INFORMATION FOR AUTHORS

MANUSCRIPT PREPARATION AND SUBMISSION

Guide to Authors

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

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

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

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

Submit manuscripts as e-mail attachment to the editorial office at: journal_bcps@gmail.com

A manuscript number will be mailed to the corresponding author within two working days.

The cover letter should include the corresponding author’s full address and telephone/fax numbers and should be in an e-mail message sent to the editor, with the file, whose name should begin with the first author’s surname, as an attachment.

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

Article Types

Five types of manuscripts may be submitted:

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

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

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

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

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

Review Process:

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

I. A. Preparing a Manuscript for Submission to JBCPS
Editors and reviewers spend many hours reading manuscripts, and therefore appreciate receiving manuscripts that are easy to read and edit. Much of the information in this journal’s Instructions to Authors is designed to accomplish that goal in ways that meet each journal’s particular editorial needs. The following information provides guidance in preparing manuscripts for this journal.

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

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

Preparation of manuscript:
Criteria: Information provided in the manuscript are important and likely to be of interest to an international readership.
Preparation:
1. Manuscript should be written in English and typed on one side of A4 (290 x 210cm) size white paper.
2. Margin should be 5 cm for the header and 2.5 cm for the remainder.
3. Style should be that of modified Vancouver.
4. Each of the following section should begin on separate page :
   o Title page
   o Summary/abstract
   o Text
   o Acknowledgement
   o References
   o Tables and legends.

Pages should be numbered consecutively at the upper right hand corner of each page beginning with the title page.

I. A. 1. a. General Principles
• The text of observational and experimental articles is usually (but not necessarily) divided into the following sections: Introduction, Methods, Results, and Discussion. This so-called “IMRAD” structure is a direct reflection of the process of scientific discovery.
• Long articles may need subheadings within some sections (especially Results and Discussion) to clarify their content. Other types of articles, such as case reports, reviews, and editorials, probably need to be formatted differently.
• Electronic formats have created opportunities for adding details or whole sections, layering information, crosslinking or extracting portions of articles, and the like only in the electronic version.
• Authors need to work closely with editors in developing or using such new publication formats and should submit supplementary electronic material for peer review.
• Double-spacing all portions of the manuscript— including the title page, abstract, text, acknowledgments, references, individual tables, and
legends—and generous margins make it possible for editors and reviewers to edit the text line by line and add comments and queries directly on the paper copy.

• If manuscripts are submitted electronically, the files should be double-spaced to facilitate printing for reviewing and editing.

• Authors should number on right upper all of the pages of the manuscript consecutively, beginning with the title page, to facilitate the editorial process.

I. A. 1. b. Reporting Guidelines for Specific Study Designs

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

I. A. 2. Title Page

The title page should have the following information:

1. Article title. Concise titles are easier to read than long, convoluted ones. Titles that are too short may, however, lack important information, such as study design (which is particularly important in identifying type of trials). Authors should include all information in the title that will make electronic retrieval of the article both sensitive and specific.

2. Authors’ names and institutional affiliations.

3. The name of the department(s) and institution(s) to which the work should be attributed.

4. Disclaimers, if any.

5. Contact information for corresponding authors. The name, mailing address, telephone and fax numbers, and e-mail address of the author responsible for correspondence about the manuscript.

6. The name and address of the author to whom requests for reprints should be addressed or a Statement that reprints are not available from the authors.

7. Source(s) of support in the form of grants, equipment, drugs, or all of these.

8. A short running head or footnote, of no more than 40 characters (including letters and spaces). Running heads are published and also used within the editorial office for filing and locating manuscripts.

9. The number of figures and tables. It is difficult for editorial staff and reviewers to determine whether the figures and tables that should have accompanied a manuscript were actually included unless the numbers of figures and tables are noted on the title page.

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

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

I. A. 4. Abstract

• Structured abstracts are essential for original research and systematic reviews. structured abstract means introduction, methods, results and conclusion in abstract

• Should be limited to 250 words

• The abstract should provide the introduction of the study and blinded state and should state the study’s purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect sizes and their statistical significance, if possible), principal conclusions. It should emphasize new and important aspects of the study or observations. Articles on clinical trials should contain abstracts that include the items that the CONSORT group has identified as essential (http://www.consort-statement.org).

• Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to be careful that they accurately reflect the content of the article
I. A. 5. Introduction
• Provide a context or background for the study (that is, the nature of the problem and its significance). It should be very specific, identify the 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 non-technical 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.

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

I. A. 13. Units of Measurement
• Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples.
• Authors should report laboratory information in both local and International System of Units (SI).
• Drug concentrations may be reported in either SI or mass units, but the alternative should be provided in parentheses where appropriate.

I. A. 14. Abbreviations and Symbols
• Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers.
• Avoid abbreviations in the title of the manuscript.
• The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

I. B. Sending the Manuscript to the Journal
• If a paper version of the manuscript is submitted, send the required number of copies of the manuscript and figures; they are all needed for peer review and editing, and the editorial office staff cannot be expected to make the required copies.
• Manuscripts must be accompanied by a cover letter, conflicts of interest form, authorship and declaration, proforma of which is available in JBCPS web site.
**Editing and peer review:** All submitted manuscripts are subject to scrutiny by the Editor-in-chief or any member of the Editorial Board. Manuscripts containing materials without sufficient scientific value and of a priority issue, or not fulfilling the requirement for publication may be rejected or it may be sent back to the author(s) for resubmission with necessary modifications to suit one of the submission categories. Manuscripts fulfilling the requirements and found suitable for consideration are sent for peer review. Submissions, found suitable for publication by the reviewer, may need revision/modifications before being finally accepted. Editorial Board finally decides upon the publishability of the reviewed and revised/modified submission. Proof of accepted manuscript may be sent to the authors, and should be corrected and returned to the editorial office within one week. No addition to the manuscript at this stage will be accepted. All accepted manuscripts are edited according to the Journal’s style.

**Submission Preparation Checklist**

As part of the submission process, authors are required to check off their submission’s compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

**Check Lists**

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

1. Forwarding/Cover letter and declaration form
2. Authorship and conflicts of interest form
3. Manuscript
   - Sample of the above documents is available in the following links: [http://www.bcpsbd.org](http://www.bcpsbd.org) (registration required for download)
   - 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
  - Double spacing
  - Font size should be 12 in arial
  - Margins 5 cm from above and 2.5 cm from rest sides.

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

• **Language and grammar**
  - Uniformity in the language
  - Abbreviations spelt out in full for the first time
  - Numerals from 1 to 10 spelt out
  - Numerals at the beginning of the sentence spelt out

• **Tables and figures**
  - No repetition of data in tables/graphs and in text
  - Actual numbers from which graphs drawn, provided
  - Figures necessary and of good quality (colour)
  - Table and figure numbers in Arabic letters (not Roman)
  - Labels pasted on back of the photographs (no names written)
  - Figure legends provided (not more than 40 words)
  - Patients’ privacy maintained (if not, written permission enclosed)
  - Credit note for borrowed figures/tables provided
  - Each table/figure in separate page

If you have any specific queries please use at [www.bcps.com](http://www.bcps.com)

**Manuscript Format for Research Article**

• **Title**
  - Complete title of your article
  - Complete author information
  - Mention conflict of interest if any
• **Abstract**
  - Do not use subheadings in the abstract
  - Give full title of the manuscript in the Abstract page
  - Not more than 200 words for case reports and 250 words for original articles
  - Structured abstract (Including introduction, methods, results and discussion, conclusion) provided for an original article and (Introduction, results and discussion, conclusion) for case reports.
  - Key words provided – arrange them in alphabetical order (three – five)

• **Introduction**
  - Word limit 150 -200 words
  - Pertinent information only

• **Material and Methods**
  - Study Design
  - Duration and place of study
  - Ethical approval
  - Patient consent
  - Statistical analysis and software used.

• **Result**
  - Clearly present the data
  - Avoid data redundancy
  - Use table information at the end of the sentence before full stop between the small bracket

• **Discussion**
  - Avoid unnecessary explanation of someone else work unless it is very relevant to the study
  - Provide and discuss with the literatures to support the study
  - Mention about limitation of your study

• **Conclusion**
  - Give your conclusion
  - Any recommendation

• **Acknowledgement**
  - Acknowledge any person or institute who have helped for the study

• **Reference**
  - Abide by the Vancouver style
  - Use reference at the end of the sentence after the full stop with superscript

• **Legends**
  - Table
  - Figures

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Chronic Pelvic Pain: Addressing a Common Debilitating Condition of Women

Chronic pelvic pain (CPP) is a common debilitating condition of women affecting perhaps one in six of the adult female, mostly in their reproductive life\(^1\). CPP accounts for substantial personal sufferings and health care expenditure for interventions, including multiple consultations, medical & surgical therapies. Chronic pelvic pain (CPP) can be defined as intermittent or constant pain in the lower abdomen or pelvis of a woman of at least 6 months in duration not occurring exclusively with menstruation or intercourse and not associated with pregnancy\(^1\). It is a symptom, not a diagnosis, though not a life threatening condition, has significant impact on quality of life and functional capability. As the underlying pathophysiology of this complex condition is poorly understood, CPP is difficult to diagnose & treat and more often difficult to get complete cure and patient’s satisfaction creating frustration for the patients as well as their attending physicians. Magnitude of problem growing day by day. Statistics reveal that CPP accounts for about 1 in 10 outpatient gynaecology visits, is the indication for an estimated 15% to 40% laparoscopies, 12% of hysterectomies and costs $3 billion US Dollar annually in United States\(^2\), reflecting heavy economic and social burdens. Limitation of activities is also alarming as evidenced by a study on 5325 US women, of which 16% reported with CPP, 11% of which limited their home activities, 15.8% took medications, 11.9% limited their sexual activities & 3.9% missed at least 1 day of work per month\(^3\). Disruption of women’s life in the form of doing endless investigations, referral & interventions, leave the women ultimately with a feeling that “nothing can be done more than that”. Aiming for accurate diagnosis and effective management from the very beginning could minimize this tragedy.

Although women with CPP are no longer different in terms of age, race, ethnicity, education, socioeconomic or employment status, demographic profile of large surveys reveals higher incidence in reproductive life among single, separated or divorced women. 40-50% women are victim of sexual abuse. Chronic Pelvic Pain symptom usually encompasses the following clinical characteristics – duration of six months and longer, incomplete relief with most treatments, significantly impaired functional capabilities at home or work, associated with signs of depression like insomnia, anorexia, weight loss and altered family roles.

Pelvic pain is associated with a wide range of conditions involving reproductive, gastrointestinal, genitourinary, musculoskeletal or psychological systems. There is frequently more than one component of CPP and the severity and consistency of pain often increases with multisystem involvement. Clinical evaluation must therefore be thorough from a medical, surgical and psychological stand points to assess the contributory factors. Thorough history taking that generates trust between care givers and patient and a pain focused physical examination should be the key to formulating a diagnosis. A useful model for understanding CPP is Steege’s integrated Model\(^4\) which includes the following elements – biological events initiating pain, alteration of life style & relationship over time, anxiety and affective disorders and the circular interaction among these elements. Initial interview should convey interest listen with attention, validate patient’s experience and avoid telling her that problem must be psychological as no visible pathology is found. To obtain focused history use of the “Review of systems” could be followed to explore the organ system involvement.

Physical examination is very different from the routine gynaecological examination, may need to defer for a second time to exam her when she is in pain. Using a pelvic pain numerical scale to obtain a feedback from patient is useful. Physical examination should always be conducted to focus on review of systems. Enquiries should be made regarding psychological and social issues as CPP is often associated with psychological instability. The multi factorial nature of CPP should be
explored & discussed from the start. As the differential diagnosis of CPP is intensive it is the challenge for the gynaecologist as well as the attending physician to think “Out of the uterus”.

Women with CPP are often subjected to endless investigations although focused history taking and examinations can guide specific diagnostic tests appropriate for particular patient. Screening for infections by blood count, culture of endo cervical swabs and urine analysis may be the first line investigations. Diagnostic imaging should only be performed rationally. Trans Vaginal Sonography (TVS) is useful for evaluation of adnexal masses but of little value to evaluate the other causes of CPP. TVS may play role to identify women who needs laparoscopy\(^5\). MRI may be an adjunct but its role to diagnose small peritoneal endometriotic deposits are doubtful\(^6\)

Diagnostic laparoscopy is regarded in the past as “gold standard” for the diagnosis of CPP, now better seen as “second line investigation” if therapeutic intervention fails\(^1\). It may have role in developing women’s belief about pain. Only diagnostic laparoscopy will not improve the pain pulsation with positive & negative findings and negative results do not exclude diseases or organic causes. So recommendation is that laparoscopy should be offered with an aim to have both diagnostic and therapeutic contribution.

Adequate time should be allowed for clinical assessment of women with CPP & diagnosis and treatment should align with positive and negative findings. Many women demand an explanation for their pain and multi factorial nature of the pain should be discussed. Integrated approach should be taken to address organic, psychological and environmental factors. Daily pain diary could explore the provoking factors and temporal association. Appropriate referral for non gynaecological component of pain should be done.

Great concern is not to dismiss organic cause as psychological and to remember that organic causes are often masked by overwhelming psychological factors. Women should not leave with a feeling that she has to live with pain.

\(\textit{(J Bangladesh Coll Phys Surg 2016; 34: 126-127)}\)

**Prof. Salma Rouf**  
Professor of Obstetrics & Gynaecology  
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**References:**

1. Royal College of Obstetricians and Gynaecologists. The initial management of chronic Pelvic pain, Green Top Guideline. No. 41, London. RCOG; May 2012


Clinical Presentation and Bacterial Etiology of Adult Community Acquired Pneumonia

MA SALAM a, MR AMIN b, QT ISLAM c

Summary:
Introduction: Pneumonia is a worldwide, serious threat to health and an enormous socio-economic burden for health care system. According to recent WHO data, each year 3-4 million patients die from pneumonia. The clinical presentations and bacterial agents responsible for community acquired pneumonia (CAP) varies according to geography and culture.

Methods: A cross sectional observational study conducted among the 53 consecutive patients with a clinical diagnosis of CAP in admitted patient in the department of Medicine, DMCH, during January 2010 to December 2010. Hematological measurements (TC of WBC, Hb%, ESR, platelet count), blood culture, chest X-ray P/A view, sputum for Gram staining and culture sensitivity, sputum for AFB, blood urea and random blood sugar were done in all cases. ELISA for IgM antibody of Mycoplasma pneumoniae and Chlamydia pneumoniae were done in sputum culture negative cases.

Results: The mean (±SD) age was 38.9±17.3 years and Male female ratio was 3:1. Fever, chest pain and productive cough were the most common clinical features. The mean (±SD) respiratory rate was 23.0±2.8/minute. COPD and DM were found in 17.0% and 5.7% of patients respectively. Blood culture was found positive in only 1.9% of the study patients. Gram positive Cocci 62.26%, Gram negative Bacilli 9.43%, mixed Gram positive cocci and Gram negative bacilli 11.32% and Gram negative Cocco Bacilli 1.9% were observed and in 15.03 % cases, no bacteria could be seen.

Sputum culture revealed 53.8% streptococcus pneumoniae, 26.9% Klebsiella pneumonia as predominant organism. Mycoplasma pneumoniae and Chlamydia pneumoniae were found in 7.4% and 3.7% respectively by serological test. For Streptococcus pneumoniae, sensitive antibiotics were Amoxyclov and Levofloxacin. For Gram negative bacilli and cocobacilli, more sensitive antibiotics were Meropenem, Ceftriaxone, and Clarithromycin. The best sensitive drug were found meropenem. The mean (±SD) duration of hospital stay was 5.0±1.7 days with ranging from 3 to 10 days.

Conclusion: Region based bacteriological diagnosis of Cap is important for selecting the best and sensitive drugs for complete cure.

(J Bangladesh Coll Phys Surg 2016; 34: 128-134)
to be 258 cases per 100,000 population and 962 cases per 100,000 persons 65 years of age. While mortality has ranged from 2% to 30% among hospitalized patients in a variety of studies, the average rate is 14%. Mortality is estimated to be <1% for patients who are not hospitalized. The incidence of CAP is highest in the winter months.

Prospective studies for evaluating the causes of CAP in adults have failed to identify the cause of 40%-60% of cases of CAP, and two or more etiologies have been identified in 2%-5% of cases. The most common etiologic agent identified in virtually all studies of CAP is *Streptococcus pneumoniae*, and this agent accounts for approximately two thirds of all cases of bacteremic pneumonia. Other pathogens implicated less frequently include *Haemophylus influenzae*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Neisseria meningitidis*, *Moraxella catarrhalis*, *Klebsiella pneumoniae* and other Gram-negative rods, *Legionella species*, *Influenza virus* (depending on the time of year), *Respiratory syncytial virus*, *Adenovirus*, *Parainfluenza virus*, and other microbes. The frequency of other etiologies, e.g., *Chlamydia psittaci* (psittacosis), *Coxiella burnetti* (Q fever), *Francisella Tularenensis* (tularemia) and endemic fungi (*Histoplasmosis*, *Blastomycosis*, and *Coccidiodomycosis*), is dependent on specific local epidemiological factors. No convincing association has been demonstrated between individual symptoms, physical findings or laboratory test results, and specific etiology. Even time-honored beliefs (e.g., the absence of a productive cough or lack of inflammatory sputum suggests etiologies such as species of *Mycoplasma, Legionella*, and *Chlamydia*) have not withstood close inspection. On the other hand, most comparisons have involved relatively small numbers of patients and the potential for separating causes by using constellations of symptoms and physical findings has not been evaluated.

The present study was done to describe the clinical presentation and the causative bacterial organism and their pattern of CAP in adult patients in DMCH and also the influence of patient age, previous antibiotic use, and the category of pneumonia on microbial patterns in this disease. Antimicrobial susceptibility of isolates from clinical specimens were also tested to estimate the prevalence of drug sensitivity and resistance pattern of common CAP-causing bacteria, especially *Streptococcus pneumoniae* and *Haemophilus influenzae*. Meanwhile the short term clinical outcome of antibiotic therapy for CAP was also observed.

**Methods:**
A Cross sectional observational study was done from January 2010 to December 2010 in the Department of Medicine, Dhaka Medical College Hospital (DMCH), in Dhaka, Bangladesh. Dhaka Medical College is situated in the center of Dhaka city. It is a tertiary care teaching and referral hospital in Bangladesh. About 27 thousands patients were treated in the Department of Medicine in 2009.

Fifty three adult patients of both sexes over 18 years of age admitted in the department of Medicine of DMCH with Fever for less than 14 days and one or more of the followings: Cough, Sputum, Haemoptysis, Pleuritic chest pain, Dyspnoea, Sign of consolidation and radiological evidence of Pneumonic consolidation were included while hospital acquired pneumonia, chemical pneumonitis ca lung, radiological evidence of fibrosis, collapse, bronchiectasis, lung abscess and tuberculosis, suspicion of immunosupression or known immuno-suppressive status like HIV, Haematological or lymphoid malignancy and pt on immunosuppressive drugs- steroids and chemotherapy were excluded.

**Procedures:**
This study was approved by the ethical review committee of Dhaka Medical College.

After admission in the indoor, any suspected case of community acquired pneumonia seen by unit doctor was screened by study physician. Evaluation was made by history and physical examination in a structured case record form (CRF) by the study physician. Patients diagnosed clinically as CAP was screened in the study. Investigations were done hematologic measurements (TC of WBC, Hb%, ESR, platelet count), blood culture, chest X-ray P/A view, sputum for Gram staining and culture sensitivity, sputum for AFB for 3 consecutive days, blood urea and random blood sugar. For scanty production of cough, patients sputum was collected after nebulization by hypertonic normal saline. Serological tests were done for the blood culture negative and sputum culture negative cases for identification of atypical organisms (e.g. *Mycoplasma*...
and *Chlamydia pneumoniae*). It was done by ELISA for IgM antibody of *Mycoplasma* and *Chlamydia pneumoniae*. Patient with positive radiological findings of consolidation was enrolled in the study. Sputum for AFB positive cases and radiology of exclusion criteria was screened out from the evaluation. The patient address (tracing) and cell number was recorded to ensure follow up. The negative sputum culture patient was also followed up as like that of culture positive cases. Antibiotic therapy of the enrolled patient was given at the discretion of the treating clinician under the supervision of respective consultant of the medicine unit. The clinical judgment of consultant was boost up by doing the CURB-65 score by the study physician.

The study used the British Thoracic Society of severe community acquired pneumonia detected by CURB-65 which includes presence of any of the following:

0. Confusion
1. Urea 7mmol/l
2. Respiratory rate 30 breath/min
3. Systolic blood pressure <90mm of Hg or Diastolic blood pressure<60mm of Hg
4. Age65 years

1 point was scored for each feature present. On the basis of points treatment protocol was adjusted.

During treatment, oral temperature was recorded and frequently physical examinations were performed up to discharge. Patients were supplied a structured questionnaire regarding changes in symptomatology and general well being. Patients were asked to report 2 weeks after completion of treatment for follow up. Any patient who failed to come for follow up in time was called upon by cell phone (contact number of patient). Thus a short term outcome after the treatment was observed.

**Microbiological evaluation**

Sputum samples were collected from all patients enrolled in the study. Representative sputum originated from the lower respiratory tract was defined as that containing >25 granulocytes and <10 epithelial cells per low power field microscopic view. Validated sputum was cultured in blood agar, chocolate agar and McConkey’s agar media. Isolation and identification of microorganism was done according to the standard method.

Blood samples (6-8 ml) were collected aseptically from patients for blood culture and serological test. Serum was separated and stored at -4°C. Primary blood culture was done in Trypticase soya broth and secondary blood culture was done on blood agar, choclolate agar and McConkey’s agar media.

**Antimicrobial susceptibility testing:**

Antimicrobial susceptibility was determined by the disc diffusion method of modified Kirby-Bauer (1966) technique using Blood agar media (for *Streptococcus pneumoniae*), Mueller-Hinton agar media (for *Escherichia coli*, *Klebsiella pneumoniae* and Pseudeononas species) and Chocolate agar media (for *Haemophylus influenzae* and antimicrobial discs (Oxoid, UK). Following antimicrobials and their concentration per disc were used for susceptibility tests:

5. For Gram positive cocci : Amoxyclav (30 microgram), Levofoxacin (5 microgram), Azithromicin (15 microgram), Cefixime (30 microgram) and Doxycligne (30 microgram).

b) For Gram negative bacilli and coccobacilli : Meropenem (10 microgram), Ceftriaxone (30 microgram), Amikacin (10 microgram), Clarithromycin (5 microgram), Ciprofloxacin (5 microgram), Amoxyclav (30 microgram) and Cefixime (30 microgram).

Methods of susceptibility testing: The agar plates were dried in an incubator at 37°C for 30 minutes before use. With a sterile wire loop, pure and isolated colonies were picked up and was suspended into a sterile tube containing 2 ml of normal saline. The turbidity of the inoculum was standardized to the equivalent to that of 0.5 of Mac Farland standard. A sterile cotton swab was immersed into the bacterial suspension and the excess suspension was removed by rotating the swab with a firm pressure against the inner side of the tube above the fluid level. The swab was then streaked evenly on the entire surface of the concerned plate. The discs were then placed on the inoculum surface by a sterile forcep 15 mm away from the edge of the petridish with 25 mm gap in between the discs. All plates were
incubated at 37°C - aerobically for Blood agar and Mueller-Hinton agar and microaerobically (by candle jar) for Chocolate agar medium. Measurement of inhibition zone: standard procedure was followed.9

Data analysis:
Categorical data was presented as frequency and percentage and continuous variable presented as mean and standard deviation. All data was analyzed by SPSS (Statistical Package for Social Science) 16 windows version.

Results:
This prospectively study enrolled 53 cases of CAP fulfilling the eligibility check list. The various characteristics of the cases are presented in table 1. The mean (±SD) age was 38.9±17.3 years with ranged from 18 to 90 years and maximum number (24.5%) of patients was found in the age group of 31-40 years.

Fever was present in all of the study patients. Chest pain 43 (81.1%) and copious productive cough 34 (64.2%) were present in the study patients. During physical examination most of the patients had 1000 -102°F temperature (71.7%) and all patients had consolidation. (Table II)

CURB-65 Pneumonia severity scoring revealed 48 (90.6%) had 0 – 1, 5 (9.4%) had 2 and none were found to have 3 while the mean (±SD) respiratory rate was 23.0±2.8 /minute with range from 18 to 32 /minute. it was observed that COPD and DM were found 9 (17.0%) and 3 (5.7%) respectively in study patients. The mean (±SD) TC was 14804±3533/cumm, Neutrophil 78.5±7.1%, Lymphocyte 17.0±6.7%, Monocyte 2.6±1.4%, Eosinophil 2.3±1.2%, Basophil 0.0±0.0% and ESR 57.6±13 mm. In blood culture Pseudomonas species was found in 1 (1.9%) of the study patients. This patient (42 yrs female) had known diabetes mellitus and presented with high continued fever and copious productive sputum for five days. At the time admission random blood sugar was 15 mmol/L. The hospitalization of this patient was 10 days and she received meropenem with slow but complete recovery.

In sputum tested by Gram stain, only Gram positive cocci were seen in 33 (62.26%) samples, only Gram negative bacilli in 5 (9.43%) samples. Mixed Gram positive cocci and Gram negative bacilli in 6 (11.32%) samples, only one sample (1.88%) showed presence of Gram negative coccobacilli. Bacteria could not be found in 8 (15.03%) samples. (Table III)

Sputum culture was done in all patients and 26 (49.1%) positive growth out of which 5 cases used antibiotics before enrolment. Twenty seven (50.9%) were found no growth where 20 cases used prior antibiotics and 7 cases did not use prior antibiotics before hospitalization. The use of antibiotics were variable in duration in positive and negative growth cases.

Streptococcus pneumoniae was identified as the sputum culture positive in 14 / 26 cases. These 14 cases are also out of 33 Gram stain positive cocci (Not shown in table). Klebsiella pneumoniae was found 7 (26.9%) as the common isolates among Gram negative cases.(Table IV)

In case of Streptococcus pneumoniae, Amoxyclav showed the highest sensitivity (78.6%), followed by Levofloxacin (64.3%). (Table V)

Most of the given antibiotics were amoxyclav (34.6%), clarithromycin (30.8%), Ceftriaxone (30.8%) and Meropenem (23.1%).(table VI)

Mycoplasma pneumoniae and Chlamydia pneumoniae were found in 2 (7.4%) and 1 (3.7%) respectively according to serological test of the study patients. The mean (±SD) duration of hospital stay was 5.0±1.7 days with ranged from 3 to 10 days.

Discussion:
In this small series of patients with Community Acquired Pneumonia (CAP), microorganism could be identified in 49% cases in sputum culture and Streptococcus pneumoniae was the most frequent organism(14/26) resulting in classical clinical features supporting the statement that Streptococcus pneumoniae was the commonest organism of community acquired pneumonia (CAP).10

Berntsson et al.11 observed Streptococcus pneumoniae 49.0% in their study. Woodhead et al.12 found Streptococcus pneumoniae 36.0% and Escherichia coli 1.0%. Fang et al.8 observed that Streptococcus pneumoniae in 15.3%, Haemophylus influenzae in 10.9% in his study. Sullivan et al.13 found Klebsiella pneumoniae 2.0% and Escherichia coli 4.0%. So it is observed that there are variable percentage in different studies especially for Streptococcus pneumoniae. In this present study about fifty percents sputum culture were negative which might be due to other aetiological
agents e.g. viral or *Legionella pneumophila* or use of antibiotic prior to hospitalization. Mamun et al.\textsuperscript{14} showed that one fifth of the patients used antibiotics by dispensing practices in rural Bangladesh. The frequency of *Streptococcus pneumoniae* in present study is like that of similar observations showed *Streptococcus pneumoniae* 20.9\%, *Klebsiella pneumoniae* 4.7\% and *Staphylococcus aureus* 2.3\% in non diabetic patients.\textsuperscript{6,11,15,17,18}

Gram positive Cocci in staining procedure was found among more than half of enrolled patients. Fang et al.\textsuperscript{8} observed 14.8\% Gram positive cocci in their study, which is less than the present study. Gram stain has been found a useful test and reliable for targeting pathogen-directed first-line antibiotic therapy in CAP patients. Moderate to large amounts of Gram-positive diplococci was seen in sputum Gram stain of purulent sputum observed by Stralin\textsuperscript{19} which is consistent with the present study. Macfarlane et al.\textsuperscript{15} and Andrews et al.\textsuperscript{16} observed *Pseudomonas species* 11.0\% and 2.0\% respectively in their study patients. Only one patient of this present study showed *Pseudomonas species* as it was observed in blood culture. Stralin\textsuperscript{19} observed *Pseudomonas species* as the rare cause of CAP in his study which is also consistent with the present one.

In this personal series sensitivity pattern of isolated strain of bacteria from CAP patients is alarming that resistant bacteria is emerging. It was observed from this study that isolated *Klebsiella* strain was mostly resistant to commonly used antibiotics for CAP. Other isolated organisms like *Pseudomonas, Escherichia coli*, were also resistant to *B*-lactamase inhibitor, Macrolides and third generation cephalosporin. *Streptococcus pneumoniae* were sensitive to commonly used antibiotic for CAP. These antibiotics are costly and not recommended by the guideline published by American thoracic society (2004) and Infectious disease society of America (IDSA 2004).

Frequently use *B*-lactam antibiotic and Macrolides for the treatment CAP are first line regimens but emerging strain are more resistant to these conventional antibiotics. Multi drug resistant to *B*-lactamase, Macrolides and Fluroquinolone is an emerging problem and complicating the management of CAP\textsuperscript{20}. In a study ICDDR B Rahman et al.\textsuperscript{21} found *Pneumococcus* serotype is resistant to penicillin and macrolides posing threat to Bangladesh and some other Asian countries. Saibal\textsuperscript{18} showed the sensitivity pattern against the *Streptococcus pneumoniae* to Amoxyclav 83\%, *Klebsiella pneumoniae* to Ceftriaxone 73.3\% which is comparable with the present study.

The antibiotics chosen by physicians were according to preference Amoxyclav, Clarithromycin, Ceftriaxone and Meropenem. Woodhead et al.\textsuperscript{12} showed almost similar given antibiotics in their study patients.

*Mycoplasma pneumoniae* and *Chlamydia pneumoniae* were found by serological test in this study patients. Sullivan et al.\textsuperscript{13}, Macfarlane et al.\textsuperscript{14} and Ngeow et al.\textsuperscript{4} observed *Mycoplasma pneumoniae* 9.3\%, 2.4\% and 9.2\% respectively in their study. Falguera\textsuperscript{17} observed *Chlamydia pneumoniae* 11.0\%, *Mycoplasma pneumoniae* 9.0\%. Sohn et al.\textsuperscript{22} showed *Mycoplasma pneumoniae* 4.8\% and *Chlamydia pneumoniae* 4.0\%, which are comparable with the current study.

In this present study, patients mean age and age range is similar to different studies. Fang et al.\textsuperscript{8} had shown in their series, the age ranged of their patients were 23 to 92 years, which closely agrees with the present study. Liapikou et al.\textsuperscript{23} and Sohn et al.\textsuperscript{22} observed higher mean age in their study, where the mean age were 68.9±17.9 years and 54.6±17.8 years respectively. This variation in their study may be due to higher life expectancy in their population.

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Liapikou et al.\textsuperscript{23} study, where the authors found male female ratio was almost 2:1 while in this personal series it was observed that more than three fourths of the patients was male which is comparable. However, Fang et al.\textsuperscript{8} and Sohn et al.\textsuperscript{22} observed male female ratio was almost 1:1. Male patients were higher in this study, which may be due to access to health care facility by male is easier than female as she had to maintain the family and children.

The frequency of fever, chest pain and cough in this series was common feature. Almost similar observations regarding the clinical presentations were also found by Andrews et al.\textsuperscript{16}, Fang et al.\textsuperscript{8}, Sohn et al.\textsuperscript{22} and Ngeow et al.\textsuperscript{4}. Ashraf et al.\textsuperscript{24} showed fever and cough were 89.0\% and 99.0\% respectively in their study children.

All patients had documented temperature during hospital stay. In a study of pediatric population of same
country Ashraf et al.\textsuperscript{24} showed 44.0\% had >102\(^{\circ}\)F temperature among the study children. Fang et al.\textsuperscript{8} observed in their study that increasing age was associated with lower temperature. Sign of consolidation were found in all cases in this series. Sohn et al.\textsuperscript{22} found consolidation in 87.5\%. Almost similar findings obtained by Andrews et al.\textsuperscript{16} and Liapikou et al.\textsuperscript{23}. Majority of the findings are similar with the present study regarding this physical sign.

Prognosis of the patient was seen in hospitalized patient through CURB score. More than 90 percent in this study is within score 1. Liapikou et al.\textsuperscript{23} observed almost similar findings regarding the CURB-65 scoring in their study. CURB-65 score was not similar with Schuetz et al.\textsuperscript{25} study, where the authors observed 1-2 score in 0.2\% of their study patients possibly because the study was done in critical care unit. Saibal\textsuperscript{18} showed CURB-65 scoring 0 – 1 in 62.8\% and 2 in 16.3\% in non diabetic patients. CAP cases in present study were not very serious to be shifted to ICU and mortality was also absent. As the sample size is small, the actual poor prognostic factors may not be reflected here.

The respiratory rate range was similar to Schuetz et al.\textsuperscript{25} who observed respiratory rate ranged from 16 to 25 /min in their study and is also corresponds with the good outcome to the patients.

Concomitant diseases of COPD and DM were observed in the study. Fang et al.\textsuperscript{8} observed COPD in 31.4\% and DM in 13.4\% in their study which was little higher frequency than present study. Berntsson et al.\textsuperscript{11} found DM 4.0\%, which is similar with the current study frequency. Figuera\textsuperscript{17} observed 16.7\% patients had DM. Liapikou et al.\textsuperscript{23} observed COPD 37.9\%, 19.4\% and 45.0\% respectively. Similarly, Liapikou et al.\textsuperscript{23} observed 19.0\% patient had DM in the study. Although random blood sugar was taken as a screening criteria in this study for DM, it may turn up to be different if Fasting or OGTT should have been undertaken.

The mean duration of hospital stay was similar to few studies. Falguera\textsuperscript{17} and Liapikou et al.\textsuperscript{23} showed the mean duration of hospital stay was 5±1.2 days and 6±1.9 days which was similar in this study. Saibal\textsuperscript{18} found the mean duration of hospital stay was 7.7±1.7 days in non diabetic patients. Ashraf et al.\textsuperscript{24} found duration of the clinic stay > 10 days was 5.0\% of the study children.

Limitation of the study: This descriptive study is a study with small sample and requires further studies from different levels of hospitals. A nationally representative surveillance system for CAP could replace periodic small studies.

**Conclusion:**

*Streptococcus pneumoniae* was common organism for CAP identified by sputum culture. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* were found by serological test. For CAP associated with *Streptococcus pneumoniae*, sensitivity results were in favour of Amoxyclav and Levofloxacin. For CAP associated with Gram negative bacilli and coccobacilli, sensitivity status were in favour of Meropenem, Ceftiraxone and Clarithromycin respectively. Common use of antibiotics in community can lead to difficulty in identifying organism was observed in this study.

**Conflicts of interest:** None declared

**References:**


Introduction:

Endometriosis is defined as the presence of endometriallike tissue outside the uterus, which induces a chronic, inflammatory reaction. The exact prevalence of endometriosis estimates approximately 10% within the general population.

Endometriosis diagnosis is based on the women’s history, symptoms and signs. While some women with endometriosis experience painful symptoms and/or infertility, others have no symptoms at all. And definitive criteria to determine that the pain is actually caused by endometriosis is lacking. So, the nature of the relationship between chronic pain and endometriosis remains poorly understood. This results in many women receiving either delayed or suboptimal care.

Laparoscopy or laparotomy allows staging of endometriosis according to the r-ASRM classification system (Revised American Society for Reproductive Medicine classification of endometriosis: 1996, 1997). This classification system assigns points to the different locations of the disease thus resulting in four stages: minimal, mild, moderate and severe.

The aim of this study is to assess the prevalence and severity of pain in patients diagnosed with endometriosis during surgery in Infertility Management Center Dhaka, a specialized center for treatment of infertility and assisted reproductive technologies from January 2008 to January 2009.

Method

This study was done in Infertility Management Center Dhaka, a specialized center for treatment of infertility and Assisted reproductive technologies. This study was conducted from January 2008 to January 2009. It was a prospective observational study. At first 112
women with regular menstrual cycles were recruited who underwent laparoscopy or laparotomy due to various reasons. Before surgery, each patient completed a questionnaire regarding age, pelvis pain and infertility if present. Severity of pain was graded according to visual analogue scale, 0-4 mild pain, 5-7 moderate pain, 8-10 severe state like incapacitation or requiring strong analgesic. Then these patients underwent laparoscopy or laparotomy according to decision previously taken. Amongst them, 65 patients with diagnosis of endometriosis during surgery were included in this study. Forty seven patients were excluded from the study as they had pain due to PID, post operative adhesions and or genital malformation. Patients who were treated for pelvic pain and endometriosis in the previous six months other than NSAID like GnRh analogues/ OCPs were also excluded from the study. During the surgical procedure all the visible lesions were noted and staged according to r-ASRM classification. In addition, color, site of lesion and presence of endometrioma were also noted.

Table-I

<table>
<thead>
<tr>
<th>Incidence of endometriosis according to age distribution (n=65)</th>
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<tbody>
<tr>
<td>Age group</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>Less than 20</td>
</tr>
<tr>
<td>21 to 25</td>
</tr>
<tr>
<td>26 to 30</td>
</tr>
<tr>
<td>31 to 35</td>
</tr>
<tr>
<td>36 to 40</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Among the symptomatic patients, 47 (92.1%) had dysmenorrhea, 19 (37.2%) patients had chronic pelvic pain, deep dyspareunia in 11 (21.6%), dyschezia in 11 (21.6%) and dysuria in 7 (13.7%) patients.

Severity of pain was graded according to the visual analogue pain scale. We observed 30% patients experienced mild form of pain, 37% with moderate pain and 33% with severe form of pain.

Infertility was the predominant cause in 85% patients and remaining 15% did not have problem regarding fertility. Those patients who suffered from infertility were mostly (n=47 =74%) in the primary group and 14 patients (26%) suffered from secondary sub fertility.

Depending on the disease pattern, 50 patients (77%) underwent laparoscopy and the remaining 15 (23%) patients had undergone laparotomy.

During the operative procedure the commonest site of endometriosis was found in uterosacral ligament (n=58=89%), ovarian endometriosis is noted in (63%) cases. The other sites were rectovaginal septum, broad ligament, peritoneum and fallopian tubes as shown in Table II

Table-II

<table>
<thead>
<tr>
<th>Distribution of endometriosis (n=65)</th>
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<tbody>
<tr>
<td>Site</td>
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<td>-----------------------------------</td>
</tr>
<tr>
<td>Uterosacral ligament</td>
</tr>
<tr>
<td>Ovaries</td>
</tr>
<tr>
<td>Recto vaginal septum</td>
</tr>
<tr>
<td>Broad ligament</td>
</tr>
<tr>
<td>Peritoneum</td>
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<tr>
<td>Fallopian tube</td>
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</tbody>
</table>
Regarding the type of endometriotic lesion, it was observed that most of the lesions (35%) were black, haemosiderin deposits followed by red, pink and vesicular blobs (Table - III)

<table>
<thead>
<tr>
<th>Type of endometriotic lesion (n=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Black, haemosiderin deposits</td>
</tr>
<tr>
<td>Red, mild pink, flame like, vesicular blobs, clearvesicles</td>
</tr>
<tr>
<td>White, peritoneal defects, yellow brown</td>
</tr>
<tr>
<td>No specific type</td>
</tr>
</tbody>
</table>

Figure 2 showed the distribution of patients according to the stage of endometriosis (r-ASRM). Majority (58.4%) of patients were in stage IV endometriosis.

Figure 3: Stages of endometriosis according to R-AFS score (n=65)

Table-IV showed the correlation of pain score with r-AFS scores and it showed strong positive correlation between severe pain and stage IV disease (Correlation co efficient 0.711). Moderate forms of pain and severity of disease did not show any positive correlation in this study (Correlation co efficient 0.390). There was in fact negative correlation between milder forms of pain with severity of disease.

<table>
<thead>
<tr>
<th>Correlation of pain score with R-AFS score (n=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score</td>
</tr>
<tr>
<td>Minimal</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
</tr>
<tr>
<td>Severe</td>
</tr>
<tr>
<td>Correlation</td>
</tr>
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</table>

Discussion:
In this study, most of the patients were 26-30 years old. A serious challenge in endometriosis diagnosis is that even though the age of onset of menstrual pain is early, there is a significant delay of 7–11 years before the average woman is diagnosed. Propst and Yeung in two different studies also showed that among adolescents who complained of dysmenorrhea, approximately 70% eventually were diagnosed with endometriosis, so this symptom warrants special attention in young women. 4, 5
This study also revealed that even though pelvic pain was predominant in most patients, about 22% patients were asymptomatic. This was also seen in a study done by Porpora in 1999, which showed that 11.1% woman had no symptom of pelvic pain even though they had biopsy proven endometriosis.

Pelvic symptoms like dysmenorrhea, chronic pelvic pain, deep dyspareunia, cyclical intestinal complaints, fatigue/weariness and infertility continue to be the leading symptoms of endometriosis. In this study the predominant symptom was dysmenorrhea (92%) followed by chronic pelvic pain (37%) and dyspareunia (21%). In one cross-sectional survey carried out in 12 tertiary care centers in 10 countries in 2013 also showed that dysmenorrhea (59%) and chronic pelvic pain (60%) were the predominant symptoms of endometriosis. Previously in a different study, Forman also concluded that dysmenorrhea was the only symptom significantly predictive of endometriosis. No differences in the rates of pelvic pain, dyspareunia or vaginal discharge were seen among women with endometriosis, compared to those with normal pelvis or adhesions. In another prospective study done by Eskenaze et al in Italy, where women scheduled to undergo various gynecological operations were interviewed concerning infertility, dysmenorrhea, dyspareunia and non-cyclical pelvic pain, none of these were predictive of the diagnosis of endometriosis. However, women eventually surgically diagnosed with endometriosis reported more intensive dysmenorrhea than those with no diagnosis of endometriosis.

In this study, we observed a strong correlation of endometriosis with infertility, mostly primary infertility. An association between endometriosis and infertility has long been noted. The prevalence of endometriosis was 47% (104/221), including stage I (39%, 41/104), stage II (24%, 25/104), stage III (14%, 15/104), and stage IV (23%, 23/104) disease. Multiple other studies, the majority of which were retrospective, also indicated that the monthly fecundity of patients with endometriosis may be decreased by half compared to women without the disease. The precise cause-effect relationship between endometriosis and infertility remains controversial. In advanced cases of endometriosis, with distorted pelvic anatomy, the mechanism of infertility is more easily explained, but there is no satisfactory hypothesis that unequivocally explains the association of early stages of endometriosis with infertility. Endocrine dysfunctions such as luteal phase defect and luteinized unruptured follicle syndrome have been proposed as the cause in many studies.

Laparoscopy with or without histological verification is widely used to diagnose and rule out the presence of endometriosis. Furthermore r-ASRM classification can be used to express the severity of the disease. However, the literature on the diagnostic value of a laparoscopy is very limited. Data on complications and adverse events are similarly limited, a reporting bias. A negative diagnostic laparoscopy in women with symptoms and signs of the disease is highly reliable for the exclusion of the diagnosis of endometriosis.

In this study 50 patients underwent laparoscopy and the rest (15) underwent laparotomy according to the decision taken previously. The commonest site of endometriosis was uterosacral ligament (n=58=89%) and ovarian endometriosis was noted in (63%) cases. But Vercellini et al conducted a study on 244 symptomatic patients and found out that ovarian endometriosis was the commonest site and found in 108 patients followed by combined peritoneal and ovarian lesion in 57 patients.

It was also observed in this study that that most of the lesions (35%) were black, haemosiderin deposits followed by red, pink, vesicular blobs in 25% cases. There were also vesicular blobs, clear vesicles and white or yellow peritoneal defects. There were even spots of endometriosis which did not fall in any specific type. (21%).This is of immense clinical importance. Because of the variation in presentation of endometriosis, it is often very difficult to diagnose the condition. Precise diagnosis regarding presence, location, and extent of endometriosis is very much necessary for further evaluation and surgical planning of endometriosis.

This study revealed that endometrioma was present in 31% patients mostly in stage IV endometriosis. This reflected that endometrioma was usually a feature of severe disease and that isolated endometrioma was unlikely without the involvement of the peritoneal cavity.

After noting the site, type and extent of the disease, the r-ASRM scoring was done and it was correlated with the pain score given preoperatively. It showed that there was a strong positive correlation between severe pain and stage IV disease (Correlation co efficient 0.711). There was no correlation between moderate pain and severity of disease (Correlation co efficient 0.390). There is a negative correlation between milder forms of pain with severity of disease. Study conducted by Vercellini also concluded that stage of endometriosis per se,
independent of the lesion site, was not correlated with the frequency or severity of dysmenorrhea and non-menstrual pain. The severity of deep dyspareunia was found to be inversely proportional to the endometriosis score. Another study by Porpora et al. similarly concluded that no significant correlation was found among revised American Fertility Society stage of endometriosis; presence and size of ovarian endometriomas; extent, type, and site of peritoneal lesions; and pain scores. This is in contrast to a study done by Mehmud in Pakistan in 2007 which showed there was a significant positive correlation between chronic pelvic pain and R-AFS scoring but not with dysmenorrhea.

So, this study further supported that in cases of pelvic endometriosis, a newer classification is needed as a supplement to the r - ASRM score. Enzian classification was first described by Haas et al. in 2013 which revealed that the locations of endometriosis in the Enzian classification correlated partially with clinical symptoms, and the classification’s severity grades correlated substantially with pain and dysmenorrhea.

Small sample size of this study does not depict the varied picture of endometriosis. This is the limitation of this study. A larger study with a bigger sample size comparing the r ASRM system and Enzian system is required for further evaluation of disease.

Conclusion:
With all those observations it was concluded that, there was no relationship between frequency and severity of pain symptoms and disease stage of endometriosis. So a new classification system is warranted for management of endometriosis related pain. In view of these clinical results, use of the Enzian classification can be recommended as a supplement to the rASRM score for detailed description of endometriosis.

References:
Treatment Seeking Behavior and the Profile of Infertile Patients Attending the Tertiary Infertility Center at Dhaka

Summary:
Background: Motherhood is an integral part of womanhood and being childless is a devastating experience for a woman in developing countries like Bangladesh. Majority of patients in developing countries have virtually no access to treatment. Few health facilities have provision for proper diagnosis and treatment for infertility. There is a general lack of awareness among the public regarding infertility. In the quest for conception, many couples adopt for alternative therapies and religious rituals killing crucial age and time.

Objective: To find out the treatment seeking behavior and the profile of infertile patients attending a tertiary infertility center at Dhaka, Bangladesh.

Methods: During a period of five years from January 2001 to December 2005, 8580 new patients attending a tertiary infertility center at Dhaka were included in the study.

Results: Treatment seeking behavior of infertile patients attending Center for Assisted Reproduction, (CARe) Dhaka revealed 30% of the patients initially go to the traditional healers for the relief of infertility, 36% consult both traditional healers and doctors and 32% consulted with GP and Gynae specialist, and only 2% came straight to the tertiary center (CARe) for their subfertility. 55% of the patients attending the clinic were from urban area and 45% were from rural area. The maximum number of patients were from Dhaka division followed by Chittagong, Khulna, Barisal, Sylhet and Rajshahi. The overall primary and secondary infertility were in 63.34% and 36.66% of the patients respectively. 90% of the patients were Muslim and 9% were Hindu and 1% were from other religion. Only 32.37% of the patients took treatment in the clinic for their infertility. Male factor problems as identified among the male partners of the infertile couples were azoosperma in 18%, abnormal semen parameter in 24%, and normal semen parameter in 58%. Among the female partners completing investigations, 17% suffered from anovulation, 20% from premature ovarian failure and 3% from ovarian failure, with a total of 40% of the women suffering from ovarian factor, 8% suffered from endometriosis, 7% from bilateral tubal block, 3% from uterine factor problem. In 42% women there was no apparent cause in the females. Untreatable causes of infertility among the infertile couples were in 3.75% of the patients. Ovarian failure was in 3% cases, testicular failure in 0.5% and uterine factor in 0.25% of cases. 75% of the women were less than thirty five years of age where as 29% of the males were less than 35 years.

Conclusion: Causes of infertility vary from region to region so also social and cultural conditions. Financial condition also affects the health seeking behavior of the patients. For the purpose of management of infertile couples the cause of infertility is important to understand so that the options of treatment and the prognosis can be discussed with the patients.

Introduction:
Access to adequate comprehensive reproductive health services, including infertility care, is a basic reproductive right. Women go through various treatment-seeking modes to avoid the adverse consequences of childlessness. We wanted to find out the health-seeking behavior of infertile patients and the major causes of infertility in patients attending a tertiary infertility center at Dhaka, Bangladesh. Since the last 12 years tertiary infertility center facility is available in Bangladesh. Awareness on infertility management and the information that infertility is treatable and the treatment is available in the country is being focused by the physicians and the print and other medias. 8-10% of the reproductive age group couples suffer from infertility affecting some 50-80 million people. In countries with poor health care facilities infertility rates are also highest. Majority of the infertile couples blame their fate for infertility. A significant part of infertile couples seek treatment from improper place for their infertility. ‘Helping Families’ is a fertility survey endorsed by the Indian Society for Assisted Reproduction (ISAR), the

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Asia-Pacific Initiative on Reproduction (ASPIRE) and according to their survey 64% of the couples studied believed in God’s will and delayed treatment. Seeking help can take many forms and is not restricted exclusively to medical services, and their long waiting can impede success infertility treatment by loosing crucial age and time. It is important to know the health seeking behavior of the patients, the etiologic factors for the proper prevention and management of the patients and to plan the health care facilities according to the demand of the patients. Local healers in the informal sector were found to be the most popular health service option among the rural childless women. The factors for utilizing them included low costs, the gender of the provider (with same-sex providers being preferred), having a shared explanatory model with the healers, and easy availability. However, despite their affiliation with modern treatment, urban childless women still believe, like their rural counterparts, that the remedy for childlessness ultimately depends on God. As a result, in addition to biomedical treatment, many return to or simultaneously pursue various traditional, spiritual or folk treatments.

Results:
During a period of five years from 2001 to 2005, 8580 new patients was enrolled in Center for Assisted Reproduction, (CARe) Dhaka, a tertiary infertility center in Dhaka, Bangladesh (Fig:1). Health seeking behavior of infertile patients attending the outdoor of Center for Assisted Reproduction, (CARe) Dhaka, Bangladesh revealed 30% of the patients initially went to the traditional healers for the relief of infertility, 36% consulted both traditional healers and doctors and 32% consulted with GP and Gynae specialists, and only 2% came straight to the tertiary center (CARe) for their subfertility. Among the patients attending the clinic 33.25% gave only one visit, when a complete history, physical examination and recording of the previous investigations done by the patients was recorded. 34.37% of the patients completed the investigations required for their evaluations and only 32.37% took treatment in the center for their infertility.

The overall primary and secondary infertility was in 63.34% and 36.66% of the patients respectively. Among the patients giving only one visit 56% were suffering from primary infertility and 43.5% suffered from secondary infertility, among the patients completing investigation 68.5% and 31.5% suffered from primary and secondary infertility, whereas 65% and 35% of the patients taking treatment in the clinic suffered from primary and secondary infertility respectively (Fig:2).

The maximum patients were from Dhaka division followed by Chittagong, Sylhet, Rajshahi, Khulna and Barisal (Fig:3). Patients taking treatment were mostly from Dhaka division. Male factor problems as identified were azoospermia, abnormal semen parameter, normozoospermia in the patients attending the clinic.


Fig.-2: Distributions of Patients attending CARe – IVF from to different divisions of Bangladesh.
were in 18%, 24%, and 58% respectively. In patients completing investigations 17% suffered from anovulation, 23% from premature ovarian failure and ovarian failure, 8% suffered from endometriosis, 7% from bilateral tubal block, 3% uterine factor problem and 42% had no apparent problem. Untreatable causes of infertility were in 3.75% of the patients, ovarian factor was in 3% cases, testicular failure in 0.5% cases and uterine factor in 0.25% of cases. In 42% women there was no apparent cause.

Discussion:
The principal objectives of this study are to improve our understanding of infertility patients’ patterns of health seeking behavior and their patterns of access to infertility treatment. Treatment seeking behavior showed that 30% of the patients initially went to the traditional healers for the relief of infertility, 36% consulted both traditional healers and doctors and 32% consulted with GP and Gynae specialist, and only 2% came straight to the tertiary center (CARe) for their subfertility. One study showed that the delay in seeking assistance may be due to poor knowledge of infertility, unavailable and/or inaccessibility of appropriate services, prior unsuccessful medical intervention and previous visits to traditional healers. [2] In another study, infertile couple seek help from native doctors and prayer groups rather than orthodox Medicare. This was observed in this study where 65.1% had previously used traditional medications. [3]

Subfertile couples consulting fertility clinics are commonly regarded as highly motivated to achieve conception [4]. Bangladesh is an economically constrain country; almost one third of our patients desiring children give only one visit where as one third of the patients complete investigation and confirm the cause of infertility and almost one third come for treatment. This high drop out is also reported in different studies.
in developed countries. In Sweden where IVF cycles were fully reimbursed, 65% of couples did not complete the full treatment program of three IVF cycles. Only 32.37% of the patients took treatment in the clinic for their infertility which is almost similar to that observed in other developed countries. Demand and the availability of infertility services in the United States increased during the 1980s and early 1990s. Of the 6.7 million women with fertility problems in 1995, 42% had received some form of infertility services. The most common services received among these women were advice in 60% and diagnostic tests 50%, medical help to prevent miscarriage 44% and drugs to induce ovulation in 35%. Another study showed approximately only 44% of women with infertility sought medical assistance which is comparable to our study.

The percentage of secondary infertility is lowest in Asia and in developed countries; 23% and 29%, respectively. In our study the overall secondary infertility was 36.6% which is higher than the other studies in Asia. In the so-called “infertility belt” of Sub-Saharan Africa, the percentage of couples with secondary infertility exceeds 30% in some countries. A study done in Mongolia showed that 43.7% of women had secondary infertility. One study showed that 66% had primary infertility and 34% secondary infertility and in another study done in Dhaka primary and secondary infertility were 56% and 44% which is similar to our study.

Belsey suggested that a higher rate of secondary infertility, compared to primary infertility, could be used as a crude indicator of the possible effects of post abortal and post partum infection.

In our study male factor problems as identified were azoospermia in 18%, abnormal semen parameter in 24% and normozoospermia in 58% whereas in a study in Mongolia azoospermia was found in 20.5% cases, abnormal semen parameter in 23.9% and normozoospermia in 55.6% attending the clinic. In our study bilateral tubal block was in 7% of the infertile women where as in a study in Nigeria tubal occlusion was in 16.9% and bilateral tubal blockage in 15.6% and 28.9% of the infertile women which are quite high than our series. Anovulation was in 17% in our study and 22.3% in other study. In another study in Bangladesh endometriosis was in 11% where as in our study, 8% was diagnosed as endometriosis.

Conclusion:
Causes of infertility vary from region to region so also social and cultural conditions. Financial condition also affects the health seeking behavior of the patients. Care for infertility in developing countries is as important as fertility control. As infertility usually does not cause any physical disability, little attention is paid at the national level. Childbearing and family are considered a right of every human being. Infertility is a public health problem that requires appropriate diagnosis and determinants. In developing countries, reproductive tract infections, including sexually transmitted diseases, complications of unsafe abortions, and puerperal pelvic infections are regarded as important causes of infertility. Proper awareness and education of the patients and medical professionals and safe and efficient treatment facility are the key factors to protect this basic right of the patient.

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Color Doppler Evaluation of Cerebral - Umbilical Pulsatility Ratio and its Usefulness in the Diagnosis of Intrauterine Growth Retardation and Prediction of Adverse Perinatal Outcome

S MAHMOODa, S CHOWDHURYb, SB CHOWDHURYc

Summary:
The purpose of this study is Evaluation of cerebral umbilical pulsatility ratio by color Doppler and to estimate the value of pulsatility index ratio of cerebral umbilical vessels in the diagnosis of small-for-gestational-age (SGA) fetuses and in the prediction of adverse perinatal outcome. Validity of the test were confirmed by determining sensitivity, specificity, accuracy, positive predictive value, negative predictive value. The study population comprised 40 pregnancies of 30-41 weeks gestation that had been diagnosed clinically as intrauterine growth retardation (IUGR) over a period of 1 year. The cerebral - umbilical pulsatility ratio (C/U ratio) were calculated. The pregnancies were followed up and the final perinatal outcome of each case were noted. Various intraparum and neonatal indicators were used to assess the outcome, with an adverse outcome being defined as the presence of one or more of these indicators. The most common adverse perinatal outcome was birth asphyxia, low apgar score, stay at NICU, still birth and caesarean section for fetal distress. Of the 40 pregnancies in the study, 30 (75%) showed abnormal C/U ratio. Among these, 32 (80%) were SGA and 32 (80%) had adverse perinatal outcome. Of the 30 out of 40 pregnancies that showed abnormal C/U ratio (<1.08), all 30 (80%) were SGA and had adverse perinatal outcome. The results were correlated with parameters of fetal outcome. Inferences drawn from the study was that C/U ratio is a tools for prediction of SGA fetuses and adverse perinatal outcome.

Keywords: Intrauterine growth retardation, pulsatility index, middle cerebral artery to umbilical artery pulsatility index ratio.

Introduction:
Intrauterine growth retardation is characterized by failure of the fetus to reach its normal growth potential. Intrauterine growth retardation is the second leading cause of perinatal death (Wolfe et al. 1989)1. IUGR is associated with significant morbidity including increased rates of meconium aspiration, hypoglycaemia, respiratory distress syndrome, intrapartum asphyxia, developmental delay and still birth (Berkowitz et al. 1988)2. Intrauterine growth retardation is associated with an increased risk of perinatal mortality and morbidity and impaired neurodevelopment (Kok et al. 1996)3. The correct detection of the compromised Intrauterine growth retardation fetus to allow for timely intervention is a main objective of antenatal care.

Umbilical artery and middle cerebral artery Doppler velocimetry is the most rigorous evaluation test among the noninvasive tests of fetal well being (Giles et al. 1985)4. Placental insufficiency, whether primary or secondary to maternal factors such as hypertension, poor nutrition etc. is the most common cause of intrauterine growth retardation which is an important obstetric problem on account of the high association perinatal mortality and morbidity. It is essential to recognize placental insufficiency early so that its hazards can be reduced (Bano et al 2010)5.

Doppler ultrasound allows a noninvasive assessment of fetal haemodynamics. Doppler ultrasound enable a better understanding of the haemodynamic changes and has therefore become one of the most important clinical tools for fetomaternal surveillance in high risk pregnancies. Doppler investigation of umbilical arteries provides information concerning perfusion of the fetoplacental circulation. Doppler value is considered as normal when the cerebral-umbilical ratio is above 1.08 and below the value is considered abnormal. (Gramellini et al. 1992)6. Bano et al.20105 Calculated the cerebral-umbilical ratio and found that it remains constant in the last 10 wks of
pregnancy therefore it is used a single cut off value of 1.08 for all the cases of 30-41 wks of gestation.
The brain sparing effect is associated with an abnormal cerebral-umbilical ratio (<1.08). However, if hypoxia persists, the diastolic flow return to the normal level. The cerebral-umbilical ratio remains constant during, the last 10 weeks of gestation and provide better diagnostic accuracy than either vessels pulsatility index alone (Fleischer et al, 1985)7. Doppler waveform abnormalities have been reported to be the most accurate predictor of poor neonatal outcome.

Materials and Methods:
This prospective study was carried out in department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period of January 2014 to December 2014 to establish the usefulness of Color Doppler evaluation of C/U pulsatility index ratio in diagnosis of IUGR and adverse perinatal outcome. Validity of the test were confirmed by determining sensitivity, specificity, accuracy, positive predictive value, negative predictive value.

Prior to commencement of this study the respective authority approved the research protocol. Proper permission was taken from the concerned department for this study. All the patients included in this study were informed about the nature of risk and benefit of the study. Clinically diagnosed as a case of IUGR in BSMMU referred to the department of Radiology and Imaging of BSMMU were included.

Patients who are very sick with medical disorders like, hypertension, multiple pregnancies, patients refusing the procedure, difference in opinion of consultant radiologist regarding Doppler flow were excluded from the study.
For this purpose, a total number of 40 patients were enrolled in this study. Patients with suspected IUGR admitted in BSMMU referred to the department of Radiology and Imaging was included in this study. All the 40 patients were subjected to a repeated USG examination after 15 days of the initial study, when the finding of the initial study were reconfirmed. The 40 patients were subjected to color Doppler examination (Siemens Sonoline, G60s), using 3.5 MHZ transducer with 3mm sample volume and medium filter. After technically satisfactory Doppler waveform had been recorded, the Pulsatility index of the umbilical artery (UA) and the middle cerebral artery (MCA) was noted and the ratio of the MCA and UA (the C/U ratio) were calculated. The pregnancies were followed up and the lineal perinatal outcome of each case were noted. Various intrapartum and neonatal indicators were used to assess the outcome, with an adverse outcome being defined as the presence of one or more of these indicators. All these information were collected in pre-designed structured data collection sheet.

Sonographic variable
C/U pulsatility index Ratio= MCA PI/ UA PI.
The cerebral umbilical PI ratio remains constant in the last 10 weeks of the pregnancy therefore a single cut-off value of 1.08 considered normal. Below that value, velocimetry was considered abnormal, according to Gramellini et al 1985, Bano et al 2010.

Diagnostic criteria:
Normal C/U Pulsatility index ratio: > 1.08
Abnormal C/U Pulsatility index ratio: < 1.08
All the findings were analyzed by appropriate standard statistical method.

Demographic and clinical variables:
Gestational age at delivery.
Presence of IUGR (Birth weight <10th percentile) for gestational age
Normal Birth weight.
Normal outcome.
Apgar score < 7 at 5 minutes.
Stay at NICU.
Still birth.
Birth asphyxia.

Result:
Out of 40 pregnancies in the study, who were evaluated by Doppler USG to identify the normal and abnormal cerebral umbilical pulsatility index ratio, most of them were found abnormal 30 (75 %) and normal were 10(25 %).
Out of 40 patients 32 had Small for gestational age and 08 had normal birth weight.
Out of 40 patients 32 had adverse perinatal outcome and 8 had normal outcome.
Among 30 cases, who had abnormal PI ratio, 28 cases were SGA and 2 had normal birth weight. Whereas, among normal pulsatility ratio only 1 was SGA. (Table-II)
Among 30 cases of abnormal PI ratio, all 30 had adverse perinatal outcome. Whereas among 10 cases of normal PI ratio only 2 had adverse perinatal outcome. (Table-III)
Tables II and III depict the diagnostic performance of various Doppler flow indices in identifying SGA fetuses.
and predicting adverse perinatal outcome. The sensitivity and positive predictive value (PPV) were higher for the C/U ratio

**Discussion:**

IUGR is a pathological condition which is strongly related to the development and function of the uteroplacental and fetoplacental circulation. An adequate fetal circulation is necessary for fetal growth. UA velocimetry correlates with hemodynamic changes in the fetoplacental circulation, with an increase in the number of the tertiary stem villi and arterial channels, as the fetoplacental compartment develop, the impedance in the UA decreases. A diastolic component in the UA flow velocity waveform appear during the early second trimester and progressively increase in the gestational age. A mature UA flow velocity waveform pattern shows low impedance and high diastolic flow with a low pulsatility index. During normal pregnancy, the MCA shows high resistance and low diastolic flow with an increase in the pulsatility index.

Gramellini et al. (1992) calculated the C/U ratio and found that remain constant in the last 10 weeks of pregnancy, therefore this study considered a single cut-off value of 1.08 for all cases of 30-41 weeks of gestation. Using the cut-off value, study population was divided into normal and abnormal.

In pregnancies with chronic fetal hypoxia, the blood volume in the fetal circulation is redistributed in favour of vitally important organs, the heart, kidneys, and brain. Vasodilatation of the MCA, with an increase diastolic flow through it, result in a decrease in its PI. The resulting hyperperfusion is considered pathological.

In IUGR, umbilical blood flow is significantly reduced, mainly due to changes in the placental vascular
resistance. Giles et al. have found that a decrease in the number of resistance vessels in the tertiary stem villi in the placenta causes an increase in resistance, leading to decreased flow through the UA and an increase in the UA PI. This is described as umbilical placental insufficiency. Fleischer and Schulman have found that in IUGR complicated by pregnancy-induced hypertension, there is inadequate trophoblastic invasion of the spiral arteries, leading to increased resistance in the spiral arteries and decreased blood flow in the placental vascular bed and in the UA, thereby resulting in an increase in the UA PI. This is described as uteroplacental insufficiency. Several blood flow classes have been defined by Hofer et al. to describe abnormal UA waveform patterns. Increasing pathological significance is ascribed to a decrease in diastolic flow, absence of diastolic flow and reversal of diastolic flow. All these patterns were associated with increased UA PI. Patients with absent end-diastolic volume (AEDV) and reverse end-diastolic volume (REDV) have the gravest outcome. Fetuses with AEDV require intensive surveillance as fetal well-being may deteriorate within a few days. Fetuses with REDV are most severely compromised. REDV is indicative of a preterminal fetal state.

In pregnancies with chronic fetal hypoxia, the blood volume in the fetal circulation is redistributed in favor of vitally important organs, i.e., the heart, kidneys and brain. Vasodilatation of the MCA, with an increase in diastolic flow through it, results in a decrease in its PI. The resulting hyperperfusion is considered pathological. This ‘brain-sparing effect’ is associated with an abnormal C/U ratio (<1.08). However, if hypoxia persists, the diastolic flow returns to the normal level. Presumably, this reflects a terminal decompensation in the setting of acidemia or brain edema.

This study dealing with a high-risk population, maximizing the sensitivity of a screening test is an ideal goal. For a screening system to be effective, it must be sensitive enough to detect the disease at an early stage so that treatment can bring a cure, sufficiently specific, acceptable to patients and adaptable to widespread screening, cost effective:

The Color Doppler study of C/U vessels has made an advancement in new generation sonography equipment and expertise, which has brought a revolution in the field of diagnostic imaging to diagnose IUGR prenatally. This non invasive imaging modality will be able to replace the other invasive diagnostic procedures.

This current study was carried out with an aim to establish the usefulness of C/U Pulsatility index ratio in diagnosis of IUGR and prediction of adverse perinatal outcome.

Our results were more encouraging for the prediction of adverse perinatal outcome rather than diagnosing IUGR. It has been estimated that 41-86% of SGA babies can be detected with the routine use of symphysis-fundal height measurements. According to one meta-analysis of USG fetal biometry, AC and estimated fetal weight (EFW) are the best predictors of fetal weight below the 10th percentile. In high-risk populations, the sensitivity of using AC below the 10th percentile is 73-95%, whereas with EFW, the sensitivity is 43-89%. In low-risk populations, the corresponding sensitivities are 48-64% for AC and 31-73% for EFW. Biophysical profile is another method for detecting IUGR, with a sensitivity of 77.7%.

We further found that when compared with other modalities, although Doppler velocimetry was relatively less sensitive for diagnosing SGA fetuses, because uteroplacental insufficiency is just one cause of IUGR, it proved to be very useful in predicting IUGR fetuses at risk for adverse perinatal morbidity and mortality. None of the other modalities has been as promising in detecting adverse perinatal outcome as Doppler velocimetry. Among the number of biophysical tests available to assess fetal well-being, the most common methods are amniotic fluid volume (AFV), biophysical profile scoring (BPS) and nonstress test (NST). A reduced AFV (either measured by maximum vertical pocket < 2 cm or a four-quadrant amniotic fluid index (AFI) < 5 cm poorly correlates with the actual AFV and does not accurately predict adverse perinatal outcome. A review of 18 studies indicated that an AFI < 5 cm was associated with an increased risk of Cesarean section for fetal distress (relative risk [RR] 2.2; 95% confidence interval [CI] 1.5-3.4) and Apgar score of ≤ 7 at 5 min (RR 5.2; 95% CI 2.4-11.3), but not with neonatal acidosis. Large observational studies have shown an association between reduced AFV and perinatal morbidity and mortality, but the precise value is poor (< 10%) and, also, there is little evidence to support intervention with...
isolated oligohydramnios (with a normal UA Doppler).\textsuperscript{14} Yoon \textit{et al.}\textsuperscript{15} attempted to compare the performance of BPS and UA Doppler velocimetry in the identification of fetal acidemia, hypoxemia and hypercarbia as determined by PH and gas analysis of fetal blood obtained by cordocentesis in 24 patients. Although they found a strong relationship between the degree of fetal acedia and hypercarbia and the results of UA Doppler velocimetry and BPS, Doppler velocimetry proved to be a better explanatory variable for these outcomes than the BPS.\textsuperscript{15} Another study was performed by Gonzalez \textit{et al.}\textsuperscript{16} to compare the efficacy of NST, BPS and abnormal Doppler findings in predicting adverse perinatal outcomes in IUGR. The PPVs of abnormal Doppler for respiratory distress syndrome and the composite of adverse outcomes were 36\% and 42\%, respectively. Of the testing modalities compared, only abnormal Doppler significantly predicted respiratory distress syndrome and the composite of adverse outcome. Hence, they concluded that in cases of IUGR, the presence of abnormal Doppler was the best predictor of adverse perinatal outcome.\textsuperscript{18} Padmagirison Radhika \textit{et al.}\textsuperscript{17} conducted prospective antenatal fetal surveillance in 55 women to compare the efficacy of Doppler velocimetry and NST in predicting fetal compromise in utero in cases of severe pre-eclampsia or IUGR. There were 29 cases with abnormal Doppler and 20 cases with abnormal NST. In addition, Doppler abnormalities preceded NST changes with a lead time of 4.14 days and there were 10 perinatal deaths, six of which occurred in the group where both the tests were abnormal. They concluded that Doppler identifies fetal compromise earlier than NST. The lead time helps to plan delivery in preterm compromised pregnancies, resulting in better perinatal survival.\textsuperscript{17}

Validity test was done by calculating sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) respectively. The present study findings were discussed and compared with previously published relevant studies.

Gramellini \textit{et al.}\textsuperscript{16} (1992) had shown their study by a C/U pulsatility index ratio of less than 1.08 had a sensitivity of 68\%, specificity 98.4\%. Positive predictive value 94.4\%, Negative predictive value 88.8\% and Diagnostic accuracy 90\% for predicting adverse perinatal outcomes in IUGR.

Schulman \textit{et al.}\textsuperscript{17} (1999) reported the sensitivity of 63\% for predicting adverse perinatal outcomes in IUGR.

Obido \textit{et al.}\textsuperscript{16} (2005) reported by a C/U PI ‘ratio of less than 1.08 had a sensitivity of 90\% predicting adverse perinatal outcomes in IUGR.

Bano \textit{et al.}\textsuperscript{5} (2010) Studied by a C/U PI ratio of less than 1.08 had a sensitivity of 83.3\%, specificity 100\%, Positive predictive value 100\%. Negative predictive value 94.3\% and Diagnostic accuracy 95.6\% for predicting adverse perinatal outcomes in IUGR.

In this study by using a C/U pulsatility index ratio of less than 1.08 and sensitivity is 96.7\%, specificity 77.7\%, Positive predictive value 93.7\%, Negative predictive value 87.5\% and Diagnostic accuracy 92.5\% for predicting adverse perinatal outcomes in IUGR.

In asymmetrical IUGR there is high umbilical artery PI and low middle cerebral artery PI. As a result, the C/U ratio is lower than normal growth retarded fetuses.

Bano \textit{et al.}\textsuperscript{5} (2010) and Obido \textit{et al.}\textsuperscript{16} (1992), have observed in their series that Doppler was significantly correlated with adverse perinatal outcome where sensitivity ranged from 83-90\%, specificity from 71-100\%. Thus the parameters provide strong evidence that Doppler analysis is of great value in evaluation of prenatal diagnosis of fetal at risk in IUGR.

The cerebral umbilical PI ratio incorporates data of both placental status (umbilical artery) and fetal response (Middle cerebral artery) in the prediction of adverse outcomes.

In this study, comparing the use of the C/U pulsatility index ratio, we found similar efficiency in the prediction of IUGR and adverse perinatal outcomes. This implies that perinatal centers can use this method in the evaluation of cases of IUGR. According to cerebral umbilical PI value 30 (75\%) were diagnosed as abnormal and 10 (25\%) as normal flow pattern.

Perinatal findings showed 32 were SGA and 8 have normal birth weight.

The validity of cerebral umbilical PI ratio for diagnosis for diagnosis of IUGR were studied by calculating sensitivity, specificity, accuracy PPV, NPV which were 96.55\%, 81.81\%, 92.5\%, 93.33\% and 90\% respectively.

The validity of cerebral umbilical PI ratio for adverse perinatal outcome were studied by calculating
sensitivity, specificity, accuracy, PPV, NPV which were 96.7% 77.7%, 92.5%, 93.7% and 87.5% respectively.

Color Doppler study over other imaging modalities is preferred due to its relative accuracy, non invasiveness, lack of ionizing radiation, less expensiveness and availability.

**Conclusion:**
In this study Color Doppler findings of cerebral-umbilical vessels and the validity test are almost identical as observed by other investigators compared with perinatal findings, so it can be concluded that color Doppler evaluation of MCA and UA PI ratio is an useful modality in diagnosis of IUGR and prediction of adverse perinatal outcome.

**References:**
Summary:
Burning Mouth Syndrome (BMS) is characterized by chronic oro-facial pain in the absence of specific oral lesions & clinically apparent mucosal alterations. It is more commonly observed in middle aged patients & postmenopausal women. It often affects tongue, cheek, lip, hard & soft palate. Usually symptoms are better observed in morning, worsen during the day and typically subside at night. The condition is multifactorial origin, often idiopathic and its etiopathogenesis remain largely enigmatic. Associated medical conditions may include neurologic and metabolic disorder, gastrointestinal, urogenital as well as drug reactions. BMS are of two types, primary & secondary. Primary BMS is essential or idiopathic where secondary BMS is caused by local, systemic and/or psychological factors. Clinical diagnosis depends on the careful history taking, physical examinations and laboratory findings. Vitamin, Zinc or Hormone replacement therapy has been found to be effective with deficiency of the corresponding factors. The drug therapy with alpha-lipoic acid, capsaicin, clonazepam, benzodiazepines, tricyclic antidepressants, anticonvulsants may be effective in symptomatic treatment of BMS. But the treatment is still unsatisfactory and there is no definitive cure.

Keywords: Burning Mouth Syndrome, Glossodynia, Review, Stomatodynia

Introduction:
The international association for the study of pain (IASP) has identified BMS as a “Distinctive nosological entity” characterized by “unremitting oral burning or similar pain in the absence of detectable oral mucosa change”\(^1\). Burning mouth syndrome is typically described by the patient as burning, stinging and/or itching of the oral cavity in the absence of any organic disease. It lasts at least for 4-6 months duration and typically located on the tongue, particularly in the tip and lateral borders, lips, hard & soft palate, alveolar ridges with the buccal mucosa and floor of the mouth being less frequently involved\(^2-5\). BMS mainly affects middle aged or old women with hormonal changes or psychological disorders\(^6-8\). BMS can be accompanied by Dysgeusia (distortion in sense of taste), Glossodynia (painful tongue), Glossopyrosis (burning tongue) & Xerostomia (dry mouth). However, careful history taking, physical examination and appropriate laboratory testing can be effective in the proper treatment planning of BMS. BMS is usually treated through a multidisciplinary approach by antidepressants, analgesics, antiepileptics, antifungals, antibacterials, sialagogues, antihistamines, anxiolytic, antipsychotics and vitamin, minerals and hormonal replacements. Moreover patients need psychological support for the long term rehabilitation.

Discussion:
Epidemiology
BMS typically observed in middle age/ old women with an age range of 38-78 years\(^3,9-11\). The condition is extremely rare in patients under 30 years and never been reported in children and adolescence\(^12\). BMS has a significant female predilection with the ratio is about 7:18-11,13. These differences between genders may be explained by biological, psychological & sociocultural factors. Prevalences of BMS reported from international studies ranges from 0.7%- 4.5%\(^11,14-18\). Epidemiological studies revealed that this condition is more common in pre and postmenopausal women which ranges upto 12-18%\(^19\).
Recent analysis showed an increase likelihood of gastrointestinal & urogenital disease in patient with BMS. Patient with BMS had a statistically higher intake of medications for gastric disease.

**Pathophysiology:**
Though the pathophysiology of Burning Mouth Syndrome is not well understood, significant differences of thermal and nociception thresholds of patients with BMS are established in comparison to control subjects. Thus a neuropathic mechanism for BMS is currently favored though the controversy remains exist between peripheral and central dysfunction. Central neuropathic mechanisms have been demonstrated following thermal stimulation of the nerve in patients with BMS. Patients with BMS show patterns of cerebral activity similar to those that appear in other neuropathic pain disorders, suggesting that the cerebral hypoactivity could be an important element in the pathogenesis of BMS.

**Etiological factors**
The exact etiology of BMS is unknown. Although there is no definitive cause of primary BMS, there are numerous potential secondary causes of the burning mouth syndrome. Several factors play an important role in the etiology of BMS. These are grossly classified to local, systemic and psychological factors. The contributing factors may be physical, chemical or biological (some bacteria and fungi). The important factors are:

1. Mechanical factors: Poorly fitted oral or dental prosthesis that produce microtrauma or local erythema.
2. Parafunctional Habits: Tongue thrust, Bruxism, clenching, Continual rubbing over the teeth & prosthesis, buccal, labial, lingual biting & compulsive movements of the tongue.
3. Local allergic reactions: High levels of residual monomers, nylon, ascorbic acid, cinnamon, nicotinic acid, dental materials (zinc, cobalt, mercury and palladium). Sodium lauryl sulfate a detergent in toothpaste may also be involved in the development of dry mouth.
4. Nutritional abnormalities: Vitamin B1, B2, B6, B12, as well as folic acid, pernicious anemia, iron deficiency anemia, Vitamin E and Vitamin C deficiencies.
6. Hormonal change: Dryness of mucosal membrane from age related reduction in estrogen & progesterone levels & increased frequency of psychological disorders of middle aged and elderly women, uncontrolled diabetes mellitus, gastrointestinal reflux, thyroid dysfunction.
7. Drugs: Antihistamine, Neuroleptics, anti-hypertensives principally those act on renin angiotensin system (captopril, enalapril, lisinopril) & ACE inhibitors.
8. Psychiatric disorders: Anxiety, depression, personality disorder, cancerophobia, higher tendency to worry about health.
10. Autoimmune disease: Sjogren’s syndrome, systemic lupus erythematosus, lichen planus.
11. Others: Loss of taste buds, depapillation of tongue, oral desquamation due to age change, side effects of radiation or chemotherapy, cranial nerve injury, Parkinson’s disease, trigeminal neuralgia, glossopharyngeal neuralgia, herpes simplex, herpes zoster, smoking.
12. Idiopathic factors

**Classification of BMS**
According to clinical symptoms BMS is classified to primary or essential/ idiopathic and secondary.

1. Primary or essential/ idiopathic: In primary BMS organic causes cannot be identified and peripheral or central neuropathological pathways are involved.
2. Secondary BMS: Result from local or systemic pathological conditions. Causes are local infection, autoimmune diseases of the oral mucosa (lichen planus), nutritional and vitamin deficiencies, glossitis, salivary disorders, allergies, irritation caused by reflux, dental-alveolar diseases, metabolic disorders, candidiasis, nerve damage, trauma, diabetes mellitus, gastrointestinal and urogenital diseases or administration of certain drugs.
According to pain pattern BMS is classified into three types\textsuperscript{4,12,14,21,41}:

1. Type-I (35%): Characterized by pain-free awakening, worsening throughout the day, and receiving its peak intensity by evening. This type is usually associated with systemic disorders such as nutritional deficiencies, diabetes mellitus.

2. Type-II (55%): Characterized by continuous symptoms throughout the day but not at night. This type is usually associated with psychological disorders.

3. Type-III (10%): Characterized by intermittent symptoms with pain-free episodes during the day. This type is usually associated with allergic reactions.

Clinical features
The chief complaint of BMS patient is oral burning. The symptom is described by individual patient as continuous & chronic discomfort, sudden or intermittent onset of pain. Pain is increased progressively during the day and pain is relieved by sleeping and eating foods (although some may worsen the pain)\textsuperscript{27,39}. Patient may also describe the symptom as tingling, scalding, annoying, tender or numb filling of the oral mucosa. The pain is primarily bilateral and typically on the anterior 2/3 of the tongue (71-78%) followed by dorsal and lateral border of the tongue, anterior portion of hard palate, labial mucosa or gingiva with no identifiable precipitating factors except stress and other psychological factors\textsuperscript{14-16,42}. To fulfill the diagnostic criteria for BMS, pain episode must occur continuously at least 4-6 months\textsuperscript{1,43}. Acidic or spicy foods may increase burning symptoms\textsuperscript{44}. BMS patient may suffer from headache & TMJ pain\textsuperscript{45}. They often show easy fatiguability, sensitivity, anxiety, muscular tension and a tendency to be more concerned about their health. Sleep disturbance may also be present. 70% of BMS patient has persistent test disorders as bitter, metallic or both\textsuperscript{3,8,46-48}. Xerostomia may be the complaints of approximately 46-67% of BMS patient\textsuperscript{6,8,11}. Other symptoms include dysgeusia, sensory disturbance and sticky sensation, dysphagia, burning irritation of lingual papilla, pruritis, and intolerance to prosthesis\textsuperscript{14,17}. Oral findings are erythema, geographic tongue, candidiasis, atrophic glossitis, lichen planus\textsuperscript{49}.

Diagnostic criteria
Taking a thorough and comprehensive history & laboratory findings are the key to diagnosis. Diagnosis of BMS is very much difficult because BMS is positively designed only by symptoms without signs or etiologies. The symptomatic triad rarely occurs simultaneously in one patient. Overlapping stomatitis may confuse the clinical presentation. However, some diagnostic work up include oral examination, salivary parameters, nutritional parameters, hormonal parameters, medication, parafunctional habits, contact allergies, psychological and psychosocial evaluation. There are various investigations that can be used to rule out secondary causes of BMS such as blood count which may reveal infections or anemia, blood level of iron, zinc, folic acid, vitamin B-complex, serum ferritin, fasting blood sugar, allergy testing, fungal or oral cultures, thyroid functions & serum autoantibodies\textsuperscript{4,44,50,51}.

Differential diagnosis of BMS
The BMS diagnosis may be confusing with stomatitis, atypical facial pain, atypical odontalgia, pemphigoid, pemphigus, denture design and tooth restoration failure, herpes simplex or herpes zoster, neoplastic lesions, trauma to lingual or mandibular nerve from dental surgery.

Treatment
Treatment of BMS patient varies in individual patient. A multidisciplinary approach is needed for the treatment of BMS. Primarily patients need psychological support. Patient must be informed about the nature of the condition. They should assured as the syndrome is common in middle aged & elderly individual and the syndrome is not any form of cancer. They should also inform that all the symptoms may not definitely disappear. The investigator should have a detailed review of patients personal, familiar, medical and dental histories and a careful interpretation of data obtained from various physical and laboratory investigations to identify the symptoms are primary or secondary. A lack of oral mucosal pathology is mandatory for the diagnosis of BMS. As the symptoms of primary BMS are idiopathic and its etiology is unknown, a variety of drug treatment is found beneficial in some research. Some drugs are used topically and some are systemically. Behavioral interaction is needed sometimes. Medications used for BMS include antidepressants, analgesics, antiepileptics,
antifungals, antibacterials, sialagogues, antihistamines, anxiolytic, antipsychotics and vitamin, minerals and hormonal replacements. Topical application of capsaicin (0.02% cream 3-4 times daily) has been used as a desensitizing agent or analgesic for treatment of oral mucosal burning. But it is usually unaccepted by the patient due to its taste. Furthermore it causes an increase in the burning sensation at the beginning of the treatment. Another topical drugs used are lidocaine, clonazepam, benzydamine, doxepin, lectoperoxidase. Clonazepam is the only topical therapy studied in a double-blind randomized placebo controlled fashion. The topical application of clonazepam (by sucking a tablet of 1 gm) two or three times a day for 14 days treatment period provided reduced burning in two thirds of the patients studied. The most commonly used local anesthetic agent lidocaine has not been shown as an effective treatment due to their short duration of analgesic action. The topical application of Aloe vera gel (0.5 ml three times a day) combined with tongue protector found to be effective. Systemic drugs for BMS treatment include gabapentin, pregabalin, amitriptyline, nortriptyline, clonazepam, pramipexole and capsaicin. Results with gabapentin were found little or no effect on BMS treatment while positive results were obtained with pregabalin use. Systemic use of capsaicin (0.25% three times a day for one month) is found a significant reduction of pain intensity. It is not recommended for extended treatment as 32% of patients experience gastric pain after 4 weeks of treatment. Systemic use of clonazepam (0.25 mg/day increasing to a maximum of 3 mg/day) has also been found better results. Combined topical and systemic use of clonazepam has found more effective. Several studies suggest that alpha lipoic acid (200 mg three times a day) can improve the symptoms in BMS at two months. This improvement is maintained during the first year in 70% of the patient. In other studies show that the combination of psychotherapy (one hour session weekly for two months) and alpha lipoic acid (200 mg three times a day for two months) was significantly more effective than psychotherapy alone or alpha lipoic acid alone. Secondary BMS is associated with causative factors. Laboratory findings are needed to identify the cause and treatment of BMS. Deficiencies of vitamin B-complex, folic acid, iron can be treated by supplemental use of these components. For the patients with zinc deficiency, zinc replacement therapy (14.1 mg per day for 6 months) has improved the condition. The prevalence of oral discomfort is higher in perimenopausal and post-menopausal women than in premenopausal women due to estrogen deficiency.

### Principal clinical features in different idiopathic orofacial pain conditions:

<table>
<thead>
<tr>
<th></th>
<th>Atypical facial pain (bone)</th>
<th>Atypical odontalgia (tooth)</th>
<th>Burning mouth syndrome (mucosa)</th>
<th>Idiopathic facial arthromyalgia (muscle, TMJ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain descriptors</strong></td>
<td>Emotional, mechanical, burning</td>
<td>Varied</td>
<td>burning</td>
<td>Spontaneous or during function or voluntary movements</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Moderate to intense</td>
<td>Moderate to intense</td>
<td>Weak to intense</td>
<td>Weak to intense</td>
</tr>
<tr>
<td><strong>Pattern</strong></td>
<td>Continuous</td>
<td>Continuous with possible remission</td>
<td>Continuous</td>
<td>Continuous with remission</td>
</tr>
<tr>
<td><strong>Localization</strong></td>
<td>Initially unilateral then bilateral</td>
<td>Initially a single tooth then may spread</td>
<td>Bilateral, symmetrical</td>
<td>Unilateral or bilateral</td>
</tr>
<tr>
<td><strong>Paroxysmal</strong></td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Pain during sleep</strong></td>
<td>No</td>
<td>No</td>
<td>Infrequent</td>
<td>Uncommon but disturbed sleep</td>
</tr>
<tr>
<td><strong>Other associated signs/ symptoms</strong></td>
<td>Bone cavity, osteoporosis</td>
<td>None</td>
<td>Dygesia, xerostomia, thirst</td>
<td>TMJ functional limitations, tenderness in masticatory/ TMJ palpation, TMJ sounds, bruxism, parafunction</td>
</tr>
<tr>
<td><strong>Neurological signs</strong></td>
<td>Dysesthesia, allodynia, paresthesia</td>
<td>Allodynia</td>
<td>Sensory, chemo-sensory anomalies</td>
<td>Allodynia (trigger point in myofacial pain)</td>
</tr>
<tr>
<td><strong>Psychological profile</strong></td>
<td>Frequently altered</td>
<td>Frequently altered</td>
<td>Frequently altered</td>
<td>Frequently altered</td>
</tr>
</tbody>
</table>

Principal clinical features in different idiopathic orofacial pain conditions: Burning Mouth Syndrome: A Review SMA Sadat et al.
However, hormone replacement therapy (conjugated estrogen for 21 days and medroxyprogesterone from day 12 through day 21) is effective in pain relief due to the presence of estrogen receptor on the oral mucosa. BMS patient with psychological cause is treated by psychotherapy alone or combined with drug therapy. Although, variety of drugs are used for the treatment of BMS but the treatment is not satisfactory and there is no definitive cure. It is important to inform patients about the nature of the disease to understand their pathology.

### Several drugs and therapies used for treatment of BMS

<table>
<thead>
<tr>
<th>Author, date</th>
<th>Drug or therapy used</th>
<th>comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sun et al. 2013 (59)</td>
<td>Vitamin supplement treatment: Supplementation with vitamin BC capsules plus relatively high doses of corresponding deficient hematines (vitamin B12, folic acid and iron)</td>
<td>Approximately 44.4% of 399 patients with BMS show complete remission of all oral symptoms</td>
</tr>
<tr>
<td>Cho et al. 2010 (57)</td>
<td>Zinc replacement treatment: A zinc supplement (14.1 mg/day) for 74 (26.8%) BMS patients with zinc deficiency</td>
<td>Zinc replacement therapy for 6 months can lower the mean numerical pain scale from 8.1 to 4.1 compared with a mean decrease from 7.7 to 6.7 in a control group</td>
</tr>
<tr>
<td>Forabosco et al. 1992 (58)</td>
<td>Hormone replacement treatment: 27 post-menopausal patients with oral discomfort are treated with conjugated estrogens (premarin) 0.625 mg/day for 21 days plus medroxyprogesteroneacetate (farlutal) 10 mg/day from day 12 through day 21 of the treatment cycle for three consecutive 21 day cycles</td>
<td>Hormone replacement therapy can relieve the symptoms and improve oral cytologic features in 15 of 27 patients with oral symptoms. The relief of oral discomfort following hormone replacement therapy is due to the presence of estrogen receptors on the oral mucosa</td>
</tr>
<tr>
<td>Epstein and Marcos. 1994 (52)</td>
<td>Topical capsaicin treatment: Capsaicin cream (0.025%) to the site of discomfort four times a day for at least 4 weeks</td>
<td>Topical capsaicin can be used as a desensitizing agent or an analgesic for treatment of oral mucosal burning</td>
</tr>
<tr>
<td>Gremeau-Richard et al. 2004 (53)</td>
<td>Topical clonazepam treatment: The patients are instructed to suck a tablet of 1 mg clonazepam with saliva at the oral pain sites for 3 mins and then to split. This protocol is repeated three times a day for 14 days</td>
<td>Clonazepam acts as an agonist of gamma-aminobutyric acid (GABA) receptors. A greater reduction of pain score in clonazepam-treated patients than in placebo-treated patients suggests that the action of this drug is related to peripheral nervous system dysfunction in patients with BMS and the presence of GABA receptors in peripheral tissues</td>
</tr>
<tr>
<td>Sardella et al. 1999 (60)</td>
<td>Topical lidocaine benzylamine hydrochloride treatment: Lidocaine or 0.15% benzylamine hydrochloride as a mouthwash</td>
<td>Lidocaine is a local anesthetic agent and 0.15% benzylamine hydrochloride has anesthetic and anti-inflammatory effect. These two agents can lessen the pain and burning symptoms in patients with BMS. But the analgesic effect is of short duration.</td>
</tr>
<tr>
<td>Lopez-Jornet et al. 2012 (61)</td>
<td>Topical aloe vera treatment: Topical application of 0.5 mL aloe vera gel at 70% to the sore areas of the tongue three times a day combined with a tongue protector.</td>
<td>This agent is effective in reducing tongue burning and pain</td>
</tr>
<tr>
<td>Petrucci et al. 2004 (54)</td>
<td>Systemic capsaicin treatment: 0.25% capsaicin three times a day for 30 days</td>
<td>The drug can reduce the pain intensity. However its use is not recommended for extended treatment as 32% of patients experience gastric pain after 4 weeks of treatment.</td>
</tr>
<tr>
<td>Grushka et al. 1998 (62)</td>
<td>Systemic clonazepam treatment: 30 patients with BMS take an initial dose of 0.25 mg clonazepam daily with an increase in dose of 0.25 mg clonazepam on a weekly basis if symptoms continue</td>
<td>Approximately 70% of patients with BMS experience pain reduction with effects at low doses</td>
</tr>
<tr>
<td>Hackmann et al. 2012 (63)</td>
<td>Systemic clonazepam treatment: 0.5 mg clonazepam per day</td>
<td>The agent is effective for reducing pain and burning sensation</td>
</tr>
</tbody>
</table>
Conclusion:
BMS is a painful condition interfering with patient’s normal livelihood. Evaluation must be focused on ruling out all secondary causes of oral burning and treating the underlying etiology. New evidence for the neuropathic basis of the syndrome is emerging. There are no well-defined data and studies to formulate a consensus on this syndrome. Therefore research in this area undertaken according to a variety of approaches is needed for a clean definition, diagnostic criteria and to establish a proper treatment planning.

References:

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<tr>
<td>Ko et al. 2012 (64)</td>
<td>Systemic clonazepam treatment: 100 patients with BMS are instructed to take 0.5 mg of clonazepam once or twice daily for 4 weeks</td>
<td>Psychological status, initial symptom severity and the presence of xerostomia and/or taste disturbance can serve as an outcome predictors of systemic clonazepam therapy for patients with BMS</td>
</tr>
<tr>
<td>Amos et al. 2011 (65)</td>
<td>Combined topical and systemic clonazepam therapy: 36 patients with BMS are asked to dissolve clonazepam tablet (0.5 mg tablet three times daily) orally before swallowing and are followed up over a 6 months period</td>
<td>About 80% of patients obtain more than a 50% reduction in pain over the treatment period and one-third of the patients have complete pain resolution.</td>
</tr>
<tr>
<td>Femiano et al. 2004 (66)</td>
<td>Systemic alpha lipoic acid treatment: 192 patients with BMS are treated with two hour psychotherapy alone weekly for two months, alpha lipoic acid (600 mg/day) alone for two months or combination therapy for two months</td>
<td>Patients with BMS receiving combination therapy for two months obtain more significant improvement of BMS symptoms than patients treated with psychotherapy alone for 2 months or alpha lipoic acid alone for 2 months.</td>
</tr>
<tr>
<td>Marino et al. 2010 (67)</td>
<td>Systemic treatment with capsaicin, alpha lipoic acid, lysozyme-lactoperoxidase (test drugs) and boric acid (control group) for 56 patients with BMS</td>
<td>A significant reduction in the symptoms scores of all patients with BMS who received the test drugs for a period of 60 days and at the end of the follow-up period (60 days after discontinuation) is found effective in the three test groups as a whole</td>
</tr>
<tr>
<td>Maina et al. 2002 (68)</td>
<td>Systemic treatment with amisulpride (50 mg/day) or selective serotonin inhibitors such as paroxetine (20 mg/day) and sertraline (50 mg/day) for 8 weeks</td>
<td>All three treatment regimens can result in a significant improvement of oral burning symptom from baseline to week 8. Amisulpride shows a shorter response latency and a better compliance than the other two drugs</td>
</tr>
<tr>
<td>Rodriguez-Cerdeira and Sanchez-Blanco. 2012 (69)</td>
<td>Systemic amisulpride treatment: amisulpride (50 mg/day) for 24 weeks</td>
<td>A significant improvement of burning mouth symptoms is found from baseline to week 24. Amisulpride seems to be effective and well tolerated by the patients as a short term treatment</td>
</tr>
<tr>
<td>Yamazaki et al. 2009 (70)</td>
<td>Systemic paroxetine treatment: Paroxetine (10 or 20 mg/day with dosage increasing to a maximum of 30 mg/day) to treat patient with BMS for 12 weeks</td>
<td>Approximately 80% of patients with BMS reported a reduction in symptoms with complete remission of pain being observed in 70% of patients by week 12</td>
</tr>
<tr>
<td>Bergdahl et al. 1995 (71)</td>
<td>Cognitive behavior therapy: Once a week for 12-15 weeks to treat patients with BMS</td>
<td>A decrease in pain intensity is observed immediately after therapy and in a follow-up of 6 months</td>
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Successful Pregnancy Outcome in Antiphospholipid Antibody Syndrome with Several Comorbidities

L CHOWDHURYa, A RAZZAKb, R KHANc, H SULTANAd

Summary: The presence of antiphospholipid antibody (aPL) has been clearly shown to have an adverse effect on pregnancy outcome. These effects may be apparent in the first trimester, presenting as recurrent pregnancy loss, or may be associated with the later development of pre-eclampsia (PE), IUGR, placental abruption, pre-term delivery, and intrauterine death. Antiphospholipid antibodies accounts for 3-5% of patients with second trimester repetitive pregnancy losses. The frequency of foetal death & recurrent abortion in untreated patient is greater than 90%. We will discuss here a 26 years old pregnant lady who was diagnosed 06 months prior to this pregnancy during pre conceptional counseling as antiphospholipid syndrome (APLS), autoimmune hypothyroidism and hypertension. She was on aspirin, heparin & thyroxine and ovulation inducing drugs before conception. After conception she was on close monitoring by the Obstetrician and Medicine specialist and ultimately on 36th week pregnancy was terminated by LSCS & a female baby was delivered. However, although the live birth rate is increased sevenfold, it should be acknowledged that these births are associated with an increased rate of prematurity and possible neonatal complications. The increased incidence of pregnancy-related complications necessitates the need for careful antenatal surveillance, and for delivery to be conducted in a unit with facilities for operative delivery and neonatal intensive care.

Key Words: Pregnancy, APS, recurrent foetal loss.

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Introduction: Antiphospholipid syndrome or antiphospholipid antibody syndrome(APS or APLS), often also Hughes syndrome, is an autoimmune hypercoagulable state caused by antibody against cell membrane phospholipid that provokes blood clots in both arteries and veins as well as pregnancy related complications. The disease is characterise by recurrent venous or arterial thrombosis, recurrent foetal loss, thrombocytopenia and presence of antibody to antiphospholipid such as anticardiolipin antibody. The antiphospholipid antibody syndrome may be primary or secondary. For all the patients with APS Female: male=2:1. Among patients with SLE the prevalence of APLS is much higher. HLA-DR7 is the risk factor for Primary APS and HLA-B8, HLA-DR2, HLA-DR3 for secondary APS, SLE or other autoimmune disorders and races like Blacks, Hispanics, Asians and Native Americans are at risk of developing secondary APS. Obstetrics manifestations of APS includes recurrent foetal loss, IUGR, pre eclampsia, postpartum syndrome. Other systemic manifestations includes-Neurologic (CVD, TIA, severe migraine, ischemic encephalopathy, seizures, peripheral neuropathy), Cardiovascular (MI, mitral or aortic valvular lesion, pseudo infective endocarditis), Dermatologic (livedo reticularis, leg ulcer, necrotizing purpura, widespread cutaneous necrosis), Haematologic (thrombocytopenia, leukopenia, Cooms’ positive haemolytic anaemia) and others such as avascular necrosis, non thrombo embolic pulmonary HTN etc.

Case Report: Mrs. Reshma 26 years, para:2-2, housewife of lower middle class family admitted in Combined Military Hospital (CMH) Dhaka on 19th March 2012 at her 22 weeks pregnancy. She was married for 11 years &
conceived after 4 years of marriage in 2005. Her pregnancy was terminated by C/S at 36 weeks gestation due to severe PE & oligohydramnios, baby died 05 days after birth due to IUGR related complications.

Second pregnancy in 2008 was also complicated by severe PE & baby was born vaginally at 28 weeks died immediately after birth due to severe birth asphyxia & low birth weight (LBW). After that she reported to GOPD with complaints of progressive weight gain, cold intolerance and irregular menstruation for 02 years. At that time she was thoroughly investigated & diagnosed as a case of Primary APS, autoimmune hypothyroidism & HTN.

With above diagnosis she was treated accordingly with joint consultation of Obstetrician & Medicine specialist. She was advised levo-thyroxine, aspirin, folic acid and ovulation inducing drug. With these advice after 02 month she conceived and report to hospital immediately after conception. At 06 weeks of gestation she reported to OPD and Inj Heparin (5000 unit S/C 8 hourly) and alpha methyldopa was added. She was under regular follow up of Obstetric & Gynae and Medicine OPD.

At 19 weeks of gestation she was admitted with severe epigastric pain and vomiting. She was nursed in ICU, examined and investigated & diagnosed to be a case of acute pancreatitis due to dyslipidaemia and hyperglycaemia. Patient was discharged from hospital with inj heparin, diet control for diabetes and follow up investigation of lipid profile & GTT after 2 weeks.

At 22 weeks she again got admitted with same complaints & treated conservatively as a case of acute pancreatitis. S. Triglyceride as 1226 mg/dl.

In ICU she was under close supervision of Intensivist, rheumatologist, gastroenterologist, Obstetrician. She remained admitted upto 34 weeks of gestation in hospital under close monitoring of Medicine specialist and regular follow up by obstetrician. Pregnancy was terminated by LSCS at 36 weeks of gestation. Before hand anticoagulant & aspirin was stopped and inj Dexamethasone was given 03 days prior to LSCS.

A female baby of 2.8 kg weight was delivered who had respiratory distress at birth, later on upper GI bleeding which was managed with Fresh Frozen Plasma transfusion & vit K. Subsequently the baby diagnosed as a case of congenital hypothyroidism.

Immediately after delivery Inj LMWH (Enoxaperin) followed by tab Warfarin was started accordingly. Patient was discharged on 16th postoperative day on tab aspirin, tab thyroxine, tab fenofibrate, tab atorvastatin, tab calcium & folic acid with advice for regular follow up in OPD. On post natal check up after 06 weeks mother & baby was found alright and barrier contraceptive was advised. She was given assurance to be pregnant again after 2-3 years.

Discussion:
The persistent presence of medium to high levels of IgG and/or IgM class anticardiolipin antibodies (aCL) and/or the lupus anticoagulant (LAC) in plasma is associated with both “recurrent pregnancy loss” and venous and arterial thrombosis. This clinicoserological entity, when diagnosed in patients with underlying autoimmune disease (usually Systemic Lupus Erythematosus, or SLE), APS is termed secondary antiphospholipid syndrome (APS). AAPS also occurs in otherwise healthy people led to the term primary antiphospholipid syndrome.

Clinical studies indicate that aPL are related to both early pregnancy losses and fetal demise in advanced pregnancy. Placental thrombosis and infarction are common findings in aPL related intrauterine fetal deaths. Apart from being risk factors for fetal demise, aPL associate with high frequencies of pre-eclampsia, intrauterine growth restriction, fetal distress, and premature delivery.

The presence of more than one class of antiphospholipid antibodies increases thrombotic risk. Patients who are test positive for all three of the major assays - positive LAC, elevated anticardiolipin...
antibodies and elevated anti-2GPI antibodies (referred to as “triple positivity”), are at markedly increased risk for thrombosis and for pregnancy complications. About 10-15% of women with recurrent miscarriage are diagnosed with antiphospholipid syndrome. Fetal loss (≥10 weeks of gestation) is more strongly associated with aPL than are earlier pregnancy losses. Lupus anticoagulant has been strongly associated with recurrent miscarriage before the 24th week of gestation. Current APS criteria include early delivery, oligohydramnios, neonatal complications such as prematurity-estimated at 30-60% and more common in SLE patients, intrauterine growth restriction (IUGR), fetal distress and rarely fetal or neonatal thrombosis, associated maternal obstetric complications like pre-eclampsia or eclampsia and HELLP syndrome, arterial or venous thrombosis and other aPL-related complications like placental insufficiency. The association between antiphospholipid antibodies and the risk of premature birth due to eclampsia or preeclampsia and intrauterine growth restriction remains controversial; studies contributing data to this area tend to be small, retrospective, and have conflicting results.

A randomized controlled study of prednisone and aspirin as compared with heparin and aspirin showed low-dose subcutaneous heparin with low-dose aspirin to be equally efficacious with less morbidity. A 2005 Cochrane systematic review concluded that women with recurrent miscarriage and antiphospholipid syndrome should be given a combination of heparin 5000 IU subcutaneously twice daily and low-dose aspirin.

Evidence-Based Clinical Practice Guidelines of American College of Chest Physicians suggest that women with antiphospholipid antibodies and a history of 2 or more early pregnancy losses or 1 or more late pregnancy losses who have no prior history of thrombosis receive treatment with combination aspirin and heparin (unfractionated or lowmolecular-weight) during pregnancy. Aspirin (81 mg/d) should be started with attempted conception; most investigators recommend, in fact, preconceptional aspirin because of its possible beneficial effect on early stages of implantation.

Most of these possible future therapies (clopidogrel, rivaroxaban, statins, rituximab, and other new anticoagulantdrugs) are for non-pregnant patients. The only new drugs for APS that pregnant women can use are dipyridamole and hydroxychloroquine. Observational studies have suggested an antithrombotic effect of hydroxychloroquine in patients with antiphospholipid antibodies, most of whom have systemic lupus erythematosus.

**Conclusion:**
APS is an uncommon disease with diverse clinical manifestations. A high clinical suspicion is required to diagnose it. With treatment and close monitoring the prognosis improves dramatically. Successful pregnancy outcome in a patient with APS require a multidisciplinary approach.

**Reference:**


Partial Hydatidiform Mole with Alive Term IUGR Foetus

R ARAa, J BEGUMB, SB KASEMC, S HOQUEd, SF NARGISE

Summary:
Gestational Trophoblastic diseases consist of a broad spectrum of conditions ranging from an uncomplicated partial hydatidiform molar pregnancy to stage IV choriocarcinoma with cerebral metastasis. Incidence of hydatidiform mole with a co-existing live fetus varies between 0.005 to 0.01% of all pregnancies. We report a case of partial molar pregnancy with alive term IUGR (intrauterine growth retardation) foetus. Diagnosis was made by sonographic findings of molar changes at her 28 weeks of gestation.

Introduction:
Gestational Trophoblastic diseases encompass a diverse group of lesions with specific pathogeneses, morphological characteristics and clinical features. The modified world health organization classification of Gestational Trophoblastic disease includes complete and partial hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumor, epitheloid, trophoblastic tumor, exaggerated placental site and placental site nodules. The Hydatidiform mole is characterized histologically by abnormalities of chorionic villi, trophoblastic proliferation and edema of villous stroma. Molar pregnancy is significantly more common in extreme age. The usual management of gestational trophoblastic diseases is evacuation of the uterus and follow-up because of higher chances to develop choriocarcinoma. But some time when molar changes are in placenta along with alive foetus, expectant management can be performed under strict surveillance. In each visit, history should be taken properly like hyperemesis, irregular per vaginal bleeding, sign of preeclampsia, features of thyrotoxicosis or any sign suggestive of metastasis. Patient is also advised to do serum β-hcg & USG for pregnancy profile. We described a case of singletone pregnancy, in which partial molar change was detected, however, the pregnancy ended in phenotypically normal term IUGR fetus.

Case Report
A 26 years old patient who was P-1+0, G-2nd admitted in the gynecological emergency at 40 weeks gestation with labour pain. Previously she had one supervised uncomplicated pregnancy. In this pregnancy she had antenatal care in primary health care facility. She didn’t give any history of vaginal bleeding, excessive vomiting and other features suggestive of molar pregnancy. Obstetric USG at her 28 weeks of pregnancy showed single live intrauterine gestation with multiple cysts involving the part of the placenta suggestive of molar changes. The risk of continuation of pregnancy was explained to the patient and the relatives. Subsequently anomaly scan was done at 29 weeks of pregnancy which showed no obvious gross foetal anomaly but growth retarded foetus and oligohydramnios and molar changes in the placenta. As there was no preeclampsia, hyperthyroidism and any other complications and the no obvious gross anomaly so pregnancy was continued with advice to regular follow up. Serum β-hcg was not done antenataly due to lack of facility. Patient was on followed up upto 34 weeks of gestation thereafter she missed follow up. Later she came in hospital at 40 weeks pregnancy with labour pain. There was no specific past and family history of molar pregnancy. Labour was....
monitored with maintenance of partograph. After 6 hrs of labour pain, she delivered a male baby of 1.5 kg with good APGAR score. Active management of third stage of labour was done. Weight of the placenta was 600 gram and almost 1/3 of the placenta was replaced by molar tissue. Umbilical cord was normal, having 3 vessels.

The baby was examined by paediatrician and no gross congenital abnormality was detected. The baby was on breast feeding. Maternal serum β-hcg 24 hours after delivery was 300mIU/ml. Baby and the mother were discharged from the hospital on 2nd postnatal day. Histopathology of the placenta showed molar changes but chromosomal study of the placenta was not done.

The patient was followed up with serum β–hcg and chest x-ray after 15 days of delivery, both were normal. Again patient came after 6 weeks for postnatal check up, serum β-hcg was normal and both the mother and the baby were fine. Her repeated USG didn’t show any features of myometrial invasion. Karyotype of the baby was done after 3 months and that was 46XY.

Discussion:
Hydatidiform mole can be separated into two entities with respect to cytogenetics, histopathology and morphology: firstly, complete, classical mole has diploid karyotype, no embryo and amnion and uniform changes of the placental villi and trophoblasts; secondly, partial mole usually has a triploid karyotype, resulting from the fertilization of a normal ovum with two sperms, the presence of ascertainable embryo, umbilical cord or an amniotic membrane and only focal changes of the placental villi and trophoblasts. Histologically molar pregnancy is characterized by layers of degenerated, attenuated or hyperplastic sheets of trophoblasts with mild to moderate atypia, the cores of the villi showed cistern formation and vessels were absent. Incidence of molar pregnancy varies from 1 in 2000 pregnancies in USA to 1 in 200 in certain part of Asia. Partial molar pregnancy with co-existing normal live fetus has been divided into three types. The first and most common is twin pregnancy with one normal fetus having a normal placenta and another complete mole, second type is a twin pregnancy with normal fetus and the placenta and another partial mole. The third and most uncommon occurrence is a singleton normal fetus with partial molar placenta similar to our case. The diagnosis of molar pregnancy with co-existing fetus is difficult. An elevated serum β-hcg with low serum placental lactogen and snowstorm appearance of placenta in USG help to diagnosis the case. This condition co-existing with viable foetus warrant for genetic analysis and search for gross congenital anomaly. Histopathology and cytogenetics help in final diagnosis.

Molar pregnancy with co-existing normal live foetus has been divided into three types. The first and most common is twin pregnancy with one normal fetus having a normal placenta and another complete mole, second type is a twin pregnancy with normal fetus and the placenta and another partial mole. The third and most uncommon occurrence is a singleton normal fetus with partial molar placenta similar to our case. The diagnosis of molar pregnancy with co-existing fetus is difficult. An elevated serum β-hcg with low serum placental lactogen and snowstorm appearance of placenta in USG help to diagnosis the case. This condition co-existing with viable foetus warrant for genetic analysis and search for gross congenital anomaly. Histopathology and cytogenetics help in final diagnosis.

Molar pregnancy with coexisting fetus carries a significant risk to mother and the fetus. Maternal risks include abnormal bleeding, preeclampsia, eclampsia, hyperthyroidism, anemia, persistent trophoblastic disease and abruption. Fetal complications include abortion, congenital anomalies, preterm, severe anemia, IUGR and IUFD. Several factors influences the outcome in partial molar pregnancy, most important being the foetal karyotype. Other factor includes the size of the molar placenta, the speed of molar degeneration and foetal anaemia.

Previously most partial molar pregnancies identified early were terminated with or without medical complications but especially when preeclampsia was also present. However termination of pregnancy is not always the only option as the pregnancy can be
managed conservatively if the foetus appears normal and healthy on ultrasound and if there are no maternal complications. Patients who develop partial molar placenta may find the pregnancy complicated by intrauterine growth restriction and oligohydramnios which were both observed in the case discussed here\textsuperscript{21}. Jones and Lauresen recommend immediate termination after the diagnosis of molar pregnancy with co-existing foetus\textsuperscript{22}. Suzuki et al, however, state that in the absence of preeclampsia or fetal abnormality the pregnancy can be allowed to continue till term\textsuperscript{2}. In our case though there was partial molar changes in placenta, baby was grossly IUGR and there wasn’t any significant symptoms or signs, so pregnancy was advised to continue. In our case prenatal karyotyping of the foetus was not possible but the postnatal karyotype of the foetus was normal 46XY, though the placental karyotyping was not done. However placenta in a partial mole with foetus in a single tone pregnancy results from dispermy and diploid karyotype in most cases\textsuperscript{23}. Hydatidiform mole with co-existing fetus can be established by partial mole syndrome or by a twin pregnancy where the other conceptus has degenerated into a mole\textsuperscript{5}. It is important to distinguish between a complete and partial mole when a foetus co-exists because it has been reported that a complete mole has a 20% tendency to become an invasive mole or even a choriocarcinoma, while the risk was far less for partial moles\textsuperscript{24}. Some Studies\textsuperscript{18,25,26} have questioned whether patients with partial hydatidiform mole require follow up observation and assessment of serum β-hcg concentration. However patients can develop choriocarcinoma if not followed up correctly and one study by Seckl et al reported the death of one such patient.

Szulman and Surti\textsuperscript{27} reviewed 86 cases of partial hydatidiform mole and reported that the overall prevalence of the disease was 4%, however Berkowitz et al\textsuperscript{25} reported a higher prevalence (9.9%) among patients who had developed persistent gestational trophoblastic disease\textsuperscript{13}. The patient in the case discussed here did not show any persistent trophoblastic disease after the birth and her serum β-hcg concentration returned to normal within 6 weeks.

Post delivery follow up includes measurement of β-hcg value at delivery and weekly values plotted on a standered regression curve, adjusted for local reference standered. This is followed by weekly values until three values are obtained below the limit. Then every second weekly for two months and then monthly for one year\textsuperscript{28}. A single asessment of a patient’s serum β-hcg concentration after the termination of pregnancy is sufficient to confirm remission in these patients\textsuperscript{24}.

The case we reported probably had sufficient placental circulation to sustain through the 1\textsuperscript{st} and 2\textsuperscript{nd} trimaster, however had severe IUGR due to limited placental circulation. Grossly two types of placental pathology have been described previously, focal and diffuse partial degeneration\textsuperscript{13}. Our case had focal molar changes allowing fetal survival until term. The genetic makeup leading to multiple congenital anomalies as well as the compromised blood supply lead to the diminished fetal survival. Normal fetal outcome is therefore barely known in this condition\textsuperscript{30}. The case discussed here the baby is running two years, milestones are normal and both the baby and mother are in good health.

**Conclusion:**
Pregnancies with normal live fetus coexistent in with partial molar placenta are extremely rare because of numerous maternal and fetal complications. In our case the foetus was born with severe IUGR but having no gross congenital abnormality, karyotyping was normal on chromosomal study and the child was continued to grow normally, the abnormal cell population appears to be confined to the placenta. The management of such rare condition should be determined on one to one basis and the possibility of increased complications and prognosis should be discussed with the family. Complete evaluation of the placental tissue is important even in cases with normal fetal outcome as molar changes which might be unsuspected antenataly might affect the future obstetrical outcome.

**References:**
AIDS with Disseminated Tuberculosis

M SANYAL, FA CADER, MA AMIN, A DAS, MA KAHHAR

Summary:
Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) have been closely linked since the emergence of the Acquired Immune Deficiency Syndrome (AIDS). Worldwide, TB is the most common opportunistic infection affecting HIV-seropositive individuals, and it remains the most common cause of death in patients with AIDS. By producing a progressive decline in cell-mediated immunity, HIV alters the pathogenesis of TB, greatly increasing the risk of disease from TB in HIV-coinfected individuals, and leading to more frequent extrapulmonary involvement, atypical radiographic manifestations, and paucibacillary disease, which can impede timely diagnosis. Although HIV-related TB is both treatable and preventable, incidence continues to climb in developing nations, wherein HIV infection and TB are endemic and resources are limited. We report the case of a 45 year old gentleman who presented with generalized lymphadenopathy, whose lymphnode biopsy was consistent with TB; however following poor response to anti-TB treatment, he was found to be serologically positive for HIV.

Key Words: Acquired Immune Deficiency Syndrome (AIDS), Human Immunodeficiency Virus (HIV), Lymphadenopathy, Tuberculosis (TB).

Introduction:
HIV associated TB remains a major global public health challenge, with an estimated 1.4 million patients worldwide, particularly in Asia and Africa. Co-infection of TB with HIV leads to challenges in both the diagnosis and treatment of tuberculosis, especially given an increase in the rates of drug resistant tuberculosis, including multi-drug (MDR-TB) and extensively drug resistant TB (XDR-TB). AIDS, first recognized in 1981, is caused by the retrovirus HIV, which progressively decreases cellular immunity. The virus has two subtypes: HIV 1 and HIV 2. HIV 1 is the cause of the global pandemic, while HIV 2 causes a similar pattern of weakness as HIV 1 but progresses slowly and is less transmissible. There are many opportunistic diseases in AIDS, varying according to the CD4 count. TB may occur at any stage of HIV disease and is frequently the first recognized presentation of underlying HIV infection. In addition, most TB/HIV-coinfected patients have extrapulmonary or disseminated forms of TB. With an estimate of 350,000 deaths per year, TB accounts for a quarter of all AIDS-related deaths, and is the most common cause of death for people living with HIV. Apart from the diagnostic and therapeutic challenges among TB/HIV co-infected patients, there is also the especial difficulty in obtaining correct history, with most patients concealing the history of sexual exposure and drug addiction, important factors in the epidemiology of HIV. Treatment of coinfection is challenging, however the principles of treatment of active TB in HIV-infected patients are the same as those for HIV-uninfected patients. All HIV-infected patients with diagnosed active TB should be started immediately on both anti-TB treatment as well as antiretroviral therapy. Close collaboration between HIV and TB control programs among clinicians, health care institutions, and public health programs is necessary in order to integrate care and improve medication adherence and TB treatment completion rates, reduce drug toxicities, and maximize HIV outcomes.

Case presentation:
A 45-year old normotensive newly diagnosed diabetic Bangladeshi gentleman presented to DMCH on 11.3.2014 with the complaints of fever for 9 months and multiple lumpy swellings in different parts of the body for 2 months. The fever was low grade, continued, not associated with chills & rigors, with no evening rise and subsided on taking antipyretics. He also complained...
of occasional cough with production of scanty sputum, whitish and non-foul-smelling. He had been initially diagnosed as a case of Pulmonary TB on the basis of blood tests, sputum and chest X-ray, and started on anti-TB therapy which he continued for two months.

With no improvement of his symptoms and gradual worsening of his general condition which included the onset of severe nausea and vomiting, he stopped taking his medications himself. However, there was no blood loss, unconsciousness, convulsion, blurring of vision, morning headache, focal deficit or bone pain. He denied any contact with TB patients, however was unsure of his BCG vaccination. He is non-smoker and non-alcoholic, with no history of blood transfusion or i/v drug abuse. He was in Dubai for 2 years and Malaysia for couple of months 10 years back. He was married, had two children, and denied any history of extramarital sexual exposure.

On examination, he was cachectic, dehydrated, severely anaemic and moderately icteric. His pulse was 94 beats/min, and blood pressure was 110/70mmHg. There were multiple non-tender enlarged lymph nodes along both cervical chains and right inguinal region, which were discrete, variable in size (largest measuring 3x3cm), firm in consistency, not fixed with underlying structures or overlying skin, with no discharging sinus. There was a tender scar over right inguinal lymph node. Systemic examination revealed no abnormality. Funduscopy was normal.

Investigations showed Hb-7.7 mg/dl, WBC-3210 /cumm, platelets- 54000/cumm. MCV-74fl. Reticulocyte count 0.89%. Peripheral blood film showed microcytic hypochromia with target cell with thrombocytopenia. Initial Serum Na⁺ was 121 mmol/l most likely due to vomiting and later corrected to 138mmol/l. Liver function test revealed elevated liver enzymes (ALT-173 U/L, AST-483 U/L) and raised serum bilirubin - 20.56mg/dl. The bilirubin levels declined to 46 ìmol/L after abandoning anti-TB treatment.

With lymphoma being one of the differential diagnoses, we also did serum LDH and Alkaline Phosphatase levels which were both raised at 729 U/L and 479 U/L respectively. GGT was elevated at 234 U/L. VDRL, HbsAg were negative. Lymph node biopsy revealed granulomatous inflammation consistent with TB with areas of caseation (Figure 1). However, on further probe into the reason for poor response to anti-TB treatment, we tested the patient for HIV. ELISA was positive for HIV1 and HIV2. With the confirmed diagnosis of disseminated TB with drug-induced hepatitis and HIV/AIDS, we proceeded to counsel his spouse and arranged for concomitant anti-retroviral as well as anti-TB treatment.

Discussion:
A cachectic patient presenting with generalized lymphadenopathy brings a variety of differential diagnoses to mind. Among them, especially in a country like Bangladesh, disseminated TB is the most plausible differential, and the commencement of anti-TB chemotherapy is justified, especially given the caseating granulomatous lesion found on lymph node biopsy. The possibility of a different diagnosis, or co-infection with
HIV arose, in the context of our patient, mainly due to the poor response to anti TB treatment despite 2 months of uninterrupted therapy. In addition, the patient had become icteric, and there was a persistent rise of liver enzymes, and the question of drug-induced hepatitis arose. The blood film showed pancytopenia with raised LDH. With an additional differential of granulomatous lesion in liver in mind, we did a GGT level too, which turned out to be elevated. Although this patient’s liver enzymes reduced following discontinuation of anti-TB treatment, they failed to return to normal; this, along with a raised GGT level leads to the possibility of TB dissemination to the liver. AIDS is a progressive deterioration of the immune status of the individual, characterized by the progressive depletion of the CD4 T lymphocyte population, which represents a major target of viral infection by the causative HIV. The clinical consequences of HIV infection encompass a spectrum ranging from an acute syndrome associated with primary infection to prolonged asymptomatic state to advanced disease, classified by the CDC according to CD4 T lymphocyte count.7

The mechanisms of immunity against M. tuberculosis and control of M. tuberculosis infection depends on a T-cell immune response comprising CD4 and CD8 cells, as well as Th1 and Th2 cytokines, including IFN-γ, tumor necrosis factor (TNF)-α and IL-2. 8

In immunocompetent persons with pulmonary TB, antigen-specific CD4 T cells accumulate in the lung.9 Progressive loss of CD4 T cells and susceptibility to opportunistic infections like TB are hallmarks of HIV-1 infection. After HIV-1 seroconversion, the risk of active TB is greatly increased in persons who are latently infected with M. tuberculosis.10 In contrast to the majority of other opportunistic infections, the risk of developing TB is substantially increased before CD4 T-cell loss is profound, with evidence of TB incidence doubling within the first year of HIV-1 infection.3

Systemic T-cell responses against M. tuberculosis, especially type 1 cytokines responses, are impaired in HIV-1–infected adults.11 T cells play an important role in maintaining the integrity of granuloma formation in the human lung.12 Susceptibility to active TB in HIV-1–infected persons who are latently infected with M. tuberculosis is likely related to the inability of local immune mechanisms to control the M. tuberculosis infection. This includes dysregulation of the interaction between lymphocytes and alveolar macrophages. Also, studies show that in addition to a total CD4 T-cell deficit, the function of mycobacteria-specific CD4 T cells is significantly impaired in the lung of HIV-1–infected persons, which may account for the HIV-1–associated elevated risk for developing tuberculosis,9 as with our patient.

Thus, when we found that our case was responding poorly to anti TB treatment, with high index of suspicion, we screened him for HIV, which turned out to be positive. Western Blot test and CD4 cell count has also been planned.

Given that our patient is a case of Category C according to CDC classification,7 his management involves simultaneous treatment with anti-retroviral therapy (ART) as well as anti TB chemotherapy Category II. As the patient had drug induced jaundice, he was to be commenced on SHE therapy consisting of Streptomycin, INH and Ethambutol for 3 months, followed by only the latter two drugs for 6 months.

As for ART, the combination of two NRTI with one NNRTI is available and it is the first choice.6 Researchers recommend that for patients with CD4 counts <50 cells/mm³, ART should be initiated within 2 weeks of starting TB treatment.

In patients with CD4 counts e50 cells/mm³, who present with clinical disease of major severity as indicated by clinical evaluation, ART should be initiated within 2 to 4 weeks of starting TB treatment. In patients with CD4 counts e50 cells/mm³ who do not have severe clinical disease, ART can be delayed beyond 2 to 4 weeks of starting TB therapy but should be started within 8 to 12 weeks of TB therapy initiation. Rifabutin is the preferred rifamycin to use in HIV-infected patients with active TB disease on a protease inhibitor (PI)-based regimen, because the risk of substantial drug interactions with PIs is lower with rifabutin than with rifampin.6

**Conclusion:**

As the incidence of AIDS is increasing at an alarming rate in Bangladesh, a high index of suspicion needs to be employed in the diagnosis and further treatment of TB showing poor response to anti TB treatment, as
there is a considerable possibility of co-infection with AIDS and in such patients, screening of the patient for HIV is of paramount importance.

References:
We report an interesting case of a neonate presenting immediately after birth with respiratory distress, inspiratory stridor and difficult intubation. During operative microfaryngoscopy, a well-delineated papilloma like elongated supraglottic mass was seen. The patient underwent surgery, and the diagnosis was confirmed histologically. Biopsy revealed tissue compatible with hamartoma including blood vessel, nerve bundle and cartilage plate. The mass was removed by direct laryngoscopy. Neonatal laryngeal hamartomas are extremely rare. In general, an excellent prognosis is associated with these lesions, and the treatment of choice is endoscopic surgical excision. To our knowledge, this is the first description of a neonatal laryngeal hamartoma in Bangladesh.

Keywords: Neonate, Larynx, Hamartoma

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Introduction:
Hamartomas are defined as a congenital malformation that consists of a focus of mature, locally derived tissue with abnormal histological architecture. Hamartomas are common among benign masses found in the lung. Head and neck manifestations are rare and can occur anywhere along the aerodigestive tract. Hamartomas affecting the larynx are extremely rare with less than twenty well-documented cases in the literature. Hamartomas of the larynx are rare benign entities that can be locally destructive and cause airway obstruction. Recurrence rate is 20%, often associated with incomplete removal.

We report a case of supraglottic hamartoma causing airway obstruction in a newborn necessitating laryngoscopic removal of the mass. The laryngeal hamartoma should be removed in the newborn period to avoid tracheostomy, because decanulation after tracheostomy in infants can be difficult.

Case report:
The patient was a full term, female newborn who presented immediately after birth with inspiratory stridor and respiratory distress (Fig.-1). The baby cried 5 minutes after birth following resuscitation. She was on mechanical ventilator just after admission to Neonatal Intensive Care Unit due to respiratory difficulty and constant lower oxygen saturation. But intubation could be done with difficulty. The baby was delivered by Lower Uterine Cesarian Section (LUCS) at term due to placenta previa and history of antepartum hemorrhage. The baby was extubated after clinical improvement but again became lethargic and cyanosed with increasing intensity of stridor within a few hours. She remained event-free when endotracheal intubation was maintained with or without ventilator support. Each time intubation was very difficult. Serial chest radiographs demonstrated intermittent atelectasis and low lung volumes with hypoventilatory changes.

Fig.-1: Newborn with laryngeal hamartoma
Then Otolaryngologist was consulted and flexible laryngoscopy at the bedside revealed a large, obstructing polypoidal mobile mass in supraglottis with suspicion of a supraglottic polyp. Operative microsurgery further characterized a well delineated, large papilloma like elongated supraglottic mass which was firm to hard in consistency. The mass was removed by direct laryngoscopy and airway was clear.

Histopathological examination confirmed a solid lesion with features of hamartoma including blood vessel, nerve bundle and cartilage plate. She was extubated on postoperative day 1 and the immediate postoperative course was uneventful. A trial of oral feeding was initiated on postoperative day 3, which resulted in increased work of breathing and concern for aspiration. Oral feedings were withheld, and the patient was brought back to the operating room for a follow up endoscopy where she was seen to have good healing. A nasogastric tube was placed for feeds.

Consequently, the baby was maintained on enteral feeds with plans for clinical re-evaluation. At a 2 month follow-up visit, the patient demonstrated no respiratory complaints or flexible fiberoptic laryngoscopy findings of recurrence. She is now 9 months old and doing well without any respiratory symptoms or feeding difficulties (Fig.-2).

**Discussion:**

Hamartomas are simple and spontaneous growth composed exclusively of components derived from local tissue. The growth produces an excessive number of cells that reach maturity and then ceases to reproduce, so that the growth is self-limiting. Hamartomas are basically benign malformations although they often present many clinical features of a neoplasm, 4.

We report an extremely rare case of a neonatal laryngeal hamartoma causing stridor and respiratory compromise since birth (Fig.-3). Linder describes a similar case of a neonatal boy presenting with respiratory distress secondary to a laryngeal hamartoma5. Windfuhr described a series of 10 pediatric patients with laryngeal hamartomas, presenting at a various ages, with an average age of 1.9 years. The most common presenting symptoms were stridor, dysphonia, and hoarseness, and most commonly affected the supraglottis1.

Another possible clinical presentation in laryngeal hamartoma is asphyxia described by Bouzouita in a case report. Our patient also presented with asphyxia. Asphyxia can occur according to the volume of the lesion, demanding prompt treatment as an emergency4. Some of these disorders were discovered during surgical procedures, when the lesion made intubation difficult5. In the case reported by us, the intubation was difficult drawing special attention to laryngeal pathology and considered consultation with Otolaryngologist and Anaesthesiologist. Our case is also similar to a case reported by Leoncini et al. however, they described a 3 month old infant who presented with progressive airway symptoms2.

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**Fig.-2:** The newborn infant with laryngeal hamartoma after recovery

**Fig.-3:** Laryngoscopic view of laryngeal hamartoma

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Clinically and histopathologically, our patient appears to have manifestations of the glandular hamartoma described by Sahhar and Leoncini et al\textsuperscript{2,6}. In addition to the unique histopathology, diagnostic yield of cross-sectional imaging with magnetic resonance imaging (MRI) is very crucial. It may be advisable to use to evaluate the lesion’s vascularity and potential involvement with other critical structures. But it has limited role in visualising neonatal larynx\textsuperscript{1}. Again, microlaryngoscopy is the primary modality for diagnosis of these lesions; the operative goal should be to primarily focus on maintaining function, as these lesions generally have an excellent prognosis\textsuperscript{7}.

The pathophysiologic mechanism underlying the origin of oropharyngeal polyp is unknown. Polypoid lesions may have many different histologic abnormalities. Therefore, it is important to consider other neoplastic and non-neoplastic conditions that may present as a polyp in the differential diagnosis. These include hamartomas, inflammatory polyps, lipomas, hemangiomas, lymphangiomas, schwannomas, and other unusual neoplasms, such as carcinoid tumors and chemodectomas\textsuperscript{8}. Histopathological examination of the resected polyp in our case revealed features of hamartoma including blood vessel, nerve bundle and cartilage plate.

In present case, the polypoidal mass was removed by direct laryngoscopy with excellent prognosis in subsequent follow up. The lesion was treated in a similar fashion, with an excellent functional result and prognosis described by Leoncini\textsuperscript{2}. The airway in another case was secured via tracheostomy, and the lesion was resected endoscopically with a carbon dioxide laser. A subtotal resection was achieved, but functionally, the patient did well and was eventually decannulated at 33 months of age\textsuperscript{5}. The lesions were fatal in two neonates in another report, but generally, an excellent prognosis can be expected with complete surgical removal as the treatment of choice. In addition, while benign, there was report of one case with histologic change observed at recurrence\textsuperscript{1}. In general, an excellent prognosis is associated with these lesions, and the treatment of choice is endoscopic surgical excision with complete recovery\textsuperscript{9}.

**Conclusion:**

Neonatal laryngeal hamartoma is extremely rare which is primarily a benign disease with excellent prognosis after complete endoscopic removal. The aim of our report is to underline consideration of laryngeal hamartoma by paediatricians as an important cause of airway obstruction in newborn with difficult intubation.

**References:**

A 65–year-old male admitted in Dhaka Medical College Hospital with the complains of pain in left flanks for 5 days and fever for 3 days. Pain was constant, severe, cramping in nature associated with nausea and vomiting. He also complained of dysuria for last 8 days. Fever was intermittent in nature comes with chills and rigor subsided with sweating. Maximum rise of temperature was 102°F (38.9°C). Following 4th day of admission he developed soft tissue swelling over his left flanks. He was diabetic for last 5 years was on oral hypoglycemic drugs but stopped drugs for last 6 months.

The vital signs showed blood pressure of 100/60 mm Hg at presentation, pulse rate of 106 beats/min, respiratory rate of 25 breaths/min, breathing was uraemic and temperature of 103°F (39.4°C) was recorded. On examination, the patient was conscious, but mildly disoriented, and there was tenderness in the left renal angle, soft tissue pitting oedema localized to left flanks, but all the other systems were normal.

CT SCAN abdomen: Emphysaematous pyelonephritis (EPN) - class IIIa with left psoas muscle inflammatory changes.

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The patient was diagnosed as a case of emphysematous pyelonephritis with Septicemia with acute renal failure. His blood sugar controlled with insulin. Antibiotic inj. Meropenum and inj. Ceftazedime started according to culture of urine (klebsiela). He responded well with medical management and become afebrile in 1st week. His WBC count reduced to 11,100/cmm after 3 weeks and renal function improved to 1.2mg/dl after 2 weeks. Due to absence of any complications or features of sepsis after 4 weeks of injectable antibiotics the patient was discharged on oral antibiotics for a further 2 weeks.

Discussion:
Emphysematous pyelonephritis is a well-known condition which mainly affects the diabetic population (90%) and seen in patients with chronic diabetes characterized by formation of gas in renal parenchyma. It has a strong female preponderance with female to-male ratio of 5:1, mean age of occurrence is around the fifth decade, and most often it involves left kidney in almost 60% of cases. Patient usually present with abdominal pain, fever and tenderness in renal angle.

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
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<tbody>
<tr>
<td>Class I</td>
<td>Gas in collecting system only</td>
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<tr>
<td>Class II</td>
<td>Parenchymal gas only</td>
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<tr>
<td>Class IIIa</td>
<td>Extension of gas into perinephric space</td>
</tr>
<tr>
<td>Class IIIb</td>
<td>Extension of gas into pararenal space</td>
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<tr>
<td>Class IV</td>
<td>EPN in solitary kidney, or bilateral disease</td>
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Management is now based on CT scan based classification by Huang and Tseng. Class I and II EPN can be managed by medical therapy alone or combined with percutaneous drainage, have a success rate of 66%, while the mortality rate for treatment with antibiotics alone ranges from 40% to 90%. For classes III and IV, antibiotic therapy and PCD may be attempted but ultimately nephrectomy may be necessary.

Investigations are given below

1. CBC
   - Hb 11.4gm/dl
   - WBC 25,000/cmm
   - Neutrophils 87%
   - Platelete count 24,000/cmm
   - ESR 32mm in 1st hour

2. Urine RME
   - Sugar +++
   - Albumin +
   - Pus cell plenty
   - RBC plenty

3. Urine C/ S- growth of klebsiella
4. Blood C/ S – No growth
   - 4.S. Cratinine 4.09 mg/dl
5. FDP 20.17Ug/ml
6. D- dimer >4.0Ug/ml
7. Blood sugar Fasting- 10mmol/L, 2 hour after breakfast- 16 mmol/L
8. Plain Xray KUB region- Gas shadow present in left renal area.
A recent case series describes eight cases of EPN with medical management alone. Of these eight cases, four were class IV EPN, five cases required haemodialysis, whereas four needed percutaneous drainage. The authors successfully used injections of imipenem for 10 days in five patients, cefoperazone + sulbactam for 14 days in two patients, and piperacillin + tazobactam for 14 days in one patient. Recent update recommended more conservative management, there are case reports of successful treatment with percutaneous drainage and antibiotics. Our patient recovered well with conservative management without percutaneous drainage and surgery. Conservative management could be done with close monitoring and follow up the patient. But nephrectomy is the best way to treat advanced disease.

References:
LETTER TO THE EDITOR

To
Editor-in-Chief
Journal of Bangladesh College of physicians and surgeons

Subject: Letter to editor on the review article ‘Probiotics and their role in GI Diseases’

Dear Sir,

I would like to thank Colonel Dr Shaila Parveen and Colonel Dr Mir Azimuddin Ahmed through you for the well articulated and informative review article on the role of Probiotics in medical practice.

This is a hot topic in the field of medical research. The article started with amazing fact that trillions of bacteria and yeasts live within our GI. They outnumber total number of human cells and genome. This beneficial symbiosis coevolve through generations and ages. Its impact on immune system and gut homeostasis has opened a new horizon of knowledge of healing different gastrointestinal diseases. In the later part of the indications and precautions on usage of probiotics has been detailed in a nice and descriptive way. Use of probiotics in recurrent Clostridium difficile associated diarrhea and necrotizing enterocolitis is life saving. It is praiseworthy that the authors mentioned the side effects of probiotics as well. I would be obliged if some of my confusions are addressed.

(a) It is mentioned that in the USA Probiotics are medical food and must be used under medical supervision. Would you please clarify the kind of supervision and recommendations of regulatory bodies like US FDA and European Food Safety Authority? Is there any recommendation of Bangladesh Pharmacy Council or food safety authority?

(b) Whether the level of evidence is available for use in maintenance of remission of Ulcerative Colitis and Crohn’s disease?

(c) Can we predict the group of persons who are vulnerable to the side effects?

(d) What are the effect of different human gut microbiome of babies born through normal delivery and cesarean section?

(e) Is there any impact of commercially available household water filters and hand wash campaign on human gut microbiome?

At last I must thank the authors again for the hard work and trouble taken by them to write the thoughtful review article at right time.

With regards

Dr. Chandra Shekhar Bala
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Dr. Gobinda Chandra Banik
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Author’s reply

To
The Editor-in-Chief
Journal of BCPS.

Sir,

The gut microbiome has now been linked to an ever increasing number of clinical fields beyond gastroenterology like immunology, rheumatology, diabetes and neurology. More so for gastroenterology as the GI system is the seat of the microbiome. The link between Helicobacter pylori and GI diseases like peptic ulcer disease and gastric cancer is considered by some to be the most significant discovery yet to have arisen from this new field of research. I shall try to address the five queries raised by the readers one by one.

(a) US FDA
Probiotics face challenges similar to other areas of development where there is a lack of conclusive findings as to the safety of an evolving product. The FDA regulates products by category. Each category is
regulated by a center that evaluates and monitors many aspects of the life cycle of a product. These may include research, manufacture, safety, efficacy, transportation, labeling and claims.

Probiotics have traditionally appeared in foods which along with cosmetics are the least regulated products consumers use in or on their bodies. The earliest probiotic products were fermented products such as kefir (a fermented milk drink), yogurts and present day products like Redness Solutions Makeup SPF 15 with Probiotic Technology made by Clinique company. Probiotics are regulated based on the product category into which they fall i.e., food, food additive, cosmetic, medical devices, dietary supplement or drug. When questions arise regarding into which category a probiotic belongs, the answer is determined on a case-by-case basis. Many Working Group members expressed concern that because probiotics fall into multiple categories, expertise about them is spread unevenly across multiple centers at the FDA. Finally, although no probiotic drug have yet been approved by the FDA, several clinical trials are under way that are studying the safety and efficacy of probiotic formulas.

b. Crohn's disease and Ulcerative colitis

Crohn's disease, ulcerative colitis and pouchitis after ileal pouch anal anastomosis in ulcerative colitis patients are often refractory to standard therapy. So the rational to use probiotics and its beneficial efficacy in the treatment of chronic inflammatory bowel disease (IBD) is increasingly under scrutiny. Most of relevant data derived from studies on probiotics report some efficacy in ulcerative colitis and in pouchitis while disappointing results are available for Crohn’s disease.\(^1\) There is emerging interest on the role of selective modulation of microflora in inducing benefits in inflammatory intestinal disorders, by as probiotics, prebiotics, synbiotics, antibiotics and fecal microbiota transplantation (FMT).

Recent developments in gene-sequencing technologies and potent bioinformatic tools have enabled new insights into the effects of microbial communities on various pathological conditions. Analysis of the microbiome using 16S rRNA sequencing confirmed that microbiota in IBD patients significantly differs from the one present in healthy individuals.\(^2\) With its diversity and bacterial load decreased assembles the characteristics of the status known as “dysbiosis”. It still remains unknown whether dysbiosis is a cause or consequence of intestinal inflammatory response in IBD.

The most convincing data for using probiotics in IBD comes from studies on commercial probiotic supplement VSL#3, a highly concentrated (450 billion bacteria/sachet) freeze-dried cocktail containing eight different bacterial species. VSL#3 cocktail, given in combination with standard UC therapy, results in higher rates of response and remission when compared to standard therapy alone. VSL#3 was also found effective in maintenance of chronic pouchitis and in prevention of pouchitis after ileal pouch anal anastomosis. Recently, researchers have taken probiotics to the next level, genetically modifying bacterial species to produce specific immunosuppressive mediators, \(i.e.,\) IL-10 and antioxidant enzymes, \(i.e.,\) superoxide dismutase (SOD). This is an interesting approach for mucosal delivery of selected proteins and could prove a feasible strategy for down regulating gut inflammation in IBD. It ultimately led to European Crohn’s and Colitis Organisation (ECCO) guidelines suggesting the use of this particular probiotic mixture both for maintenance of antibiotic-induced remission and for prevention of pouchitis.

\(E.\ coli\) Nissle 1917 and VSL#3 both received a very strong “A” recommendations in American Recommendations for probiotic use for the maintenance of remission in UC. ECCO guidelines also recognized the role of VSL#3 probiotic mixture for treating relapsing, mild-to-moderate UC. The reports on the use of probiotics in Crohn’s Disease do not suggest any disease improvement, so probiotics are not advocated for this patient population.

c. Safety

In people who are generally healthy, probiotics have a good safety record. On the other hand, there have been reports linking probiotics to severe side effects, such as dangerous infections in people with serious underlying medical problems. The people who are at risk of severe side effects include critically ill patients, those who have had surgery, very sick infants and people at extremes of age with weakened immune system. Even for healthy people, there isn’t enough information right now to answer some safety questions. Most of our knowledge about safety comes from studies of \(Lactobacillus\) and \(Bifidobacterium\); less
is known about other probiotics. Information on the long-term safety of probiotics is limited and safety may differ from one type of probiotic to another. For example, even though a study showed that a particular kind of *Lactobacillus* appears safe in healthy adults of age 65 and older this does not mean that all probiotics would necessarily be safe for people in this age group.

d. NVD and C/S
It has become clear that the gut microbiota not only plays a major role in priming and regulating mucosal and systemic immunity but the immune system also contributes to host control over microbiota composition. These two ways of mutual communication between the microbiota and the immune system were coined as “outside-in” and “inside-out” respectively.

In comparisons with other mammals, scientists have noted that human mothers produce a much more varied number of complex sugars called oligosaccharides (more than 200 have been identified to date). These sugars cannot be digested by babies and are more likely to be food for the microbiome as they selectively provide nourishment to one bacterial subspecies that in turn produces adhesive proteins with immunoprotective and anti-inflammatory qualities. A recent study showed that the microbiome of children who were exclusively breastfed differed significantly from those who were given formula and even from those who alternated between the two. Same is the case with babies born by NVD who are exposed to mothers birth passage commensal microbiota than with those born in aseptic condition by C/S.

e. Handwash Campaign
The microbiome’s delicate ecologic balance has given rise to the theory that modern hygienic practices (overuse of antibiotics, improved sanitation, too much hand washing, non-touch way of living) have actually weakened aspects of our health by reducing exposure to the bacteria on which we thrived for thousands of years. Kids today don’t play with mud. They just stay inside and text. They are not exposed to anything or anybody. Isolated hunter-gatherer tribes in South America have been shown to have considerably more diverse microbiomes than those from industrialized populations. The same progress that may be hurting us has also given us the means to unravel the reasons potentially to intervene and correct it.

Regards,

Colonel Shaila Perveen
Senior Gastroenterologist,
CMH, Dhaka.
Dear Fellows,

AssalamuAlaikum. I am glad that the July 2016 issue is published, though late due to the intervening long ‘Eid vacations’. I am thankful to my Obstetrics and Gynecology fellows for contributing the most in this issue and bringing up some fantastic topics. The original article ‘Endometriosis: correlation of severity of pain with stages of disease’ perfectly addresses a common misconception among junior doctors and general practitioners that ‘more the pain, severer the disease’. Rather, the study shows that only severe pain has strong positive correlation with stage IV disease and mild to moderate pain has no correlation. 85% of the 65 patients were infertile, which is a major concern prevailing in our society. P Fatima et al has successfully highlighted the matter in their original article: ‘Treatment seeking behavior and the profile of infertile patients attending a tertiary infertility center in Dhaka’. Though understandable in our society, it is alarming that 30% go to traditional healers and 36% consult both traditional healers and GP. We need to act together to increase awareness at all levels immediately.

Thanking you all.

Prof. Khan Abul Kalam Azad
Editor-in-Chief
Journal of BCPS