi Medical College, Rajshahi	Surgery
085-8682	Ruhina Alam	Dhaka Medical College, Dhaka	Surgery
085-8689	Most. Bilkis Fatema	Rajshahi Medical College, Rajshahi	Surgery
085-8692	Mohammed Shafayet Ullah	MAG Osmani Medical College, Sylhet	Surgery
085-8701	Md. Shahid-Ul-Islam Khan	Dhaka Medical College, Dhaka	Surgery
085-8702	Abdullah Md. Abu Ayub Ansary	Mymensingh Medical College, Mymensingh	Surgery
085-8712	A. N. M. Jane Alam	Sir Salimullah Medical College, Dhaka	Surgery
085-8713	Masrur Akbar Khan	Chittagong Medical College, Chittagong	Surgery
085-8720	Mohammad Mashiur Rahman	Rajshahi Medical College, Rajshahi	Surgery

The following candidates satisfied the Board of Examiners and are declared to have passed the MCPS Examinations held in July, 2014 subject to confirmation by the council of Bangladesh College of Physicians and Surgeons

Roll No.	Name	From where graduated	Subject
085-9007	Shamim Ara Begum	Comilla Medical College, Comilla	Anaesthesiology
085-9017	Md. Golam Robbani	Sir Salimullah Medical College, Dhaka	Clinical Pathology
085-9025	Md. Raihan -Ul Arefin	Chittagong Medical College, Chittagong	Dental Surgery
085-9027	Md. Emdadul Haque	Rajshahi Medical College, Rajshahi	Dental Surgery
085-9032	Tahmina Akter	Ibrahim Medical College, Dhaka	Dermatology and Venereology
085-9041	Raqib Uddin Ahmed	Rajshahi Medical College, Rajshahi	Dermatology and Venereology

Roll No.	Name	From where graduated	Subject
085-9043	Nandita Ghosh	Rangpur Medical College, Rangpur	Dermatology and Venereology
085-9044	Isabela Kabir	Rajshahi Medical College, Rajshahi	Dermatology and Venereology
085-9046	Tasnuva Ashraf	Rangpur Medical College, Rangpur	Dermatology and Venereology
085-9047	Kaniz Shahali Reza Snigdha	Sir Salimullah Medical College, Dhaka	Dermatology and Venereology
085-9523	Kazi Md. Ainul Islam	Rajshahi Medical College, Rajshahi	Family Medicine
085-9052	Mamtaz Ara	Rangpur Medical College, Rangpur	Forensic Medicine
085-9054	Tarana Chowdhury	Z.H. Sikder Women's Medical College, Dhaka	Forensic Medicine
085-9055	Biswajit Kumar Das	Gonoshasthaya Samajvittik Medical College	Forensic Medicine
085-9057	Palash Kumar Bose	Rajshahi Medical College, Rajshahi	Forensic Medicine
085-9071	Taslima Akter	Dhaka Medical College, Dhaka	Medicine
085-9072	Md Aminul Islam	Rangpur Medical College, Rangpur	Medicine
085-9089	Goutam Kumar Ghosh	Khulna Medical College, Khulna	Medicine
085-9111	Md Zahid Amin	Dhaka Medical College, Dhaka	Medicine
085-9122	Ashim Chakraborty	Sir Salimullah Medical College, Dhaka	Medicine
085-9126	Palash Kumar Deb Nath	Sir Salimullah Medical College, Dhaka	Medicine
085-9140	Marina Arjumand	MAG Osmani Medical College, Sylhet	Medicine
085-9147	Mohammad Salim	Dhaka Medical College, Dhaka	Medicine
085-9182	Md. Khairul Islam	Sir Salimullah Medical College, Dhaka	Medicine
085-9188	Md. Nazibur Rahman	University of Science & Technology Chittagong (USTC)	Medicine
085-9189	Md. Ashikur Rahman	Sher-E-Bangla Medical College, Barisal	Medicine
085-9198	Shahana Parvin	Sir Salimullah Medical College, Dhaka	Medicine
085-9206	Kazi Nazmul Hossain	Dhaka Medical College, Dhaka	Medicine
085-9214	Monira Sarmin	Mymensingh Medical College, Mymensingh	Medicine
085-9220	Ashraf -Ur- Rahman	Dhaka Medical College, Dhaka	Medicine
085-9225	Muhammad Abdul Hannan	Sir Salimullah Medical College, Dhaka	Medicine
085-9228	Md. Guljar Hossain	Mymensingh Medical College, Mymensingh	Medicine
085-9237	Sadia Jerifa	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-9273	Bindu Rani Gope	Chittagong Medical College, Chittagong	Obst and Gynae
085-9282	Rokeya Gulshan Ara	Rajshahi Medical College, Rajshahi	Obst and Gynae
085-9288	Dipu Das	Jalalabad Ragib-Rabeya Medical College, Sylhet	Obst and Gynae
085-9300	Sharmin Naz	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-9308	Rowson Ara Jaman	Jalalabad Ragib-Rabeya Medical College, Sylhet	Obst and Gynae
085-9313	Sabina Yeasmin	Chittagong Medical College, Chittagong	Obst and Gynae
085-9317	Rubina Bari	Dhaka Medical College, Dhaka	Obst and Gynae
085-9328	Rehena Nasreen	Kumudini Womens' Medical College, Tangail	Obst and Gynae
085-9330	Sanjukta Chowdhury	Dhaka Medical College, Dhaka	Obst and Gynae
085-9336	Kaniz Fatema	Sher-E-Bangla Medical College, Barisal	Obst and Gynae
085-9339	Dilruba Akhter	Dhaka Medical College, Dhaka	Obst and Gynae
085-9343	Amina Jannat Peea	Sir Salimullah Medical College, Dhaka	Obst and Gynae
085-9355	Most. Nuri Zunnatul Fardous	Z.H. Sikder Women's Medical College, Dhaka	Obst and Gynae
085-9381	Shamim Ara Yeasmin	Rajshahi Medical College, Rajshahi	Ophthalmology
085-9393	Mostafa Kamal Arefin	Dhaka Medical College, Dhaka	Otolaryngology
085-9455	Md. Khayrul Islam	Shaheed Ziaur Rahman Medical College, Bogra	Psychiatry
085-9457	Md. Fazlul Bari	Shaheed Ziaur Rahman Medical College, Bogra	Psychiatry
085-9460	Md. Shahab Uddin	Rangpur Medical College, Rangpur	Radiology & Imaging
085-9517	Ashrafun Nessa	Sir Salimullah Medical College, Dhaka	Surgery
085-9522	Kashfia Islam	Chittagong Medical College, Chittagong	Transfusion Medicine

FROM THE DESK OF EDITOR in CHIEF

(J Banagladesh Coll Phys Surg 2014; 32: 251)

Dear Fellows

Wish you all had a wonderful Eid and Durga Puja. October has turned out to be a month of festivity throughout the nation. The joyous occasion of the two major religion of Bangladesh has created a vibe of unification, happiness and the strength to go further in all sectors. The Journal of BCPS has also geared up its momentum in full swing. All issues are up-to-date, there are no back logs, more and more publications are being submitted with great enthusiasm and the editorial team is working relentlessly to keep up with your esteem. I would like to thank you for your constant support and would like to remind you of our online system for submission of articles that makes publication smoother for all.

With your support we are only inches away from being indexed on medline. Keep supporting.

Professor HAM Nazmul Ahasan
Editor-in-Chief
Journal of Bangladesh College of Physicians
and Surgeons

Obituary

(J Banagladesh Coll Phys Surg 2014; 32: 252)

The following fellows who died on July to September, 2014

Professor A K M Nazimuddowla Chowdhury

Professor A K M Nazimuddowla Chowdhury died on 25thSeptember, 2014.He own fellowship without examination in Psychiatry, 1983from Bangladesh College of Physicians and Surgeons (BCPS).