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MANUSCRIPT PREPARATION AND SUBMISSION

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

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

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

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

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Article Types
Five types of manuscripts may be submitted:

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

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

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

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

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

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

I. A. Preparing a Manuscript for Submission to JBCPS

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

Conditions for submission of manuscript:
- All manuscripts are subject to peer-review.
- Manuscripts are received with the explicit understanding that they are not under simultaneous consideration by any other publication.
- Submission of a manuscript for publication implies the transfer of the copyright from the author to the publisher upon acceptance. Accepted manuscripts become the permanent property of the Journal of Bangladesh College of Physicians and Surgeons and may not be reproduced by any means in whole or in part without the written consent of the publisher.
- 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:
   - Title page
   - Summary/abstract
   - Text
   - Acknowledgement
   - References
   - 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).

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The title page should have the following information:

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

2. Authors’ names and institutional affiliations.

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

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• 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).

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• Provide a context or background for the study (that is, the nature of the problem and its significance). It should be very specific, identify the specific knowledge in the aspect, reasoning and what the study aim to answer.
• State the specific purpose or research objective of, or hypothesis tested by, the study or observation; the research objective is often more sharply focused when stated as a question.
• Both the main and secondary objectives should be clear.
• Provide only directly pertinent primary references, and do not include data or conclusions from the work being reported.

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

I. A. 6. b. Technical Information
• Identify the methods, apparatus (give the manufacturer’s name and address in parentheses), and procedures insufficient detail to allow others to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and brief descriptions for methods that have been published but are not well-known; describe new or substantially modified methods, give the reasons for using them, and evaluate their limitations. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration.
• Authors submitting review article should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

I. A. 6. c. Statistics
• Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals).
• Avoid relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size. References for the design of the study and statistical methods should be to standard works when possible (with pages stated).
• Define statistical terms, abbreviations, and most symbols.
• Specify the computer software used.

I. A. 7. Results
• Present results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Please keep the result the sequence of specific objective selected earlier.
• Do not repeat all the data in the tables or illustrations in the text; emphasize or summarize only the most important observations. Extra or supplementary materials and technical detail can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.
• When data are summarized in the Results section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them.
• Restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables.
• Avoid nontechnical uses of technical terms in statistics, such as “random” (which implies a randomizing device), “normal,” “significant,” “correlations,” and “sample.” Where scientifically appropriate, analyses of the data by such variables as age and sex should be included.

I. A. 8. Discussion
• Emphasize the new and important aspects of the study and the conclusions that follow from them in the context of the totality of the best available evidence.
• Do not repeat in detail data or other information given in the Introduction or the Results section.
• For experimental studies, it is useful to begin the discussion by briefly summarizing the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies, state the limitations of the study, and explore the implications of the findings for future research and for clinical practice.
• Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses when warranted, but label them clearly as such.

I. A. 9. References
I. A. 9. a. General Considerations Related to References
• Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible.
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I. A. 9. b. Reference Style and Format
• References should be numbered consecutively in the order in which they are first mentioned in the text.
• Identify references in text, tables, and legends by Arabic numerals in superscript.
• References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure.

I. A. 10. Tables
• Tables capture information concisely and display it efficiently.
• Use tables/fig that are relevant to study
• Try to limit the number of tables/figure
• Type or print each table with double-spacing on a separate sheet of paper. Number tables consecutively in the order of their first citation in the text and supply a brief title for each.
• Do not use internal horizontal or vertical lines. Give each column a short or an abbreviated heading. Authors should place explanatory matter in footnotes, not in the heading. Explain all nonstandard abbreviations in footnotes, and use the following symbols, in sequence:
  *, †, ‡, §, _, ¶, **, ††, ‡‡, §§, _ _, ¶¶, etc.
• Identify statistical measures of variations, such as standard deviation and standard error of the mean.
• Be sure that each table is cited in the text. If you use data from another published or unpublished source, obtain permission and acknowledge that source fully.

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• 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)
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• Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples.
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• 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.

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

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

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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

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**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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## OBITUARY  

Chronic Kidney disease (CKD) is a world-wide public health problem. Incidence and prevalence are rising worldwide with poor outcome and high cost of treatment. CKD is defined as kidney damage or decrease in glomerular filtration rate GFR below 60ml/min per 1.73 m² for 3 months or more irrespective of cause with or without kidney damage. Kidney damage is defined by structural or functional abnormalities of the kidney with or without decreased GFR, manifested by either pathological abnormalities or marker of kidney damage such as abnormalities of blood, urine, or in the imaging tests. Markers of kidney damage are proteinuria, microalbuminuria, haematuria and presence of casts with cellular elements.

Chronic kidney disease is classified in 5 stages based on glomerular filtration rate (GFR).

### Classification of CKD based on GFR

<table>
<thead>
<tr>
<th>CKD Description</th>
<th>GFR (ml/min/ stage 1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Kidney damage with normal or ↑GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2. Kidney damage with mild ↓GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3. Kidney damage with moderate ↓GFR</td>
<td>59-30</td>
</tr>
<tr>
<td>4. Kidney damage with severe ↓GFR</td>
<td>29-15</td>
</tr>
<tr>
<td>5. Kidney Failure</td>
<td>≤15</td>
</tr>
</tbody>
</table>

Classification of CKD based on GFR as proposed by the kidney Disease Outcome Quality Initiative (KDOQI) guidelines. The true incidence and prevalence of CKD in our community are difficult to ascertain as early to moderate CKD is usually asymptomatic and due to lack of enough studies in our country.

However, different studies were carried out to find the prevalence of diabetes mellitus, hypertension and proteinuria. Prevalence of diabetes was 4.1%, hypertension 11.6% and proteinuria 7.7%. Low eGFR (<60ml/min/m²) was found 14.8% using Cockcroft-Gault (C-G) formula and 12.1% using modification of Diet in Renal Disease (MDRD) formula. Another study showed prevalence of Diabetes 4%; hypertension 11% and proteinuria 6% in rural area of Bangladesh.

National Health and Nutrition Evaluation Survey (NHANES) observed chronic kidney disease is 15.2%; out of which diabetes constitute 7.7% in community prevalence in USA in 2003-2006. Community prevalence of early kidney disease in Australia observed haematuria 5.6%; proteinuria 2.4%; albuminuria 6%, chronic kidney disease 12%. The community prevalence of chronic kidney disease in Norway showed diabetes mellitus 4.4%; hypertension 24%; microalbuminuria 6%; proteinuria 2% and chronic kidney disease 10.5%. Global kidney disease prevention describe prevalence CKD varies 11 to 33%, microalbuminuria 12 to 19%, dipstick proteinuria 6 to 31%, eGFR 60ml/min/1.7m² in 2.5 to 18%. The disease profile of the world is changing and chronic diseases accounts for the majority of global morbidity and mortality rather than infectious disease. The causes of chronic kidney disease reflects this change. Diabetes and hypertension is now major cause of end stage renal failure worldwide. Primary causes of renal failure in USA are diabetes 43.8% followed by hypertension 26.5%; glomerulonephritis 7.6%, cystic disease of kidney 2.3%, urological disease 2%, other causes 17.5%. However, the causes of chronic kidney disease in Bangladesh are glomerulonephritis 47%, diabetes mellitus 24%, hypertension13%, obstructive uropathy 8%, undetermined 6%.

Incidence of end stage renal disease (ESRD) refers to the number of patients with ESRD beginning renal replacement therapy (RRT) during a given time (usually a year) in relation to population (usually in a year), it is expressed as number of patients per million population for year. Usually the incidence of ESRD does not take into account patients not treated by RRT, so it underestimate the overall true incidence of ESRD (CKD stage 5). The prevalence of ESRD encompasses both new and continuing patients on RRT. The incidence and prevalence of ESRD vary widely from country to country. Incidence and prevalence of renal replacement therapy...
therapy (RRT) in United States 360 of 1625 respectively per million population (PMP) in 2006. In Australia, the incidence and prevalence cases on RRT are 115 of 778 respectively per million population in 2006. In UK this RRT rate are 113 of 725 PMP. In Bangladesh, prevalence of all new and old cases in haemodialysis from 1998 to 2010 are 2411. The prevalence of all transplant cases is 685 from 1988 to 2010 and prevalence of CAPD patients 420 from 1998 to 2010. Risk factors for CKD are susceptibility, initiation and progression factors. Susceptibility factors predispose to CKD, initiation factors directly trigger kidney damage and progression factors one associated with worsening on already established kidney damage. The initiating factors are systemic hypertension, diabetes mellitus, cardiovascular disease dislipidaemia, obesity (metabolic syndrome), hyperuricemia, smoking, low socioeconomic status and nephrotoxic expose (NSAID, analgesic, heavy metal) and progression factors are older age, male gender, genetic predisposition, poor blood pressure control, poor glycemic control, proteinuria. The risk factors are classification as modifiable and nonmodifiable. Modifiable risk factors include hypertension, proteinuria, metabolic factors, smoking, alcohol consumption and drugs. Patients with early stage of CKD is 5 to 10 times more likely to die from cardiovascular events before reaching ESRD. Many CKD patients with GFR below 60 ml/min/1.73 m² die from cardiovascular or other causes before they reach ESRD. Cardiovascular risk factors for CKD patients are divided traditional and nontraditional. Traditional risk factors are same as initiating factors. However, nontraditional risk factors are albuminuria, anemia, abnormal Ca/P, high PTH level, ECF overload, Vit D analogue, electrolyte imbalance, inflammation, malnutrition, oxidative stress, thrombogenic factors and homocysteine.

The cost of treating patients with ESRD is substantial and has an impact on health care system of the country. Globally it assumed, 2 million individual was treated with RRT in 2010 at cost of US $1 trillion during the decade. The great majority (90%) of those treated who live in high economies. More them 100 of 212 countries of the world with low and middle economies do not have enough provision for RRT. Therefore, low and middle economies countries ESRF is a death sentence.

In Bangladesh only 10% of ESRD patient can afford renal replacement therapy in the form of haemodialysis, continuous ambulatory peritoneal dialysis and kidney transplantation. Cost of ESRD patients care by maintenance haemodialysis or renal transplant in our countries about US$ 6000/per patient/ year and for CAPD US$ 8000/Patient/ year. Therefore to solve the problem, early detection and prevention of CKD is the answer. To create public awareness, to know about their kidneys “World Kidney Day” stated in 2006 with different theme every year. World kidney day is a joint initiative between the International Society of Nephrology (ISN) and International Federation of Kidney foundation (IFKF). In Bangladesh, every year world kidney day is observed with the other countries of the world. Kidney disease is a “silent killer” which will largely affect the quality of life. In 2011, world kidney day prescribe 7 golden rules or easy ways to reduce of risk of developing kidney disease. The seven golden rules are (1) Keeping fit and active (2) Keep regular control of blood sugar level (3) Keep blood pressure control (4) Eat healthy and keep your weight in check (5) Not to smoke (6) Not to take over the counter pill on a regular basis and finally (7) Check your kidney function if you have one or more of the high risk factors such as (a) If you have diabetes (b) if you have hypertension (c) if you are obese (d) if you or one of your family members suffer from kidney disease (e) if you are African, Asian or Aboriginals is origin.

In summary, chronic kidney diseases is one of the leading causes of death in the world. In Bangladesh, prevalence of CKD is 14.8%, and prevalence of hypertension varies form 11.6% to 19%, diabetes mellitus 4.1%, and proteinuria varies from 6 to 7.7%. Causes of end stage renal disease are glomerulonephritis 47%, diabetes mellitus 24%, hypertension 13%, obstructive uropathy 8% undetermined 6% cases. About 30,000 patients developed ESRD per year in Bangladesh. Only 10% of those patients can afford to bear the cost of treatment for renal replacement therapy. More than 100 nephrologists, equal number urologists, 20 transplant surgeons about 200 dialysis nurse and
twenty dialysis engineers constitute existing manpower in Bangladesh. If we consider 18 million people are suffering from CKD and 100 nephrologists for this group of patients is very few which means average 800 patients per nephrologist/ day. Considering this situation, prevention and early detection of CKD cases is the answer to face the problem of kidney disease in Bangladesh.

*(J Bangladesh Coll Phys Surg 2013; 31: 1-3)*

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2. KS. Alam, M.N Huda, HU Rashid, Prevalence of Diabetes mellitus, Hypertension, Proteinuria and Association of these risk factors with estimate Glomerular Filtration Rate (eGFR) in adult disadvantaged population. Bang. Renal J. 2010; 29 (1): 1-6
Secondary Alveolar Bone Graft with the Cancellous Iliac Crest in Cleft Patient: Outcome Study

MM HASAN\textsuperscript{a}, M RAHMAN\textsuperscript{b}, W ALI\textsuperscript{c}, M AHMED\textsuperscript{d}

Summary:
Cleft palate is the second most of all body congenital anomalies and the most common congenital anomaly to affect the oro-facial region. Reconstruction of cleft alveolus is an integral part of the cleft patient management. The aim of this study was to restore the form of maxillary arch, closure of oronasal communication and eruption of tooth in the cleft area. Nine patients were selected for the study, age ranges from 8-11 years and was referred by the orthodontist. Cancellous bone from the Iliac crest was grafted in cleft area and subsequently evaluated for graft success using radiographs. Good alveolar bone with trabeculation was observed and teeth were erupted in the cleft area with complete arch form. There were no complication in terms of pain, infection, exposure of graft, rejection of graft, and wound dehiscence at the recipient site. There were also no major complications in the donor site. It was found that secondary alveolar grafting during the mixed dentition period is beneficial for patient. This erupted tooth as well as the grafted bone gives the complete arch form and function of the cleft patient which is important for the orthodontist for subsequent arch expansion and establishment of correct occlusal relationship.

\textsuperscript{(J Bangladesh Coll Phys Surg 2013; 31: 5-10)}

Introduction:
Cleft palate is the second most of all body congenital anomalies and the most common congenital anomaly to affect the oro-facial region. Management of the cleft lip and palate patient is a multistage and multi disciplinary procedure. So repair of cleft lip and palate is done primarily by many discipline of medical science with success but it failed mostly in the area of the nostrils and alveolar ridges along with that of teeth in the cleft alveolus region\cite{1}. Attention has been made to these problems in the developed countries but in the developing country it is still overlooked due to the lack of team approach for treating the cleft patient. Repair of the cleft alveolus is the integral part of the cleft management. This paper presents 09 cases (referred cases in the duration of July 2009 to December 2010) of alveolar cleft referred by the orthodontist after expansion of the collapsed arch, with a view to have complete arch form, closure of oro-nasal communication and to erupt the canine. The orthodontist during their treatment procedure for the eruption of the canine and build the arch form with correct occlusal relationship referred the patient to the maxillofacial surgeon for alveolar bone grafting but not by the primary operating cleft surgeon. Then after completion of the arch form and eruption of canine and closure of oro-nasal communication the occlusal relationship of the patient will be followed up by the referral orthodontist. Study showed that patients who underwent maxillary expansion prior to surgery were more successful.\cite{2} But conflicting claims have been made with regard to success and time of surgery in the cleft alveolus cases. Among these the studies of Bohn,\cite{3} Bjork and Skieller,\cite{4} Waite and Kersten \cite{5} and Boyne and Sands \cite{6} are important. Alveolar bone grafting should be timed between 6 years of age and prior to eruption of teeth in the cleft region.\cite{1} Secondary bone grafting of the maxilla and the repair of residual alveolar cleft at the stage of mixed dentition preceding eruption of the canine has become an adjunctive procedure aiming to further improve the functional and esthetic rehabilitation of...
patient with unilateral or bilateral cleft lip and palate.\textsuperscript{7} Fresh autogenous bone is the ideal bone graft material because it supplies living immunocompatible bone cells essential for osteogenesis.\textsuperscript{8} The bone can be harvested from several sites. The ilium is the most frequently used, as access is easy and a large amount of bones can be obtained from the area.\textsuperscript{6,8,9} The use of allogenic material for alveolar bone grafting did not show a statistical benefit.\textsuperscript{10} During repair of the alveolar cleft with bone it should be kept in mind that the defect area should be covered with keratinized mucosa for the ease of eruption.\textsuperscript{11} For the present study 09 cases of residual alveolar cleft with unilateral or bilateral cleft lip and palate of mixed dentition period irrespective of sex and socio-economic status were selected. The study was done in the department of Oral and Maxillofacial Surgery, Dhaka Dental College and Hospital in the duration of July 2009 to December 2010. Postoperative clinical and radiological evaluation was done to evaluate formation of bone in the cleft region and restore form of the clefted maxillary segments, closure of oro-nasal communication and the eruption of canine.

**Materials and Methods:**

The present study was done on nine (09) patients having cleft alveolus in the period of July 2009 to December 2010. Out of these eight were unilateral and one was bilateral cleft. Patient selection was done irrespective of sex (six patients were male and three were female) and age range of the patients were 08-11 years. The cases were diagnosed on the basis of clinical and radiological (CBCT and intraoral occlusal views) features and also the history of previous cleft palate surgery. Informed written consent was taken from the patient or from the guardian describing the surgical procedure. Post operative follow up was given at 3 months interval up to 18 months for all of the patient. Trabecular pattern of the grafted bone was evaluated by comparing the x-ray of the patient at clefted site and normal site using a standard scale (Gray scale) with image processing software. The first focus was from the healthy portion of maxilla and the second focus was from the grafted bone. In the image study those who had the gray scale score similar to that of normal bone was called complete trabecualtion. When the image showed complete trabecualtion it was termed as complete bone formation. Tooth eruption was evaluated by visual examination by evaluating the crown height.

Operative procedure:

The procedure was performed under general anesthesia with naso/oroendotracheal intubation. The surgical site was prepared with 10% povidone Iodine solution. Incisions were made along the cleft margins splitting the labial/nasal and palatal/nasal mucosa (Fig:3). Nasal layer was dissected carefully from the labial layer and sutured to make the nasal floor. Labial incision was extended for adequate exposure. Two gingival flaps were then raised. Palatal mucoperiosteal flaps were elevated to visualize the cleft and ease of closure.

The palatal mucoperiosteal flaps were then approximated medially with interrupted 4–0 absorbable Arch form was compared with the pre and post operative model by the orthodontist. Oro nasal communication was checked with gutta-percha point.

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**Fig.-1:** *Cleft alveolus (Preoperative)*

**Fig.-2:** *Incision around the cleft alveolus*
sutures, thus creating a soft tissue pocket between nasal floor and palatal mucosa to accommodate the bone graft. The cancellous bone graft were harvested from the ipsilateral iliac crest, mixed with blood and was packed tightly to completely fill the bony cleft and restore the thickness and height of the nasal floor and the maxilla as close to normal as possible. Any permanent teeth erupting through the cleft was covered with bone graft. Finally, the previously raised gingival mucoperiosteal flaps were sutured together and inferiorly to the palatal flaps to provide complete coverage of the bone graft (Fig.-3). The flaps were further secured with a few interrupted sutures between the flap and papilla while the area of the back cut posterior was left open to heal secondarily. The surgical site was covered and stabilize with the custom made vaccu formed occlusal splint (Fig.-4). Cancellous graft from iliac crest was harvested by lateral approach and iliac crest was opened by Tschopp approach\(^{12}\) (pedicles the iliac crest on the external oblique muscle. The wound of the donor site was closed in layers and suction drain was kept in situ.

![Fig.-3: Sutured mucoperiosteal flap](image)

![Fig.-4: Erupted canine and bone formed](image)

**Results:**

Present study comprised 09 individuals having cleft alveolus (8 unilateral and 1 bilateral). Out of 09 patients 06 were male and 3 were female with a male female ratio of 3:1. Age range of all the patients were 8 to 11 years.

Every patient was followed up at 3-month interval with the recording of X-rays, and clinical photograph up-to 18 months. The following observations were noticed and results were obtained from this study.

At 1 month postoperative trabeculae formation was absent in 100% cases and was present at 3 months postoperatively in 66.66% cases. In remaining 33.33% cases trabeculae formation was seen within 6 months follow-up (Table.1)

<table>
<thead>
<tr>
<th>Trabeculae formation</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>9(100)</td>
<td>0</td>
</tr>
<tr>
<td>3 months</td>
<td>3(33.33)</td>
<td>6(66.66)</td>
</tr>
<tr>
<td>6 months</td>
<td>0(0)</td>
<td>3(33.33)</td>
</tr>
</tbody>
</table>

Table I showed no trabeculae was found in 1 month follow up but at 3 months follow up trabeculation was

![Fig.-5: Vaccuform splint in situ](image)
found in 66.66% cases remaining 33.33% cases trabeculation completed in 6 months.

Regarding tooth eruption in the grafted bone of the clefted portion 22.22% showed tooth eruption within 12 months of bone graft and 33.33% showed tooth eruption at 15 months and 44.44% showed at 18 months (Table 2). Oro nasal communication was not persist in any of our post operative cases. Arch form was satisfactory in all the cases (100%) according to the orthodontics plaster model evaluation.

Table-II

<table>
<thead>
<tr>
<th></th>
<th>No eruption n(%)</th>
<th>Eruption n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>9(100)</td>
<td>0(0)</td>
</tr>
<tr>
<td>3 months</td>
<td>9(100)</td>
<td>0(0)</td>
</tr>
<tr>
<td>6 months</td>
<td>9(100)</td>
<td>0(0)</td>
</tr>
<tr>
<td>9 months</td>
<td>9(100)</td>
<td>0(0)</td>
</tr>
<tr>
<td>12 months</td>
<td>7(77.77)</td>
<td>2(22.22)</td>
</tr>
<tr>
<td>15 months</td>
<td>4(44.44)</td>
<td>3(33.33)</td>
</tr>
<tr>
<td>18 months</td>
<td>0(0)</td>
<td>4(44.44)</td>
</tr>
</tbody>
</table>

Table 2 showed that in 22.22% cases tooth erupted within 12 months of bone graft and 33.33% showed tooth eruption at 15 months and 44.44% showed at 18 months.

Table-III

<table>
<thead>
<tr>
<th></th>
<th>Closed</th>
<th>Persists</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>9(100)</td>
<td>0</td>
</tr>
<tr>
<td>3 months</td>
<td>9(100)</td>
<td>0</td>
</tr>
<tr>
<td>6 months</td>
<td>9(100)</td>
<td>0</td>
</tr>
</tbody>
</table>

Table-III Showed Oro nasal communication was closed in all of the cases at 1 month follow up. and none of the cases showed persistence of oro nasal communication.

Regarding donor site, pain was present in all cases (100%) till second postoperative week but after that nobody complains of pain at the donor site. There was no infection at the donor site in any patient from immediate postoperative to sixth week follow-up. Paresthesia was absent in all the patients from immediate postoperative to sixth week postoperative follow-up.

Discussion:

Present study comprised 09 individuals having cleft alveolus (8 unilateral and 1 bilateral). In this study six patients were male and three patients were female with a male female ratio of 3:1. Stevenson and Johnson stated that cleft lip with or without cleft palate is more common in males with the ratio of approximately 2:1 over females. This study correlates the above study.

Earlier primary bone grafting was used to obtain closure of the residual alveolar cleft. But according to Bohn this procedure interfered in mid-facial growth and creates anterior and posterior cross bite. Jackson IT showed that the increase in width in anterior maxilla is minimal after age 6–7 years; accordingly surgical interference with the primary palate after the age of 7–8 years would have little effect on growth. The presented study was done for the patient of age range 8-11 years which will not produce any affect on growth. Secondary osteoplasty is performed in patients between the ages of 6 and 12 years (the period of mixed dentition). The exact timing of grafting is determined by the position of the crown of the tooth. The optimum time is when the root of the permanent canine has formed by approximately one-fourth to two-thirds of its length that is in between 8-9 years. Bone grafting, before or after arch expansion has still controversy. Literature showed that bone grafting of alveolar cleft patients is commonly done after expansion of the maxilla. Sheats RD etal. Reviewed and showed that after arch expansion, grafting of the cleft area with bone will maintain arch form and allow long-term retention of the maxillary expansion. He also reviewed that no matter what procedures are done and what type of retention is used, maxillary expansion of cleft sites is doomed for relapse. In all of these study cases arch expansion was done by the orthodontist before the bone grafting.

The coverage of the mucosa over the alveolar cleft must be with keratinized mucosa which requires for tooth eruption. In this regard gingival flap is preferable as tooth eruption into the bone grafted alveolar cleft may
still occur. In this study eruption of tooth in the cleft region was seen 22.22% after 12 months and 33.33% after 15 months and 44.44% after 18 months. Teeth eruption through bone grafts has been a controversial topic. Some report showed spontaneous eruption in 95% of patients whereas others indicate a remarkably low rate of eruption and emphasize the need for surgical uncovering. In this study 100% of cases had spontaneous eruption and no surgical intervention or orthodontic traction were needed. In this study it was observed that 100% of the cases trabeculae formation of the grafted bone was completed within 6 months of bone graft that is bone transformed into the functional alveolar bone which responded to the eruption. This finding matches with the observations made by Abyholm, Bergland, and Semb and Bjork and Skiller. In their study 75% subjects showed eruption of tooth without orthodontic assistance.

For the reasons of ease, simplicity, and low expense, the dental and occlusal radiograph has become the most frequently used tools for reporting and comparing the bone formation after secondary bone grafts. In this study 100% evidence of trabeculae formation was noted after 6 months follow-up which coincides with the findings made by Abyholm, Bergland, and Amanat. The studies of Albertksson showed that cancellous bone grafts were fully revascularized after 3 weeks but transformation of graft into a normal trabecular pattern was not completed before 3 months. The finding of Albertksson was observed in all cases reported in this study. Sinder-Pederson and Enemark showed in a study of bone grafting in cleft lip and palate reported 100% success for bone grafting and their mean follow-up was 7.2 months only. In the presented study success rate was 100% at 18 months follow-up.

The ribs, iliac crest, calvarium, mandibular symphysis and tibia are the most common donor sites. Cancellous bone from the iliac crest is generally considered the best material for bone grafting of alveolar clefts. The presented study uses cancellous iliac bone from anterior iliac crest in all of the cases. Bone grafts harvested from the posterior iliac crest in general have less morbidity, but for the presented surgical procedure as the patient need postural change while the patient is under general anesthesia so it is avoided. Studies showed that endochondral cancellous specimens have a higher percentage increase in bony volume than cortical membranous and cortical endochondral bone grafts. The presenting study uses endochondral cancellous bone only.

Postoperative pain was primarily due to muscular injury and could be significantly reduced when the fascial attachments of the abdominal wall musculature were detached from the crest without cutting through the thigh or abdominal wall muscles. There was no sign of morbidity at donor site in 100% cases. This finding correlates with the findings of Cohen and Figueroa, Schafer and Aduss. In the presented study there was pain at donor site in 100% cases up to the second postoperative week after that all the patients were free of pain. This finding correlates with the that of Laurie et al. who stated that all patients experienced moderate postoperative pain lasting 2 weeks to 2 months with an average of 6 weeks.

A watertight repair of the palatal cleft and the nasal lining and a secure closer of the soft tissue across the anterior alveolus are essential. Accurate and extreme care must be taken to improve oral hygiene prior to surgery. In all of these cases oral hygiene was maintained meticulously and did not find complete failure in any of cases. This finding was similar as reported by Bergland et al. and Turvey et al.

Conclusion:
Eruption of the tooth in the cleft site is the paramount important for the alveolar cleft patient. This erupted tooth as well as the grafted bone gives the complete arch form and function of the cleft patient which is very important for the orthodontist for subsequent arch expansion and establishment of correct occlusal relationship. So treatment of alveolar cleft patient without alveolar bone graft and subsequent orthodontic treatment would not be completed. Mixed dentition period (8-11 years) is the right time for the correction of alveolar cleft and benefit of the patient. In this regard multidisciplinary team approach is obvious. Further study with large sample size and different donor site is recommended.

References:
Anaesthetic and Analgesic Effects of Adding Dexamethasone to Bupivacaine in Supraclavicular Brachial Plexus Block – A Comparative Study

M TALUKDAR\textsuperscript{a}, H BEGUM\textsuperscript{b}, MM SHOMAN\textsuperscript{c}, UHS KHATUN\textsuperscript{d}

Summary:
The present study was designed to observe the analgesic and anaesthetic effects of adding dexamethasone to bupivacaine in supraclavicular brachial plexus block for upper limb surgery.

Sixty patients of ASA grade 1 and II were randomly enrolled in this study, thirty in each group after taking informed consent and particulars of patients. Group A received only bupivacaine and Group B received dexamethasone in bupivacaine. Group A was considered as control group. Patients demographic variables and perioperative haemodynamics characteristics (pulse, BP, respiratory rate, \textit{Po2} saturation) change were not statistically significant between two groups. This study showed that earlier onset of sensory and motor blockade were seen in group B and also showed that duration of sensory and motor blockade were quite prolonged in Group B.

Prevalence of sedation in Group B slightly higher but not statistically significant. The incidence of other side effects was not statistically significant. Comparison between groups regarding onset and duration of both sensory and motor block were highly significant differences. There were no significant difference of inter group haemodynamic variables which was observed up to 8 hrs of postoperative period.

But intensity of pain measured on VAS, Group A experienced highest VAS (worse pain) at 8 hrs of postoperative period and Group B shows highest VAS at 12 hrs thereafter.

Result of duration of effective analgesia (time from supraclavicular block to first analgesic demand) study Group B had significantly longer mean duration of analgesia in comparison to control Group.

(J Bangladesh Coll Phys Surg 2013; 31: 11-17)

Introduction:
Brachial plexus regional anaesthesia has been a mainstay of the anaesthesiologist armamentarium since Hall et al first reported the use of cocaine to block upper extremity nerves in 1884.\textsuperscript{1}Regional nerve block avoids the unwanted effects of anaesthetic drugs used during general anaesthesia and the stress of laryngoscopy and tracheal intubation.

Various approaches (Interscalene, supraclavicular, infracavicular, axillary) can be used to block brachial plexus providing anaesthesia and analgesia for upper extremity surgery.\textsuperscript{2}Interscalene approach is most optimal for procedures on the shoulder, arm and forearm. In contrast, the axillary to the brachial plexus is most optimal for procedure from elbow to hand. The supraclavicular and infracavicular approach to brachial plexus result in a more even distribution of local anaesthesia and can be used for procedures on the arm, forearm and hand \textsuperscript{2}. In supraclavicular approach the plexus is blocked where it is most compactly arranged at the level of nerve trunks with rapid onset can be achieved, with high success rate for elbow, forearm, hand surgery because all the branches of the brachial plexus can be reliably blocked.\textsuperscript{3} It avoids the sparing of the ulnar nerve that frequently occur with an intersclene block and produces good musculo-cutaneous anaesthesia which is often missed with an axillary block\textsuperscript{4}.

Now-a-days different drugs have been used as an adjuvant with local anaesthetic in brachial plexus block to achieve quick, dense and prolonged blocked.\textsuperscript{5} Drugs like Morphine, Pethedine, Clonidine, Fentanyl, Dexamethasone, Midazolam are commonly used along with anaesthetic for this purpose. However their use is limited because of side effects like heavy sedation, respiratory depression and psychomimetic effects.

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Steroids relieve pain by reducing inflammation and by blocking transmission in nociceptive c fibres as well as suppressing ectopic neuronal discharge. They decrease inflammation by inhibiting the action of phospholipase A₂. The block prolonging effect may be due to its local action on nerve fibers and not a systemic one. Dexamethasone with local anaesthetics cause faster onset of action and prolong duration of analgesia. Most of the orthopedic surgeries are of uncertain duration. Local anaesthetic produces 3-4 hours of block, which is sufficient for most upper limb surgeries but not enough duration for elective postoperative analgesia. Addition of dexamethasone with local anaesthetics prolongs analgesic period. This study was carried out to compare the analgesic and anaesthetic effects of local anaesthetic with or without dexamethasone in supraclavicular brachial plexus block in respect of duration of analgesia & onset time of anaesthesia as well as the quality of block by adding dexamethasone.

Materials and methods:
This clinical study on comparison of supraclavicular brachial plexus block with or without dexamethasone in upper limb surgery was carried out at the Department of Anaesthesia, pain management and ICU, Dhaka Medical College Hospital, Dhaka, Bangladesh. Subjects were recruited and grouped randomly after clear explanation and written consent. After approval of the Ethical Review Committee of DMCH patients belonging to ASA grade I and II, aged between 18 to 60 years undergoing elective operation for upper limb (elbow, forearm and hand) were included and patients with coagulopathy receiving anticoagulant, H/O allergy to local anaesthetics, H/O hypertension, peripheral neuropathy, COPD, inadequate block those were not interested to be included in the study were excluded. A total 60 patients of upper limb surgery were divided into two groups by card sampling containing 30 patients in each group. Group A: Received bupivacaine (0.25%) 38ml + Normal saline 2ml (total 40 ml). Group B: Received bupivacaine (0.25%)38 ml+ Dexamethasone 2ml (8mg) (total 40ml) .

In the operation room patients Pulse, BP, Respiratory rate, Heart, Lungs, Base line pain score were recorded. Patients were hydrated with IV fluid infusion at a rate of 30 drops per minute with 18G canula. With all aseptic precaution supraclavicular brachial plexus block were done using paresthesia technique. Patient should be supine position, head turned to the opposite side and arm placed medially towards the body, using 22G IV cannula stylate. After getting paresthesia drugs were deposited with repeated aspiration. The time of block was noted, patients were monitored with pulse oxymeter. The onset of sensory block was assessed every 5mins with application of cold spirit swab and by response to a traumatic prick with blunt needle in different areas innervated by radial, ulnar, median, musculocutaneous nerve. The time of complete sensory block was noted. The motor block was assessed every 5 mins by asking the patients to raise their hands or move their fingers. When the patient could not move the finger or raise the hand, this was considered as complete motor block (modified Bromage scale) and the time was noted. The duration of analgesia was noted according to 0-10 cm visual analog scale (VAS) for pain at every .5 hr, 1 hr, then 2hrs interval up to 24 hrs. Sedation, nausea, vomiting, hypotension, arrhythmia, shivering were recorded.

The data were compiled and analyzed statistically using mean standard deviation independent student t-test, ANOVA, chi-square test, Fisher’s Exact test as appropriate. A p-value <0.05 were regarded as significant. The statistical calculations were done by using Statistical Package for Social Science (SPSS) version -12.

Results:
This study was intended to observe the outcome of dexamethasone as adjuvant therapy to bupivacaine for Supraclavicular brachial plexus block in upper limb surgery. 30 were assigned to Group A (received 38 ml of 0.25% bupivacaine along with 2ml normal saline) and 30 to Group B (received 38 ml of 0.25% bupivacaine along with dexamethasone (8mg) 2ml ). Changes in pulse, systolic and diastolic blood pressures, respiratory rate, Spo2 and pain measured on VAS scale were compared at different time interval perioperatively. Demographic variables demonstrate that mean age of Group B and Group A were 29.5±11.2 and 33.1±13.2 years respectively with no significant differences between the groups in terms of sex and weight (P=0.559 and p=0.160 respectively).

The mean duration of surgery was although slightly higher in Group B than that in Group A, the difference was not statistically significant (p=0.413). Onset of sensory block was significantly early in Group B than those in Group A(p < 0.001). Duration of sensory block was significantly higher in Group B than in Group A (P=0.001). The onset and persistence of motor block were significantly higher in Group B than those in Group A (p=0.026 and p<0.001 respectively).
The mean pulse rate of Group B was 80/min at baseline which gradually decreased to 68/min at 90 minutes interval and did not vary much throughout the whole period of observation in Group A. There was no significant difference in respect to changes in pulse rate (p=0.068).

The changes of systolic blood pressure at different time interval showed that the mean systolic blood pressure of Group B at baseline was 118.8mmHg and 114.7 mmHg in Group A which experienced a gradual fall up to 90 minutes interval. The changes of systolic blood pressure were similar in both groups throughout the observation (p=0.129). The mean diastolic blood pressure in Group B and Group A decreased insidiously from 76.1 and 74.2 mmHg respectively at baseline to 68.3 and 71.9 mmHg respectively at 90 minutes interval. The overall changes in diastolic blood were not statistically different (p=0.500).

Repeated measure ANOVA statistics was employed to analyze the data and P refers to overall differences between groups.

The changes in postoperative systolic and diastolic blood pressure at different time interval observed, with no significant difference (p=0.128). The mean diastolic blood pressure of Group B at 30 minutes was 74.3 mmHg without any demonstrable change over time and in Group A was 70.6 mmHg which experienced a gradual rise up to 8 hrs.

The intensity of postoperative pain measured on visual analog scale (VAS) showed that in Group B had no pain from 0.5 hour to 6 hours period. Then worst pain (VAS=8-10) after 12 hours, considered that the analgesic action of the drug was terminated and an analgesic dose was needed. No pain was observed in Group A at 0.5 hour. It increases insidiously to 2.9 cm at 4 hours interval, 7.7 cm at 6 hours interval, 8.3 cm at 8 hours interval which decreased sharply to 2.5 cm and 1.2 cm at 10 and 12 hours interval respectively following an analgesic dose.

<table>
<thead>
<tr>
<th>Table-II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Comparison of post operative pain VAS between groups</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pain VAS (cm)</th>
<th>Group P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GroupA (n=30)</td>
</tr>
<tr>
<td>Pain VAS at 0.5 hr</td>
<td>0.0±0.2</td>
</tr>
<tr>
<td>Pain VAS at 1 hr</td>
<td>0.8±0.4</td>
</tr>
<tr>
<td>Pain VAS at 2 hr</td>
<td>2.9±2.7</td>
</tr>
<tr>
<td>Pain VAS at 3 hr</td>
<td>7.7±2.2</td>
</tr>
<tr>
<td>Pain VAS at 4 hr</td>
<td>8.3±1.4</td>
</tr>
<tr>
<td>Pain VAS at 5 hr</td>
<td>2.5±1.9</td>
</tr>
<tr>
<td>Pain VAS at 6 hr</td>
<td>1.2±1.1</td>
</tr>
<tr>
<td>Pain VAS at 7 hr</td>
<td>1.1±0.9</td>
</tr>
<tr>
<td>Pain VAS at 8 hr</td>
<td>0.9±0.7</td>
</tr>
</tbody>
</table>

Student’s t Test was done to analysis the data; s= significant.

The mean Spo2 in Group B and in Group A were 99.1% and 98.5% respectively at baseline which gradually declined 98.5% and 98.2% in Group B and Group A respectively at the end of 90 minutes. No significant difference between the groups was noted in terms of changes in Spo2 (p=0.245) (Fig. 1).
Repeated measure ANOVA statistics was employed to analyse the data and \( p \) refers to overall differences between groups. \( S = \) significant.

**Table-III**

<table>
<thead>
<tr>
<th>Group</th>
<th>Duration of effective analgesia (hours)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>3.16±0.48</td>
<td>0.000*</td>
</tr>
<tr>
<td>Group B</td>
<td>12.75±5.33</td>
<td></td>
</tr>
</tbody>
</table>

Student’s t Test Was done to analysis the data and presented as mean ± SD; * = significant.

Four(13.3%) in Group A required 1\(^{st}\) analgesic dose within 6 hours after operation, while none in Group B required analgesics within the same period.

**Table-IV**

<table>
<thead>
<tr>
<th>Analgesic required 1 hr after 1(^{st}) analgesic dose</th>
<th>Group A (n=30)</th>
<th>Group B (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>4(13.3%)</td>
<td>0 (0.0%)</td>
<td>0.056**</td>
</tr>
<tr>
<td>No</td>
<td>26(86.7%)</td>
<td>30(100%)</td>
<td></td>
</tr>
</tbody>
</table>

Fisher’s Exact Test was done to analyse the data; NS = not significant.

**Table-V**

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group A (n=30)</th>
<th>Group B (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep sedation*</td>
<td>0(0.0)</td>
<td>3 (10.0)</td>
<td>0.834</td>
</tr>
<tr>
<td>Bradycardia*</td>
<td>3(10)</td>
<td>2(6.7)</td>
<td>0.217</td>
</tr>
<tr>
<td>Nausea*</td>
<td>2(6.7)</td>
<td>4(13.3)</td>
<td>0.341</td>
</tr>
<tr>
<td>Hypotension*</td>
<td>6(20.0)</td>
<td>4(13.3)</td>
<td>0.135</td>
</tr>
<tr>
<td>Shivering#</td>
<td>4 (13.3)</td>
<td>2(6.7)</td>
<td>0.335</td>
</tr>
</tbody>
</table>

\( \# \) Chi Square (\( x^2 \)) test was employed to analyze the data, *Student’s t test was done to analyze the data.

Table V demonstrates 3 (10%) subjects in Group B had deep sedation but not in Group A at all (\( P=0.834 \)). Other side effects like bradycardia, nausea, hypotension were not significant. Shivering was higher in Group A than in group B, without statistically significant.

**Discussion:**

Supraclavicular brachial plexus block is widely employed regional nerve block to provide anaesthesia and analgesia for the upper extremity surgery. Supraclavicular block provide anaesthesia of the entire upper extremity in the most consistent manner of any brachial plexus techniques. Local anaesthetics are used for this purpose. Currently available local anaesthetics can provide analgesia for limited period of time when used as single injection. Plain Bupivacaine when used alone in brachial plexus block, has been claimed to produce block as long as 3 – 8 hrs\(^9\). Practically the result could not be produced in series of study with sole bupivacaine. It is cardiotoxic and slower onset of action but has got long duration of action of certain duration. Relative duration of action with bupivacaine is 2 – 4 hrs.\(^{10} \)
Nowadays different drugs have been used as adjuvant to achieve quick, dense and prolong block. Adjuvant improves analgesia, reduces systemic side effects and reduce total dose of local anaesthetic required. Drugs like Morphine, Pethidine, Clonidine, Butorphanol, Midazolam are commonly used along with local anaesthetics for this purpose. Since Morphine, Pethidine, Butorphanol are associated with side effects like heavy sedation, respiratory depression and psychomimetic effects.

Dexamethasone is selected as adjuvant to local anaesthetics in brachial plexus block in this study because respiratory depression is not a major problem with its use. Steroids have nerve block prolonging effects. They block the nociceptive impulse transmission along the myelinated C fibres. Steroids are very potent anti-inflammatory and immunosuppressive agents. Perineural injection of steroids is reported to influence postoperative analgesia. A study in axillary plexus block suggest that dexamethasone when added to lignocaine significantly prolonged duration of analgesia. In 1998 Drager Christiane, reported prolonged intercostals nerve block by using bupivacaine and dexamethasone. Perineural injection of steroid is reported to influence postoperative analgesia in a study on intercostal nerve blockade. The early onset of action in steroids group is due to the synergistic action with local anaesthetic on blockage of nerve fibres. Addition of dexamethasone as an adjuvant to local anaesthetics in brachial plexus block results in significantly early onset and markedly prolonged duration of analgesia without any unwanted effects. In 2003 Shrestha BR et al have been found addition of 4-6mg of dexamethasone effectively and significantly prolongs the duration of the analgesic as well as producing earlier onset of action. When steroid alone is used in regional blocks, the blockade is not produced. Steroids might bring about this effect by altering the function of potassium channels in the excitable cells.

Epidural steroids were used for treatment of back pain and sciatica. Various steroid has been used for this purpose. But dexamethasone, a 9α derivative synthetic glucocorticoid is preferred because of its highly potent anti-inflammatory property, about 25 – 30 times as potent as hydrocortisone and without any mineralocorticoid activity thus was found to be safer and devoid of potential side effects. The onset of motor block was faster than the sensory block in either of the group in this study. As described by Winnie in 1977 the outer motor fibers are blocked earlier than the sensory fibers which are situated deeper in the brachial plexus at the level of trunk and division. Our study showed the same result that the motor block was quicker than the sensory block. The duration of analgesia with dexamethasone in brachial block in the study by Shrestha BR et al was 12 hrs but only 4 hrs with local anaesthetics. Duration of analgesia in terms of hours, it was nearly matched with this present study. Many previous workers have included dexamethasone in Bupivacaine micro-spheres to see the block effect in animal models and found prolonged duration of block (7-11 days) when steroid was used together. Additional of small amount of dexamethasone to bupivacaine micro-capsules prolongs the local analgesia when compared to micro-capsules with plain bupivacaine after subcutaneous placement in humans. Kopacz DJ, Lacouture PG et al explored the effect of dexamethasone in bupivacaine micro capsules for intercostal blockade in healthy human volunteers and concluded that dexamethasone increased the duration of intercostal block to at least 96 hours. Methylprednisolone added to local anaesthetic in axillary block produced the prolong nerve block in the study conducted by Stan, Goodman et al. Onset of anaesthesia with dexamethasone in brachial plexus block in the study by Yadav RK et al was 16.3+/−4.3 mins and only with local anaesthetics was 9.5+/−3.6 mins which was statistically significant. In another study by Shrestha BR et al also showed that onset of action was 10-30 mins in local anaesthetic group (mean 18.15+/−4.25) and 10-20 mins (mean 14.5+/−2.10) in local anaesthetic plus steroid group. Statistical analysis revealed a significant difference between the two groups (P<0.005). Onset of anaesthesia in terms of minutes, it was nearly matched with this present study. Regarding analgesic demand between two groups, four (13.3%) of 30 patients in Group A required 1st analgesic dose within 6 hours period after operation while none of the patient in Group B required analgesic within same period (P=0.056) that was not significant. In this study 3(10%) subjects in Group B had deep sedation which was not observed in Group A at all (P=0.834). Other side effects like bradycardia, nausea, hypotension were observed in Group B (P=0.217, P=0.341, P=0.136).
shivering was higher in Group A than that in Group B although the difference was not statistically significant (P= 0.335). None of the patients had respiratory complication in perioperative period.

Steroids have block prolonging effect according to their anti inflammatory potency. Dexamethasone prolongs the action of local anaesthetics when used together.25 The pharmacodynamics and pharmacokinetics of the drugs when administered in regional nerve block is difficult to explain. There are some proposed mechanisms of action of glucocorticoids when used with bupivacaine micro- spares to extend the block effect.26 The dense and earlier motor block in the steroid group is due to the synergistic action with local anaesthetic on blockade of nerve fibers.25 The block prolonging effect of dexamethasone is due to its local action and not a systemic one.26,27 It has been found that this effect of steroid is mediated via steroid receptors.28 When steroid alone was used to block the nerves the effect was not prolonged.25,15 The action of steroid has been related with the alteration of function of potassium channels on the excitable tissues25,26

Conclusion:
The randomized comparative study of brachial plexus block with local anaesthetics, with or without dexamethasone has revealed that there was significant faster onset of action and prolonged duration of analgesia in the dexamethasone group than in the other group without any unwanted effects. This helps to minimize the cost and provides patient comfort.

Reference:
4. Telziaff JE. Periheral nerve block in Morgan GE ; Mikhail MS , Edition 2; 1995, p. 249


Comparative Safety of 0.1% Tazarotene with 0.05% Tretinoin in the Treatment of Acne Vulgaris

MH RAHMANa, MS SIKDERb, L KHONDKERC, MSI KHANd, MRU SIDDIQUIe, A NAHIDf

Summary:
A controlled clinical trial was done in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, (BSMMU), Dhaka, Bangladesh. The duration of the study was from September 2009 to February 2010. Patients of mild type acne vulgaris attending outpatient Department of Dermatology (BSMMU), Dhaka were selected by simple random sampling method. A total number of 60 patients were primarily selected and they were divided into two groups (Group-A and group-B), group A was treated with 0.05% tretinoin cream and group B with 0.1% Tazarotene cream. Mean age of Group A patients was 21.73 ± 4.30 and Group B was 19.70 ± 3.44. 43.3% of group A and 53.3% of group B was male and 56.7% of group A and 46.7% of group B was female (p=0.438). At baseline mean of total acne score was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B and at final follow up it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively (p>0.05). Side effects recorded in group A were desquamation (13.3%), dry skin (6.7%), burning sensation (3.3%) and irritation (3.3%) and in group B were desquamation (10.0%), dry skin (13.3%), burning sensation (10.0%), irritation (3.3%) and erythema (3.3%) (p>0.05). But 73.33% of tretinoin treated patient and 60% of tazarotene treated did not experience any side effects. Finally we can conclude that 0.1% tazarotene cream and 0.05% tretinoin cream is individually safe in the treatment of acne vulgaris. And the safety of 0.1% tazarotene cream is comparable with 0.05% tretinoin cream in the treatment of mild type of acne vulgaris.

Key words: Safety of 0.1% tazarotene, Safety of 0.05% tretinoin, Acne vulgaris.

Introduction:
Acne vulgaris is an extremely common disorder affecting up to 95% of the adolescent population and virtually everyone at some point in life. It can lead to significant psychological distress and long-lasting scarring.1 Acne vulgaris comprises lesions of varying morphology, from comedones, papules, and pustules to nodules and cysts.2 The pathogenesis of acne is multifactorial. Excessive sebum production, sebaceous follicles with abnormal epithelial hyperkeratinization, the presence of microbial organisms, notably the anaerobic diphtheroid Propionibacterium acnes and inflammation are the key factors involved.3 The management of acne can be challenging because of the variability in response to treatment and the need for long-term therapy.4 Currently, there is a variety of topical and systemic therapies that are recommended for the treatment of acne, including retinoids, antibiotics, benzoyl peroxide, and hormone therapy.1 Topical retinoids are an integral part of acne therapy and are considered appropriate first-line therapy, either alone or in combination with antimicrobials, for all cases of acne with the exception of the most severe.4 The abnormal desquamation of follicular epithelium can be normalized by topical tretinoin. This agent decreases the cohesion of corneocytes, minimize microcomedo formation and in time, decrease both clinical noninflammatory and inflammatory lesions.5 The newer synthetic retinoid derivative- tazarotene have demonstrated effectiveness in the treatment of acne. But lack of proper research on safety background, many dermatologists’ have confusion about tolerance of...
tazarotene in acne. To the best of my knowledge no study exploring the safety of topical Tazarotene comparing with topical tretinoin in the treatment of acne vulgaris has yet been conducted in Bangladesh. The current study was aimed to evaluate comparative safety of tazarotene cream 0.1% and tretinoin cream 0.05% in the treatment of mild acne vulgaris.

**Materials and Methods:**
A controlled clinical trial was done in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, (BSMMU), Dhaka, Bangladesh. The duration of the study was from September 2009 to February 2010. Patients of mild acne vulgaris attending outpatient department of dermatology (BSMMU), Dhaka were selected by simple random sampling method after considering the inclusion and exclusion criteria of patient selection. Inclusion criteria were age 13 to 40 years of both sexes, patients conformed to the following washout periods: 14 days for topical acne medications, 30 days for systemic antibiotics and 12 weeks for estrogen or birth control pills and 12 months for oral retinoids and female who agreed to practice appropriate contraceptive measure. Exclusion criterias were skin disorders likely to affect drug absorption or disorders requiring medical treatment within 5 days before the start of the study; known case of topical tazarotene or tretinoin hypersensitivity; history of serious allergic reactions to drug treatment; pregnancy, lactation and/or use of oral contraceptives with a specific anti-androgenic action or any oral contraceptive treatment initiated within 3 months before or during the study and patients suffering from moderate or severe type acne or nodulocystic acne.

**Ethical issues:**
The researcher was duly careful about ethical issues related to this study. In this study the following criteria was set to ensure maintaining the ethical values:
1. All patients were given an explanation of the study including the potential risks and obtainable benefits.
2. All patients were included in the trial after taking their informed consent.
3. The researcher also explained them that they have the right to refuse or accept to participate in the study.
4. All data obtained during study period from the patients remained confidential.

**Procedure of data collection:**
A total number of 60 patients were primarily selected and they were randomized using computer-generated codes into two groups (group-A and group-B), each of which included 30 patients. Complete history, general physical and dermatological examinations were done for all enrolled patients. For women of reproductive age reproductive history, menstrual history, lactation and pregnancy plan was carefully judged. History and physical findings were recorded in a structured questionnaire. Finally those patients, who matched the inclusion and exclusion criteria according to history, physical examination and freely gave their informed consent, were selected for the study.

**Intervention:**
Patients were divided into two groups (Group-A and group-B), group A was treated with 0.05% tretinoin cream and group B with 0.1% tazarotene cream. Both preparations had to be administered in once-daily regimen on both sides of the face at bedtime, and the duration of the total treatment period was 12 weeks. Unused medication were collected after the last assessment. Patients were clinically assessed monthly for three months. Each time the severity index of the disease were calculated and recorded and clinical photographs were taken. The final clinical assessment was done and the severity index was calculated and adverse effects were noted at the end of the third month. Then the patient was followed up monthly in the post-treatment period for monitoring of all adverse effects.

**Data processing and analysis:**
Data were edited, coded and entered into the computer. Statistical analysis was done and level of significance was measured by using appropriate procedures like chi square test ($\chi^2$), relative risk (RR) measurement, t-test, and proportion ($d$) test and others where applicable. Level of significance ($p$ value) was set at 0.05 and confidence interval at 95%.

**Results:**
Mean age of Group A patients was $21.73 \pm 4.30$ and Group B was $19.70 \pm 3.44$. 50.0% of group A and 58.3% of Group B was from the age group d”20 and 50.0% of group A and 33.3% of group B was from the age group of >20. 43.3% of group A and 53.3% of group B was male and 56.7% of group A and 46.7% of group B was female ($p=0.438$). At baseline mean of total acne score
was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B, at 1st follow up it was 20.50 ± 13.64 and 21.17 ± 16.94 respectively in group A and B, at 2nd follow up it was 16.23 ± 12.74 and 15.83 ± 15.29 and at final follow up it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively in group A and B (p>0.05). Percent reduction of acne severity from base line to final follow up was 69.20 ± 23.41 in group A and 74.77 ± 23.30 in group B (p=0.360). The table II showed that 73.33% of tretinoin treated patient and 60% of tazarotene treated patient did not experience any side effects. Side effects recorded in group A were desquamation (13.3%), dry skin (6.7%), burning sensation (3.3%) and irritation (3.3%) and in group B were desquamation (10.0%), dry skin (13.3%), burning sensation (10.0%), irritation (3.3%) and erythema (3.3%) (p>0.05).

The side effects experienced by patients of different groups in their first follow up were shown in table IV. In 1st follow-up visit, in group A- desquamation, dry skin, burning sensation, irritation and erythema were present in 6.7%, 3.3%, 3.3%, 0% and 3.3% of patients respectively. In group B desquamation, dry skin, burning sensation, irritation and erythema were present in 3.3%, 3.3%, 3.3%, 3.3% and 3.3% of patients respectively. In 3rd follow-up visit, in group A- dry skin, burning sensation were present in 3.3% and 3.3% of patients respectively and desquamation, irritation and erythema were absent in group A. In group B dry skin, burning sensation, irritation and erythema were absent and only desquamation was present in 3.3% cases in 3rd follow-up visit.

### Table-I

**Distribution of age by groups**

<table>
<thead>
<tr>
<th>Age (in year)</th>
<th>Group A (n=30)</th>
<th>Group B (n=30)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>15 (50.0)#</td>
<td>20 (58.3)</td>
<td></td>
</tr>
<tr>
<td>&gt;20</td>
<td>15 (50.0)</td>
<td>10 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30 (100.0)</td>
<td>30 (100.0)</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>21.73±4.30</td>
<td>19.70 ±3.44</td>
<td>0.48</td>
</tr>
</tbody>
</table>

*unpaired t test was done to measure the level of significance
#Figure within parentheses indicates in percentage.

Group A = Tretinoin .05% , Group B = Tazarotene cream (0.1%)

### Table-II

**Distribution of side effects observed in the study**

<table>
<thead>
<tr>
<th>Safety</th>
<th>Tretinoin group</th>
<th>Tazarotene group</th>
</tr>
</thead>
<tbody>
<tr>
<td>N %</td>
<td>N %</td>
<td></td>
</tr>
<tr>
<td>With side effects</td>
<td>8 26.67%</td>
<td>12 40%</td>
</tr>
<tr>
<td>Without side effects</td>
<td>22 73.33%</td>
<td>18 60%</td>
</tr>
</tbody>
</table>

### Table-III

**Distribution of side effects by groups**

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Groups</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desquamation</td>
<td>Group A 4 (13.3)</td>
<td>3 (10.0) 0.688</td>
</tr>
<tr>
<td></td>
<td>Group B 3 (10.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Dry skin</td>
<td>Group A 2 (6.7)</td>
<td>4 (13.3) 0.389</td>
</tr>
<tr>
<td></td>
<td>Group B 4 (13.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>Group A 1 (3.3)</td>
<td>3 (10.0) 0.301</td>
</tr>
<tr>
<td></td>
<td>Group B 3 (10.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Irritation</td>
<td>Group A 1 (3.3)</td>
<td>1 (3.3)   0.999</td>
</tr>
<tr>
<td></td>
<td>Group B 1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Erythema</td>
<td>Group A 0 (0.0)</td>
<td>1 (3.3) 0.313</td>
</tr>
<tr>
<td></td>
<td>Group B 1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
</tbody>
</table>

*Chi-square test was done to measure the level of significance.
Table IV

<table>
<thead>
<tr>
<th></th>
<th>1st follow up</th>
<th>3rd follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
</tr>
<tr>
<td>Desquamation</td>
<td>2 (6.7%)</td>
<td>1 (3.3%)</td>
</tr>
<tr>
<td>Dry skin</td>
<td>1 (3.3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
</tr>
<tr>
<td>Irritation</td>
<td>0 (0%)</td>
<td>1 (3.3%)</td>
</tr>
<tr>
<td>Erythema</td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
</tr>
</tbody>
</table>

Discussion:
The efficacy of tazarotene in acne is well established. The current study was conducted to evaluate the safety of topical 0.1% tazarotene cream in the treatment of acne vulgaris comparing with topical 0.05% tretinoin gel. Equal of thirty patients of acne vulgaris were treated with topical 0.1% tazarotene cream and 0.05% tretinoin gel. Mean age of Group A (Tretinoin) was 21.73 ± 4.30 and Group B (Tazarotene) was 19.70 ± 3.44, and mean age of acne onset was 19.37 ± 4.07 years and 17.42 ± 3.12 years in group A and group B respectively. Different previous studies have reported acne in 28-61% of school children in the age group 10-12 years; 79-95% in the age group 16-18 years; and even in children in the age group 4-7 years. In India, prevalence data from a dermatology clinic in a teaching hospital in Varanasi reported acne in 50.6% of boys and 38.13% of girls in the age group 12-17 years. There are believed to be no gender differences in acne prevalence, although such difference are often reported and, very likely, represent social biases. In present study, 43.3% of group A and 53.3% of group B was male and 56.7% of group A and 46.7% of group B was female, with no significant statistical difference (p>0.05). Total acne score was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B respectively at entry level and at the final follow up at the end of the third month it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively in group A and B (p>0.05). Percent reduction of acne severity from base line to final follow up was 69.20 ± 23.41 in tretinoin group and 74.77 ± 23.30 in group tazarotene (p=0.360). Preliminary data from well-controlled clinical trials suggest that the tolerability of tazarotene in the treatment of acne vulgaris appears to be clinically comparable to that of both tretinoin and adapalene.

Side effects were more in tazarotene group than tretinoin group. Side effects recorded in tretinoin treated group were desquamation (13.3% of patients), dry skin (6.7% of patients), burning sensation (3.3% of patients) and irritation (3.3% of patients). Side effects observed in tazarotene treated group were desquamation (10.0% of patients), dry skin (13.3% of patients), burning sensation (10.0% of patients), irritation (3.3% of patients) and erythema (3.3% of patients). There is no significant difference between two groups (p>0.05). And side effects observed were only mild or trace. 73.33% of tretinoin treated patient and 60% of tazarotene treated did not experience any side effects. So both tretinoin 0.05% and tazarotene 0.1% is safe individually in the treatment of mild acne vulgaris. And safety & tolerability of 0.1% tazarotene is comparable to 0.05% tretinoin in the treatment of mild acne vulgaris.

Conclusion:
Finally we can conclude that 0.1% tazarotene cream and 0.05% tretinoin cream is individually safe in the treatment of mild acne vulgaris. And the safety of 0.1% tazarotene cream is comparable with 0.05% tretinoin cream in the treatment of mild acne vulgaris. Further multicenter, randomized, double-blind, controlled study should be conducted with large sample size, in future.

References:
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12. Kircik L. Comparative efficacy and tolerability results of tretinoin microsphere gel pump 0.04% and tazarotene cream 0.05% in the treatment of mild to moderate facial acne vulgaris. J AM Acad Dermatol 2009; 60(3): 14
Summary:
Background: Iron overload has been implicated in the etiopathogenesis of diabetes mellitus, but limitations of the existing markers and involvement of confounding variables have made it difficult to ascertain its precise role in diabetes. Investigation in prediabetic states (Impaired Fasting Glucose or IFG, Impaired Glucose Tolerance or IGT, and combined IFG & IGT or IFG-IGT) may help to clarify the causal relationship between iron overload and diabetes.

Objectives: The present study was undertaken to explore the body iron status in prediabetic subjects. With the above objective a group of nine IFG, twenty four IGT and twelve combined IFG-IGT subjects were studied along with a group of nineteen healthy controls subjects, matched by Age and BMI were included in the study.

Methodology: Serum fasting glucose was measured by glucose-oxidase method and lipid profile was measured by enzymatic-colorimetric method. Insulin secretory capacity (HOMA B %) and insulin sensitivity (HOMA S %) were analyzed by Homeostasis Model Assessment. Serum ferritin was measured by chemiluminescence-based ELISA technique.

Results: Age and BMI were matched among the study subjects. Systolic blood pressure (Mean±SD) among control, IFG, IGT and IFG-IGT subjects were 113±7, 122±22, 123±24 and 122±22 respectively. Systolic blood pressures of IGT subjects were significantly higher (p=0.05) compared to control. Regarding lipid levels, only cholesterol level was significantly higher (p=0.04) in IGT than in controls.

Fasting serum glucose (mmol/l) expressed as median range were significantly higher in IFG (p=0.0001) and IFG-IGT (p=0.0001) compared to the control. Moreover, the IFG subjects showed a significant β cell dysfunction (p=0.02) as evident from HOMA%B. The insulin sensitivity was significantly (p=0.01) lower in IFG-IGT subjects than in controls as evident from HOMA%S. Fasting serum ferritin (ng/ml) expressed in Median (range) among control, IFG, IGT, and IFG-IGT were 43.9 (7.5-151.0), 51.6 (11.8-158.0), 53.9 (11.3-272.0) and 93.0 (41.8-285) respectively. IFG-IGT subjects (p=0.02) had significantly higher levels of serum ferritin level compared to the controls.

Conclusion: No association was found between serum ferritin and any other biochemical parameters. Serum ferritin did not seem to have a causal role in the pathophysiology of type 2 diabetes and the reported iron overload in diabetic patients seemed to be secondary to other metabolic disorders developed in the disease state.

Key Words: Prediabetes, Impaired Fasting Glucose, Impaired Glucose Tolerance, Ferritin, Insulin resistance, IFG, IGT.

Introduction:
In recent years there has been considerable interest in the possibility that excessive tissue iron stores may contribute to the pathogenesis of diabetes. Extensive clinical, epidemiological, and basic studies suggest that excessive tissue iron may contribute to impaired glucose tolerance, diabetes mellitus (DM), and the complication of DM1-2.

Higher serum ferritin concentration has been proposed to be a component of insulin-resistance syndrome. It has been found that serum ferritin measurement was closely correlated with body iron stores in healthy individuals3.

Several studies had been conducted to explore the relationship of body iron stores with insulin resistance syndrome in type 2 DM. In cross-sectional analysis, it had repeatedly been shown that a third or more of adults
with type 2 DM had elevated serum ferritin4-5. Elevated serum ferritin levels independently predicted incidence of type 2 diabetes in prospective studies in apparently healthy men and women6. In another study a positive association was found between elevated iron stores measured by serum ferritin level and the prevalence of metabolic syndrome, particularly serum triglyceride and plasma glucose as well as other markers of insulin resistance syndrome7. Among 9,486 adults in the United States, about half of men and women with previously unsuspected diabetes (negative history of diabetes but fasting serum glucose e126mg/dl) had elevated serum ferritin8. Further, in adult population serum ferritin had been found to correlate strongly with levels of glucose, insulin, and HbA1c . In a prospective study of 1,038 randomly selected men, those with calculated body iron stores in the highest quartile were found to be 2.4 fold more likely than others to develop diabetes during four years of follow-up9. In another study, it was found that serum ferritin could be employed as a marker of not only glucose homeostasis but also insulin resistance in type 2 diabetes10.

As ferritin can be considered as a risk factor for diabetes type 2, then it should be elevated in prediabetes stages such as subjects with impaired fasting glucose (IFG) who are prone to develop overt hyperglycemia. This study was designed to investigate the association between serum ferritin and IFG, IGT and combined IFG and IGT subjects in Bangladesh.

**Materials and Methods:**

Forty Five IGT subjects and nineteen controls subjects were collected from the Out-Patient Department (OPD) of the BIRDEM Hospital. The study subjects comprised of the following groups: subjects were considered as IFG or IGT using recently published WHO guidelines (IFG: fasting serum glucose 6.1-6.9 mmol/l and 2h serum glucose <7.8 mmol/l, IGT: fasting serum glucose 6.1-6.9 mmol/l and 2h serum glucose 7.8-11.0 mmol/l).

Nineteen age, sex and BMI matched healthy subjects without family history of diabetes were recruited as controls from the friend circle of the IGT subjects considering as the same socio-economic status. A questionnaire was developed to obtain relevant information of demographic and socio-economic data such as age, educational status, and occupational status.

**Results:**

A total number of 64 subjects were participated in this study where 09 were isolated IFG, 24 were isolated IGT and 12 were combined IFG-IGT. As a Control group 19 healthy subjects without family history of DM and IGT were recruited.

**Table-I**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (n=19)</th>
<th>IFG (n=09)</th>
<th>IGT (n=24)</th>
<th>IFG+IGT (n=12)</th>
<th>Control vsIFG</th>
<th>Control vsIGT</th>
<th>Control vsIFG+IGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(Yrs)</td>
<td>38 ± 6</td>
<td>43 ± 6</td>
<td>41 ± 7</td>
<td>43 ± 8</td>
<td>1.61/0.10</td>
<td>1.09/0.28</td>
<td>1.93/0.06</td>
</tr>
<tr>
<td>BMI( kg/m²)</td>
<td>25.4 ± 3.6</td>
<td>25.8 ± 2.9</td>
<td>25.4 ± 4.6</td>
<td>27.7 ± 2.5</td>
<td>0.38/0.70</td>
<td>0.06/0.95</td>
<td>2.17/0.03</td>
</tr>
<tr>
<td>WHR</td>
<td>0.93 ± 0.25</td>
<td>0.94 ± 0.04</td>
<td>0.92 ± 0.01</td>
<td>0.92 ± 0.01</td>
<td>1.41/0.17</td>
<td>1.60/0.11</td>
<td>1.12/0.27</td>
</tr>
<tr>
<td>Neck (cm)</td>
<td>34.4 ± 3.2</td>
<td>35.2 ± 3.1</td>
<td>33.1 ± 5.5</td>
<td>36.0 ± 3.3</td>
<td>0.65/0.52</td>
<td>0.90/0.36</td>
<td>1.34/0.19</td>
</tr>
<tr>
<td>MUAC(mm)</td>
<td>297 ± 21</td>
<td>297 ± 21</td>
<td>301 ± 47</td>
<td>316 ± 33</td>
<td>0.70/0.49</td>
<td>0.84/0.40</td>
<td>2.35/0.03</td>
</tr>
<tr>
<td>-Triceps(mm)</td>
<td>15.5 ± 4.5</td>
<td>17.1 ± 4.1</td>
<td>20.3 ± 7.1</td>
<td>21.2 ± 4.8</td>
<td>0.90/0.37</td>
<td>2.65/0.01</td>
<td>3.22/0.004</td>
</tr>
<tr>
<td>BFM(%)</td>
<td>29.2 ± 6.2</td>
<td>29.3 ± 7.3</td>
<td>29.7 ± 6.0</td>
<td>29.2 ± 0.5</td>
<td>-0.07/3.76</td>
<td>-1.00/1.24</td>
<td>-0.35/2.88</td>
</tr>
<tr>
<td>S_BP(mmHg)</td>
<td>113 ± 7</td>
<td>122 ± 22</td>
<td>123 ± 24</td>
<td>122 ± 22</td>
<td>1.7/0.09</td>
<td>2.04/0.05</td>
<td>1.6/0.12</td>
</tr>
<tr>
<td>D_BP(mmHg)</td>
<td>75 ± 8</td>
<td>77 ± 11</td>
<td>81 ± 14</td>
<td>79 ± 13</td>
<td>0.7/0.5</td>
<td>1.7/0.10</td>
<td>1.11/0.27</td>
</tr>
</tbody>
</table>

Data were expressed as Mean ± SD. Differences among the groups were calculated using Student ‘t’ test as the test of significance at 5% significance level. n=number of subjects, BMI=Body mass index, WHR=Waist hip ratio, MUAC=Mid upper arm circumference, Sub_S=Subcapular, BFM=Body fat mass, S_BP=Systolic blood pressure, D_BP=Diastolic Blood Pressure.
Age (Mean±SD) among the Control, IFG, IGT and IFG-IGT subjects were 38±6, 43±6, 41±7 and 43±8 years respectively. BMI (kg/m²) was expressed as Mean±SD and the value among control, IFG, IGT and IFG-IGT were 25.4±3.6, 25.8±4.6, 25.8±2.9, and 27±2.5 respectively. BMI was significantly higher in IFG-IGT subjects (p=0.03) compared to control. Fasting serum ferritin (ng/mL) expressed in median (range) among Control, IFG, IGT, and IFG-IGT were 43.9(7.5-151.0), 51.6 (11.8-158.0), 53.9 (11.3-272.0) and 93.0 (41.8-285) respectively. IFG-IGT subjects (p=0.02) have shown significantly higher levels of serum ferritin level compared to control.

Table-II

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (n=19)</th>
<th>IFG (n=09)</th>
<th>IGT (n=24)</th>
<th>IFG-IGT (n=12)</th>
<th>Control vs IFG</th>
<th>Control vs IGT</th>
<th>Control vs IFG-IGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>F_Glu (mmol/l)</td>
<td>5.2 (4.4-7.1)</td>
<td>6.3 (6.1-6.7)</td>
<td>5.4 (4.3-6.09)</td>
<td>6.2 (6.1-6.9)</td>
<td>-3.7/0.0001</td>
<td>-1.1/0.02</td>
<td>-4.14/0.0001</td>
</tr>
<tr>
<td>2h_Glu (mmol/l)</td>
<td>6.2 (3.6-7.4)</td>
<td>6.6 (4.2-7.7)</td>
<td>9.0 (7.8-10.92)</td>
<td>9.7 (8.2-10.73)</td>
<td>-6.4/0.05</td>
<td>-5.57/0.001</td>
<td>-4.6/0.0001</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>103.0 (56.0-361.0)</td>
<td>145.0 (67.0-386.0)</td>
<td>144.0 (67.0-254.0)</td>
<td>146.0 (88.0-319.0)</td>
<td>-1.5/0.11</td>
<td>-1.6/0.09</td>
<td>-1.7/0.08</td>
</tr>
<tr>
<td>Chol (mg/dl)</td>
<td>171.0 (150.0-261.0)</td>
<td>208.0 (169.0-239.0)</td>
<td>192.5 (145.0-273.0)</td>
<td>189.0 (149.0-269.0)</td>
<td>-2.4/0.13</td>
<td>-2.0/0.04</td>
<td>-1.18/0.24</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>27.0 (21.0-40.0)</td>
<td>37.0 (28.0-57.0)</td>
<td>35.5 (20.0-55.0)</td>
<td>36.00 (24.0-57.0)</td>
<td>-2.9/0.004</td>
<td>-2.8/0.005</td>
<td>-2.5/0.01</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>120.0 (90.8-194.2)</td>
<td>132.0 (100.6-171.0)</td>
<td>123.1 (69.2-218.6)</td>
<td>115.3 (59.4-203.4)</td>
<td>-1.05/0.29</td>
<td>-0.307/0.76</td>
<td>-0.324/0.75</td>
</tr>
<tr>
<td>SGPT (U/L)</td>
<td>24.0 (12.0-65.0)</td>
<td>10.0 (10.00-16.0)</td>
<td>10.0 (10.0-35.0)</td>
<td>10.0 (10.0-25.10)</td>
<td>-3.9/0.0001</td>
<td>-4.8/0.0001</td>
<td>-3.9/0.0001</td>
</tr>
<tr>
<td>S_Crea (mg/dl)</td>
<td>1.0 (0.8-1.3)</td>
<td>1.1 (0.8-1.4)</td>
<td>1.0 (0.9-1.5)</td>
<td>1.0 (0.8-1.3)</td>
<td>-1.3/0.18</td>
<td>-0.80/0.41</td>
<td>-0.69/0.49</td>
</tr>
</tbody>
</table>

Data were expressed as Median (range). Mann-whitney u test was performed as the test of significance 5% significance level. Values in column with different superscripts are significantly different from each other. N= number of subjects. F_Glu= Fasting glucose; 2h_Glu= 2 hour after glucose; TG= Triglyceride; Chol= Total cholesterol; HDL= High Density Lipoprotein cholesterol; LDL=Low Density Lipoprotein cholesterol; SGPT= Serum glutamate pyruvate transaminase; S_Crea= Serum creatinine

Table-III

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (n=19)</th>
<th>IFG (n=09)</th>
<th>IGT (n=24)</th>
<th>IFG-IGT (n=12)</th>
<th>Control vs IFG</th>
<th>Control vs IGT</th>
<th>Control vs IFG-IGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>F_Ins (µIU/l)</td>
<td>5.0 (1.1-14.8)</td>
<td>8.3 (3.3-12.2)</td>
<td>6.8 (2.1-30.1)</td>
<td>11.8 (3.7-66.00)</td>
<td>-3.8/0.0001</td>
<td>-1.1/0.27</td>
<td>-4.4/0.0001</td>
</tr>
<tr>
<td>Ins:Glu</td>
<td>0.6 (0.3-5.1)</td>
<td>0.7 (0.5-1.8)</td>
<td>0.8 (0.1-1.6)</td>
<td>0.5 (0.1-1.6)</td>
<td>-1.6/0.110</td>
<td>0.66/0.50</td>
<td>-1.2/0.22</td>
</tr>
<tr>
<td>HOMA%B</td>
<td>99 (21.0-187.0)</td>
<td>71.6 (39.0-93.0)</td>
<td>77.5 (51.0-264.0)</td>
<td>85.7 (40.0-121.0)</td>
<td>2.5/0.01</td>
<td>-0.94/0.35</td>
<td>-1.05/0.29</td>
</tr>
<tr>
<td>HOMA%S</td>
<td>79.6 (44.0-554.0)</td>
<td>74.6 (51.0-185.0)</td>
<td>87.1 (111.0-218.0)</td>
<td>58.9 (34.0-161.0)</td>
<td>-0.117/0.86</td>
<td>-0.42/0.68</td>
<td>-2.4/0.015</td>
</tr>
</tbody>
</table>

Data were expressed as Median (range). Mann-whitney u test was performed as the test of significance 5% significance level. Values in column with different superscripts are significantly different from each other. N= number of subjects; F_Ins= Fasting Insulin; HOMA %B= B cell function assessed by homeostasis model assessment; HOMA %S= Insulin sensitivity assessed by homeostasis model assessment; Ins: Glu= Insulin Glucose ratio.
Discussion:
It is known that iron interferes with insulin inhibition of glucose production by the liver. Hepatic extraction and metabolism of insulin is reduced with increasing iron stores leading to peripheral hyperinsulinemia\(^1\). The initial and most common abnormality seen in iron overload conditions is liver insulin resistance. Ferritin has long been known as the main site for intracellular storage of excess iron in mammalian tissues. Liang Sun et al, also found that elevated ferritin concentrations frequently cluster with well-established risk factors of diabetes including obesity, metabolic syndrome, chronic inflammation, and altered circulating adipokines\(^12\). Although considerable evidence has been generated on the association of serum ferritin with Type 2DM, its causal role in the development of the metabolic disorder has not yet been established and iron overload as a risk factor for diabetes has remained largely speculative\(^13\).

The present study was designed to investigate the association between serum ferritin concentration in IFG, IGT and combined IFG-IGT subjects in a Bangladeshi population.

Forty five IGR (9 IFG, 24 IGT and 12 IFG-IGT) subjects and 19 controls were included in this study. The median serum ferritin level in Bangladeshi control subjects \(43.90\) ng/l was comparable with the mean value in an Iranian population where they found it as \(49.4\) ng/l \(^14\). In our study serum ferritin concentration was not significantly higher in isolated IFG and IGT subjects but it was significantly higher in combined IFG-IGT subjects than the control subjects (\(p=0.02\)). This is in contrast with the findings where it was found that ferritin concentration was higher in IFG subjects, compared with normal control subjects\(^15\). Serum ferritin concentrations were remarkably increased in type 2 diabetes\(^16\). The marginal increase in the IFG-IGT group does in our study not seem to be associated with the diabetic condition as no correlation was found between serum ferritin and any parameter of glycemic (fasting / 2-hour post load glucose) or insulinemic (serum insulin / insulin secretory capacity / insulin sensitivity) status. This finding was also in contrast where a positive association was found between type 2 diabetes and high plasma ferritin concentrations. More recently, a report of 1,013 Finnish men also showed a positive association between ferritin and diabetes\(^17\).

Conclusions:
On overall analysis of the present data it can concluded that serum ferritin does not seem to have a causal role in the pathophysiology of Type 2 diabetes and the reported iron overload in diabetic patients seem to be secondary to other metabolic disorders developed in the disease state.

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Metastatic Bone Disease: A Pathophysiologic Overview

SG BANU, GMJ HOSSAIN

Summary:
Bone is a common site for metastasis of malignant tumours occurring elsewhere in the body. High blood flow in the red marrow and favorable bone-marrow microenvironment help metastatic tumour cells survive, proliferate and infiltrate the bone matrix. The cancer cells produce and secrete a number of osteoclastogenic and osteoblast stimulating factors which recruit and activate osteoclasts and osteoblasts respectively at the metastatic foci. Osteoclasts together with proteolytic enzymes released by tumour cells cause resorption and destruction of bone. On the other hand, stimulated osteoblasts lay down new bone in response to factors released by tumour cells. Degradation products of this bone turnover and tumour-derived proteins are important bio-markers of metastatic bone disease, measures of which also reflect disease prognosis and treatment efficacy. Specific tumour-bone interactions occurring in metastatic bone disease are targets of new strategies of anti-metastasis therapy.

Key words: Metastatic bone disease, bone-marrow microenvironment, osteoclastic bone resorption, osteoblastic metastasis.

Introduction:
Malignant tumour arising in an organ other than bone and subsequently spreading to bone is termed as metastatic bone disease (MBD). Bone is the third most common organ involved by metastases, the first two being lung and liver. On the other hand, metastases constitute the most common group of skeletal malignancies. Cancers of thyroid gland, breasts, lungs, prostate and kidneys account for 75-80% or more of skeletal metastases in adults. Tumours that less commonly metastasize to bone are cancers of urinary bladder, colon and other parts of the gastrointestinal tract. In children, metastases to bone originate mostly from neuroblastoma, Wilm's tumour, rhabdomyosarcoma, Ewing sarcoma and teratocarcinoma. Soft tissue sarcomas in adults rarely metastasize to skeletal system. Melanoma, lymphoma, and virtually any cancer can metastasize to bone.

Bone metastasis:
Bone is a common site for metastasis owing to the high blood flow in the red marrow. Mineralized bone matrix is a rich storehouse of growth factors, such as insulin-like growth factor, transforming growth factor-β, bone morphogenetic proteins and others. Adhesion molecules present on metastatic tumour cells bind them to stromal cells of the bone-marrow. The tumour cells secrete angiogenic factors and bone resorbing factors which stimulate their proliferation and make their access into the resorbing bone matrix. Growth factors released by the resorbing bone matrix provide a fertile soil for further growth of metastatic tumour cells.

Types of bone metastases:
Bone metastases are typically characterized as osteolytic or bone destroying, osteoblastic or sclerotic or bone forming, and mixed, according to the radiographic and pathologic appearance of the lesion. Osteolytic bone metastases are presumed to be caused by release of osteoclastogenic factors in the bone microenvironment by the metastatic tumour cells. Osteoblastic lesions are the result of release of factors from the tumour cells that stimulate proliferation, differentiation and activation of osteoblasts leading to bone production. Osteolysis is the commonest pattern of bone metastasis which also accompanies the osteoblastic lesions.
**Distribution of bone metastases:**
Axial skeleton is the most common site affected by metastases. It comprises the spine, ribs, pelvic bones, skull and sternum. Femur and upper end of humerus are the highest in frequency among long bones. These bony sites contain areas of marrow that demonstrate high levels of red blood cell production, responsible for carriage of oxygen to the tissues. Vertebral metastases are most frequently found in the lumbar spine, followed by thoracic, cervical and sacral portions. Spread of tumour cells occurs through Batson’s plexus to the basivertebral veins; as a result, posterior part of the vertebral body near the entry of the vessels is involved first. In long bones, metaphyses are involved, sometimes with bilateral distribution. Small bones and intervertebral discs rarely have metastases.

**The bone marrow microenvironment—tumour-host cell interaction:**
Once tumour cells from a distant primary colonize bone, their growth and inhabitation are helped by local cells of bone and bone-marrow. Though cancer cells in advanced metastasis can destroy or lay down bone matrix directly, the effects are mostly mediated by the local cells. Among the host cells, osteoblasts, osteoclasts, endothelial cells, platelets and mesenchymal stem cells play key role in growth and survival of the metastatic tumour cells. Cancer cells produce and secrete both osteolytic and osteoblastic factors. Transforming growth factors (TGF-α and TGF-β), parathormone related protein or peptide (PTHrP), interleukins (IL-6,8,11), prostaglandins and powerful osteoclast cytokines such as tumour necrosis factor and interleukin-1 are produced by metastatic tumour cells. TGF-α is a potent stimulator of osteoclast formation and osteoclastic bone resorption. TGF-β can stimulate both osteoblast and osteoclast activities, with the later predominating in most tumours.

**RANKL promotes differentiation, activation and survival of osteoclasts leading to bone resorption.** This resorption releases factors from bone matrix (particularly TGF-β), which in turn change the phenotype of the tumour cells, further increasing the PTHrP production. Thus a vicious osteolytic cycle between the bone and the tumour cells is established.

On the other hand, osteoblastic metastases are mediated by stimulation of osteoblasts by cytokines released from tumour cells, either directly, or via release of factors from osseous stroma. Prostatic cancer cells produce osteblast stimulating factor, bone morphogenetic proteins (MBPs), urokinase-type plasminogen activator and basic fibroblastic growth factor. Breast cancer cells produce TGF-α and endothelin.

All these stimulate osteoblasts which produce collagen, osteocalcin and alkaline phosphatase. As a result new bone is laid down. In some of the breast cancers metastasizing to bone, new bone formation occurs as a physiological attempt to bone repair following bone destruction.

**Changes in bone in metastasis:**
Carried by systemic circulation, metastatic tumour cells colonize bone in areas of active marrow. They are attached to endothelial cells and bone matrix proteins like laminin and fibronectin, probably mediated by adhesion protein integrins. The tumour cells proliferate, form nests or cell mass and replace marrow material. They destroy and invade bone by secreting proteolytic enzymes including matrix metalloproteinases. However, they more predominantly grow in osteolytic defects produced by activated osteoclasts. Radiologically, well-defined, often expansile or moth-eaten lucent or lytic lesions (geographic bone destruction) are usually documented, sometimes with periosteal reactions. The lesions may be solitary or multiple. Histologically tumour nests are seen filling the resorption lacunae or pits, often populated by osteoclasts. In primarily osteoblastic type metastasis, new bone is laid down on trabecular bone surfaces or in the marrow cavity as primitive woven bone. There may also be periosteal bone formation which can mimic osteosarcoma. The new bone is usually poorly mineralized, and in about 50% of cases of
metastatic prostate cancer, evidence of osteomalacia is seen\(^6,12,35,36,37\). However, bone formation can be so extensive as to make the skeleton appear uniformly dense\(^6,35,37\). Mixed osteolytic-osteoblastic changes are common in many, particularly in metastatic breast carcinomas. Reactive immature woven bone is present in about 40% of all bone metastases, irrespective of the primary site of the tumour. It is often associated with capillary and fibroblast proliferation as well as with infiltration of inflammatory cells and macrophages\(^6,38\).

**Markers of metastatic bone disease:**

Biochemical markers of bone turnover in metastatic bone disease can be detected in patient’s blood and/or urine. These markers are usually proteins or peptides released by tumour or bone cells, or degradation products of cellular activities\(^12,39\).

Markers of bone resorption are measured both in serum and urine. These include fragments of bone collagen, enzymes of osteoclasts e.g. tartrate-resistant acid phosphatase (TRAP) and cathepsin K, and factors that regulate osteoclast recruitment and activity e.g. receptor activator of nuclear factor kappa B (RANK), RANK ligand (RANKL) and its decoy receptor osteoprotegerin. Fragments of bone collagen are hydroxyproline, collagen cross-linking amino acids e.g. pyridinoline and deoxypyridinoline, and cross-link containing fragments of collagen e.g. N-telopeptide and C-telopeptide of collagen type I (NTx and CTx respectively)\(^39,40,41\).

Markers of bone formation are measured in serum. These include total and bone alkaline phosphatase, osteocalcin, procollagen type I propeptides from amino- and carboxy-terminal ends of synthesizing collagen (called P1NP and P1CP respectively). The later propeptides are cleaved from the ends of procollagen molecule, released in circulation and reflect the amount of newly synthesized collagen\(^39,40,41\).

The markers of bone turnover are excellent indices of disease activity in metastatic bone disease. They have both diagnostic and prognostic value. Moreover, efficacy of treatment can be established by normalization of the test results. Immunoassays selectively measure NTx and CTx in serum and urine. Serum CTx level is found highly sensitive and serum P1NP highly specific for predicting bone metastasis. Bone alkaline phosphatase is an ideal biomarker of bone turnover. Urinary pyridinoline and deoxypyridinoline are also relatively selective bone markers. Urinary hydroxyproline, however, lacks specificity of bone resorption as hydroxyproline is common to almost all forms of collagen\(^39,40,41,42\).

**Targeting pathophysiology in therapy of MBD:**

Treatment of metastatic bone disease (MBD) is primarily palliative. Aims of treatment in MBD are relief of pain, hypercalcemia and other symptoms, local tumour control, skeletal stabilization and restoration of function. Treatment modalities include chemotherapy, hormone therapy, immunotherapy, radiation, surgery and bone marrow transplantation. Often a multi-modality approach is deployed\(^12,43,44\).

Treatment strategies are being developed targeting specific tumour-bone interactions. An important target is osteoclastic bone resorption. The bisphosphonates group of drugs are readily taken up by osteoclasts, cause a loss of their resorptive capacity, and more importantly, induce their apoptosis\(^12,14,45\). Diminished osteoclastic bone resorption in turn causes a loss of growth factors from bone matrix resulting in reduced stimulation to the tumour cells. Bisphosphonates may also be taken up directly by the tumour cells causing their death\(^14\). A modified recombinant version of osteoprotegerin inhibits osteoclast formation, activity and survival. It has decreased osteolytic destruction and tumour burden in bone in animal model. Prevention of bone resorption effectively reduces bone pain\(^14\).

Other targets of therapy are mostly under clinical trial which include PTHrP neutralizing antibody, inhibitor of gene promoter for PTHrP transcription in tumour cells, drugs against RANKL, TGF-\(\alpha\), Cathepsin K and integrins\(^14,44\). Inhibitors of PTHrP transcription were tested in animal models with humoral hypercalcemia of malignancy and found effective in reducing osteoclastic bone resorption. These agents also make a less favorable environment in bone for tumour growth\(^14\). Adjuvant anti-resorptive therapy can prevent bone loss due to sex steroid ablation induced by chemotherapy itself in prostate and breast cancers\(^14\). The drug tested to date that targets osteoblastic bone metastasis is endothelin A receptor antagonist. In a mouse model with breast cancer cell lines, it has dramatically reduced bone metastasis and tumour burden\(^14,46\).

**Conclusion:**

About two-thirds of the patients with cancer develop bone metastasis\(^47\). Bone metastasis adds greatly to the
patient morbidity, specially when osteolytic in nature. Reduction in morbidity is an important part of palliation. Understanding of pathogenesis of bone metastasis is essential to target specific tumour-bone interactive processes in anti-metastasis therapy. This short review focuses on key pathogenetic processes occurring in bone metastasis and their role in targeted therapy. Biomarkers of bone resorption or formation are indicators of treatment efficacy and important predictors of prognosis.

Reference:
Croup (Acute Laryngotracheobronchitis): An Update
MAH MOLLAHa, M PERVEZb

Croup (Acute laryngotracheobronchitis) is the most common cause of upper airway obstruction of under 5 children. The word “croup” is derived from the Anglo-Saxon word *kropan* which means “to cry aloud”. It is caused by various viral agents and is characterized by varying degrees of inspiratory stridor, barking cough, and hoarseness as a result of laryngeal and/or tracheal obstruction. Although most children are deemed to have a mild and short-lived illness, many a times the presentations are frightening and worsen during the early hours of morning. Historically, before the advent of corticosteroids and racemic epinephrine for treatment of severe croup, intubation, tracheotomy, and death were the typical outcomes.

**Epidemiology**
It is primarily a disease of infants and toddlers, with a peak incidence from age 6 months to 36 months. Incidence peaks in the second year of life, at 5-6 cases per 100 children. The disease is most common in late fall and early winter but may be seen at any time of year. The incidence in boys is about 1.4 times that in girls.

**Aetiology**
Parainfluenza viruses (types 1, 2, 3) are responsible for as many as 80% of croups and type 1 accounts for about 66% of cases and majority of hospitalizations. Less commonly, Adenovirus, RSV, Enterovirus, Coronavirus, Rhinovirus, Echovirus, Reovirus, Metapneumovirus, Influenza A and B are involved. Rarely, Measles, herpes simplex, varicella viruses and Mycoplasma pneumoniae has been found to be involved with croup.

**Pathogenesis**
After entering through nose and nasopharynx, viruses eventually settle and cause inflammation in subglottic larynx (the narrowest part of the airway in children) and trachea. Inflammation ultimately gives rise to edematous swelling of airway wall, narrowing of airway lumen and airflow limitation as well as decreased mobility of the vocal cords. This results in seal-like barking cough, turbulent airflow & stridor, chest retractions and hoarseness. In severe cases, fibrinous exudates and pseudomembrane may develop, causing even greater airway obstruction and all these events culminate into poor air entry, impaired alveolar ventilation, ventilation-perfusion mismatch and hypoxaemia.

**Clinical features**
The onset of the disease is sudden and the affected children usually presents with low grade fever, characteristic barking cough, inspiratory stridor, hoarseness of voice, respiratory distress, suprasternal recession and may be cyanosis. Sometimes, similar manifestations may be present in acute epiglottitis, bacterial trachectitis, foreign body aspiration, retropharyngeal abscess, laryngeal diphtheria etc. and most of these conditions can be diagnosed through their unique presentation as follows.
Acute epiglottitis is caused by *H. influenzae* B and the disease is characterized by sudden onset of high fever, drooling, dysphagia, anxiety and a preference to sit upright and in the so-called sniffing position (i.e. sitting forward with their head extended) to open the airway is very characteristic.

Bacterial tracheitis presents with worsening respiratory distress, a “croupy” cough, and high fever. They have a toxic appearance and do not respond favorably to treatment with nebulized epinephrine. The most frequently isolated pathogen is *Staphylococcus aureus*.

Peritonsillar or retropharyngeal abscess presents with low-grade fever, dysphagia, drooling, stridor, dyspnoea, tachypnoea, a muffled “hot potato” voice, neck stiffness, unilateral neck pain and unilateral cervical lymphadenopathy. It is associated with the presence of trismus, which results from irritation of the internal pterygoid muscle.

Laryngeal diphtheria is characterized by low-grade fever, hoarseness and barking cough along with dysphagia and inspiratory stridor, and the characteristic pseudomembrane is seen on throat examination.2, 3

**Severity of croup**

Croup may be of any severity ranging from mild to a state of respiratory failure as follows:

- **Mild** - Occasional barking cough, no audible stridor at rest, and either no or mild suprasternal and/or intercostal retractions
- **Moderate** - Frequent barking cough, easily audible stridor at rest, and suprasternal and sternal wall retractions at rest, with no or minimal agitation
- **Severe** - Frequent barking cough, prominent inspiratory (and occasionally expiratory) stridor, marked sternal wall retractions, significant agitation and distress
- **Impending respiratory failure** - Barking cough (often not prominent), audible stridor at rest, sternal wall retractions may not be marked, lethargy or decreased consciousness, and often dusky appearance without supplemental oxygen support.

**Scoring system**

To assess the degree of respiratory compromise, croup scores have been developed. The most commonly cited is the Westley scoring system. The score evaluates the severity of croup by assessing the following 5 parameters, with a score range of 0 to 17:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>0 point</th>
<th>1 point</th>
<th>2 points</th>
<th>3 points</th>
<th>4 points</th>
<th>5 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspiratory</td>
<td>None</td>
<td>Upon</td>
<td>At rest</td>
<td>stridor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retractions</td>
<td>None</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air entry</td>
<td>Normal</td>
<td>Mild</td>
<td>Decrease</td>
<td>Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyanosis</td>
<td>None</td>
<td>Normal</td>
<td>Sleep</td>
<td>Sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of</td>
<td>Normal</td>
<td>Normal,</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>consciousness</td>
<td>including</td>
<td>including</td>
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A score of < 3 represents mild disease; 3-6 represents moderate disease; and a score > 6 represents severe disease.

**Diagnosis**

Croup is basically a clinical diagnosis. However, X-ray neck AP view shows steeple sign (*narrowing of air column*) which is characteristic of croup.

**Treatment**

Treatment of croup is mainly supportive with a view to minimize respiratory distress, ensure proper oxygenation, and ventilation.

- The child should be kept as comfortable as possible, allowing him to remain on the arms of parent. Unnecessary painful interventions should be avoided as these may cause agitation, worsen airway obstruction and increased oxygen requirements by the child.
• Along with that child may need IV fluid if he/she is unable to take oral feeds.

• If patient is kept on bed he/she should be placed in a neck extended position to keep the airway open. Clearing of air passage through oropharyngeal and nasopharyngeal suction may be needed.

• Monitoring of vital parameters, e.g. pulse, blood pressure, oxygen saturation and other parameters should be done routinely.

Oxygen inhalation
Oxygen inhalation by nasal cannula (2L/min) or by face mask (3-5 L/min) if SPO₂ in room air is <92%. Oxygen can also be given via a plastic hose with the opening held within a few cm of the nose and mouth (blow-by oxygen) which will render minimum irritation to the patient.

Corticosteroid
The effectiveness of oral corticosteroids in croup is well established. They reduce subglottic oedema through their anti-inflammatory action and significant relief is obtained by 6 hours of administration. Steroids either IV or oral form is adequate to control mild and most cases of moderate croup. In mild croup, steroids reduce the rate of hospitalization, hospital stay and most importantly reduce the need for subsequent intervention such as epinephrine administration. In severe croup, steroids significantly reduce the rate of intubation and also the duration of intubation.

Corticosteroids recommended are single dose of either i) dexamethasone: 0.6 mg/kg (same efficacy if administered intravenously, intramuscularly, or orally) or ii) Nebulized Budesonide: 2 mg in 4 ml of water (expensive in comparison to dexamethasone or prednisolone). A single dose of oral prednisolone (1 mg/kg) may be given but it is less effective and is associated with more return to hospitals. Prednisolone is less potent to reduce inflammation and shortened half-life (18-36 hrs) than that of dexamethasone (36-54 hrs). There are no controlled studies examining the effectiveness of multiple doses of corticosteroids.

Adrenaline/epinephrine
Nebulized racemic epinephrine is an accepted treatment for moderate-to-severe croup and this option of treatment substantially reduces the number of intubation or tracheotomy. Its effect is immediate and lasts for 90-120 minutes. Epinephrine causes constriction of the precapillary arterioles, thereby decreasing capillary hydrostatic pressure through beta adrenergic receptors. This in turn leads to fluid resorption from the interstitium and improvement in the laryngeal mucosal edema. It also causes bronchial smooth muscle relaxation and bronchodilation.

Racemic epinephrine at a dose of 0.25 to 0.5 ml to be diluted in 2.5-3 ml of normal saline can be used as often as every 20 minutes. Alternatively, L-epinephrine (1:1000 dilution) 5 ml is equally effective and does not carry the risk of cardiovascular side-effects. The duration of activity of racemic epinephrine is about 2 hours. Therefore, patients who received epinephrine should be observed for at least 3 hours because of concerns for a rebound phenomenon of bronchospasm, worsening respiratory distress, and/or persistent tachycardia. Patients can be discharged home only if they demonstrate healthy color, good air entry, baseline consciousness, and no stridor at rest and have received a dose of corticosteroids.

Analgesics and antipyretics
The use of analgesics or antipyretics is reasonable for the benefit of reduction of fever or discomfort in children with croup.

Antibiotics
Since laryngotracheitis and spasmodic croup are viral illnesses, there is no reason to treat them with antibiotics unless clinical manifestations or laboratory values suggest secondary bacterial infection. Moreover superinfections, such as bacterial tracheitis and pneumonia, are described. However their rare frequency (<1 per 1000 cases of croup) makes use of prophylactic antibiotics unreasonable.

Humidified air
Throughout the 19th and most of the 20th century, cool mist administration was the mainstay of treatment of croup. Hospitals had “croup rooms” filled with cool mist. Theoretically, mist moistens airway secretions, decreases their viscosity, and soothes the inflamed mucosa. Despite the observation of beneficial effect of cool mist, Cochrane review has found no evidence supporting its use in croup. Moreover, mist tents can disperse fungus and molds if not properly cleaned and, more importantly, separates the child from the parent, causing anxiety and agitation, worsening the patient’s symptoms. Hot humidified air can cause scald injuries.

Heliox
Helium is an inert low-density gas with no inherent pharmacological or biological effects. Administration of helium-oxygen mixture (heliox) to children with severe respiratory distress can reduce their degree of
distress since the lower density helium gas decreases airflow turbulence through a narrow airway. Helium decreases the force necessary and facilitates the movement of oxygen through the airways and decreases the mechanical work of respiratory muscles. This clinical response reduces respiratory distress.

Both heliox and racemic epinephrine were associated with similar improvements in croup score over time. However, since heliox has yet to be shown to offer greater improvements than standard treatments and can be difficult to use in unskilled hands, there is insufficient reason to recommend its general use in children with severe croup.

Cough and cold medications: Use of antitussive and decongestants are ineffective and not indicated.

Bronchodilators: In view of the pathophysiology of croup as an upper-airway disease, there is no reason to use short-acting \( \alpha_2 \) agonists for treatment of the disease.

**Stepwise management of croup according to severity**

- **Mild**
  - Give oral or intramuscular dexamethasone, 0.6 mg/kg
  - Discuss with parents likely course of illness and when to seek additional care if further respiratory distress occurs

- **Moderate**
  - Give oral or intramuscular dexamethasone, 0.6 mg/kg
  - Minimize situations that may cause distress in child, such as separation from parents and unnecessary examination
  - Observe for improvement for 1-4 hr

- **Severe**
  - Minimize situations that may cause distress in child, such as separation from parents and unnecessary examination
  - Provide oxygen if cyanosis is present
  - Give oral or IM dexamethasone, 0.6 mg/kg
  - Administer epinephrine by nebulization, either racemic epinephrine 2.25%, 0.5 ml in 2.5 - 3 ml of saline, or L-epinephrine (1:1000 dilution) 5 ml

If patient improves — as evidenced by no stridor at rest and no chest-wall indrawing — then discuss with parents likely course of illness and when to seek additional care

If no or minimal improvement after 4 hr, consider hospitalization

If good response to epinephrine, observe for 2 hr

If severe respiratory distress recurs, repeat nebulized epinephrine

If only mild symptoms persist (i.e., croupy cough) and there is no recurrence of stridor at rest or of chest-wall indrawing, then discuss with parents when to seek additional care

If good response, observe for 2 hr; if only mild symptoms persist and there is no recurrence of stridor at rest or of chest-wall indrawing, then discuss with parents when to seek additional care

If poor response, repeat nebulized epinephrine; if poor response to second treatment, admit child for ICU care and probable workup for secondary bacterial infection
**Prognosis**
The prognosis for croup is excellent, and recovery is usually complete. The majority of patients are managed successfully as outpatients, without the need for inpatient hospital care.²

**Conclusion:**
Although croup is an important cause of severe respiratory distress from upper airway obstruction of young children, it is often overlooked. If there is suspicion in clinician’s mind, diagnosis is easy through its unique clinical presentations. However, outcome of the disease is rewarding through prompt intervention with corticosteroid, epinephrine and other supports.

**References:**


Summary:
Accidental tooth avulsion is common among the children. Management of avulsed tooth within alveolar socket by re-implantation becomes a challenge for the clinician due to extra oral time and media of transportation. Although the long-term prognosis of re-implantation is poor, the time during which the tooth remain within the arch will guide the development of alveolar bone completely. Moreover, the re-implantation will maintain anatomical, functional and esthetic rehabilitation of the patient. In this case report, we presented a case of accidental avulsion where re-implantation was performed. After 12 months follow-up the periodontal space was healed perfectly without any resorption or ankylosis.

Key words: Trauma, avulsion, replantation.

Re-implantation of Accidentally Avulsed Tooth

SS CHOWDHURYa, MR HOWLADERb

CASE REPORTS

Introduction:
Dental injuries can occur at any age; however they are most common between the age of 7 to 10-year-old age group, when the children are very much active1,2. Certain predisposing factors like protruded maxillary incisors and insufficient lip closure may affect the extent of the dental trauma.3, 4 Avulsed teeth usually lost at the accident scene and both accident victims and those attending them may neglect it. But the public should be aware of the possibilities that avulsed tooth can be saved by re-implantation. Immediately after re-implantation inflammatory process in periodontal tissues induced the re-organization of new attachment apparatus to induce healing. The healing process will be directly related to extra-oral period and condition in which the tooth was preserved prior to re-implantation. Depending upon severity of injury four types of healing may occur in periodontal ligament area as: (i) healing with normal periodontal ligament: Complete regeneration of the periodontal ligament along the root surface usually takes about 7-10 days. This will occur if the periodontal ligament cells remain vital; (ii) Healing with the surface resorption:- Histologically, areas of the localized resorption on the root surface are seen. Subsequently, these areas become repaired with normal cemental tissues. Clinically the tooth is asymptomatic and has a normal percussion tone; (iii) Healing with replacement resorption:- Histologically, fusion of the bone and the root surface is observed. Clinically, the tooth is not mobile. It may become infra-occluded over time and give a high percussion tone; (iv) Healing with inflammatory resorption:- Histologically it is characterized by areas of resorption in bone and adjacent root surface. This may progress till the tooth becomes mobile and extruded. Clinically, the percussion tone is dull and patient may present with pain. More than one type of reaction may present at any one time.5

For this reason, accidental avulsion of tooth is a true emergency since timely attention to re-implantation could save many teeth.3Emergency management of accidentally avulsed tooth is spectacular but unfortunately has a low range of success ratio compared with routine endodontic therapy. However, one should consider the avulsed tooth as a foreign body when it is replaced and is therefore subjected to all functions of the body that may be employed to counteract such intruders. So, re-implantation success should not be compared with other type of endodontic therapy in which the treated tooth remains in its alveolar housing and benefited by the periodontal attachment.6 Although lower success rate, the procedure is beneficial to retain alveolar bone and

References:

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4. Received: 11 March, 2010 Accepted: 7 September, 2012

(4) Bangladesh Coll Phys Surg 2013; 31: 39-44
tooth-to-tooth relationship for a period of time. Additionally, shortly after accident it might be difficult to prepare adjacent teeth as abutment for fixed partial denture. Because in youngsters the pulp canal size is commonly large. So, the precious time has been gained to allow for diminution of the pulp canal size of abutments which will permit future fixed prosthesis.3,7

Case Report:
A 8-year-old boy came to the department of Conservative Dentistry and Endodontics, Faculty of Dentistry, BSMMU with the complaint of accidental missing of one of his upper anterior tooth during playing. The patient’s medical history was not contributory and had history of tetanus immunization. He had come after 24 hours of the accident with the missed tooth on his hand which was immersed within normal saline. On clinical examination, he had missing left central incisor and the gum tissue was lacerated there Fig.-1. On OPG examination, there was no other dental or bony damage in his mouth but the area was tender on palpation. After discussion of all the treatment options with the patient’s guardian, it was decided to re-implant the tooth within the socket after appropriate endodontic preparation. A proper access cavity was prepared outside the mouth by holding the tooth only by crown with the help of a piece of gauze. Extirpation of pulp tissue was done and normal saline was used for irrigation of the root canal. Endodontic preparation was completed by hand protaper instruments in standardized technique. Canal was then obturated and retrograde filling was done by glass ionomer filling to prevent any peri apical leakage.

The traumatized socket was inspected for any bone and tooth fragments. As the blood clot was present, gentle irrigation with normal saline was done. A straight elevator was introduced into the socket for repositioning of the bone into its normal position as there might be chance of bone collapse.

Root filled avulsed tooth was then replanted carefully into the prepared socket by holding it with the fingers to avoid contact with the root [Fig.-2(b)]. Complete re-implantation was determined by comparing the incisal edge of replanted incisor with the incisal edge of the adjacent incisor.

After re-implantation, facial and lingual soft tissues covering the alveolar bone was compressed with the fingers. The replanted tooth was in slightly rotated

Fig.-1: Pre-operative view

Fig.-2: (a) Placement of endodontically treated avulsed tooth in the socket, (b) Immediately after re-implantation.
position but the guardian told that before avulsion the child's original tooth was in the same position so it was accepted by the guardian [Fig.-2(b)]. The re-implanted tooth and each adjacent two teeth then acid-etched and light cured along with an orthodontic wire to form a functional splint. [Fig.-3, OPG-1&Radiograph-1]. To ensure complete placement of the reimplanted tooth within the socket, the patient was asked to bite gently and the occlusion found normal. The immobilization was done by that functional splint for 3 weeks as it was extremely mobile.

Patient was advised to take soft food, not to bite with the tooth and maintain proper oral hygiene for one week. Chlorhexidine mouth wash advised while the splint was in place. Antibiotic Cephradine (500 mg) was prescribed 6 hourly for 7 days to negate bacterial contamination or rapidly progressing root resorption.

Anti-inflammatory drugs was also been prescribed. The patient came at recall visit after 7 days of replantation for evaluation of healing process. Then superficial scaling was done and the light cure filling was polished as he had complained about rough feeling by lips [Fig.-4(a)]. After 3 weeks of replantation patient was available for second recall visit. The tooth was assessed clinically and radiographically but did not find any pathology and the tooth was not mobile at that stage, so we removed the splint.

After 6 months, there was evidence of apical bone formation and periodontal area was under healing process with cementum (Radiograph-3). After 1 year, there was increased rate of alveolar bone formation and no sign of tooth resorption [Fig.-4(b)]

![Fig.-3: After functional splint](image1)

![Fig.-4: (a) Follow-up after seven days, (b) Follow-up after one year](image2)
Discussion:
Prognosis of re-implantation of the permanent dentition is primarily dependent upon root development and extra oral dry time\(^8\). The root has the best prognosis if replanted immediately. If the tooth cannot be re-implanted within 5 minutes, it should be stored in a medium that will help to maintain the vitality of the periodontal ligament fibre.\(^9\)-\(^11\) If the extra-oral dry time is extended the transport media will be a critical factor for re-implantation. The transport media for avulsed teeth include via span, Hanks Balanced Salt solution (Tissue culture medium), cold milk, saliva (buccal vestibule), physiologic saline or water. Tooth storage in a cell compatible medium for a limited period of time prior to replantation has produced a similar healing result as compared with immediately replanted teeth.\(^12\) The risk of ankylosis increases significantly with an extra oral dry time of 60 minutes because it is unlikely that periodontal cells remain viable when extra-oral dry time is more than 60 minutes.\(^13\) In this case report, although the extra-oral time of avulsed tooth was 24 hours, being emerged in normal saline and management by proper technique, the tooth was re-implanted successfully within the

## Radiographs:

**Radiograph-1:** immediately after treatment  
**Radiograph-2:** Follow-up after six months of fixation  
**Radiograph-3:** Follow-up radiograph after one year

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Frequency Evaluation:  
Prognosis of re-implantation of the permanent dentition is primarily dependent upon root development and extra oral dry time. The root has the best prognosis if replanted immediately. If the tooth cannot be re-implanted within 5 minutes, it should be stored in a medium that will help to maintain the vitality of the periodontal ligament fibre. If the extra-oral dry time is extended the transport media will be a critical factor for re-implantation. The transport media for avulsed teeth include via span, Hanks Balanced Salt solution (Tissue culture medium), cold milk, saliva (buccal vestibule), physiologic saline or water. Tooth storage in a cell compatible medium for a limited period of time prior to replantation has produced a similar healing result as compared with immediately replanted teeth. The risk of ankylosis increases significantly with an extra oral dry time of 60 minutes because it is unlikely that periodontal cells remain viable when extra-oral dry time is more than 60 minutes. In this case report, although the extra-oral time of avulsed tooth was 24 hours, being emerged in normal saline and management by proper technique, the tooth was re-implanted successfully within the
socket. The case was periodically examined up to 12 months and during the time tooth mobility, periodontal status, occlusal balance and pain on percussion was assessed and after 12 months the patient was perfectly all right with the replanted tooth both functionally and aesthetically. The long term prognosis for re-implantation was poor, but the recent studies found significant increase in success rate. Further studies in university of North Carolina verified that the longer the period between the traumatic extraction and re-insertion, the greater is the chance of failure. Therefore the technique for re-implantation should follow the standard protocol within a shorter period of time. If the time is more than 15 minutes, the tooth should be taken quickly to the dental office, hopefully in a suitable transport media, where a dentist is able to re-implant it.

A study by Sherman indicated that the presence of the original periodontal ligament on the root surface of re-implanted teeth improved the prospect for secondary cementum deposition and root resorption repair. When the original periodontal ligament was scraped and the tooth re-implanted with absorbable surgical sponge, root resorption was more extensive and progressive and a greater degree of ankylosis took place compared with the non-scraped replants. Two undesirable conditions may occur to re-implanted teeth- tooth resorption and or ankylosis. For this reason we should take follow-up regularly at six months interval while radiographs would reveal the resorption process. Resorption can be seen radio graphically on the lateral surface of root, in irregular bays. In ankylosis tooth fail to passive eruption therefore, eventually appear shorter than the adjacent tooth. The long-term prognosis for re-implantation was thought to be poor but the recent studies found a significant increase in the success rate. So, we should develop awareness among the general people as well as dental professionals about the management of avulsed tooth. As extra oral time and transporting media is of crucial importance to survival of the tooth, general people should get the message of urgency of arrival at the dental office with the avulsed tooth/teeth as early as possible.

**Conclusion:**
As the patient was in growing stage it was wise to attempted for re-implantation. Although it was thought that there is low success rate of re-implantation when the extra oral time after accidental avulsion is more than 60 minutes. But in my case report, the tooth was properly re-implanted after 24 hours of avulsion. After 12 months follow-up, none of the features of resorption and ankylosis were evident so, we can conclude the case as successful.

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Acute Appendicitis in a Duplicated Vermiform Appendix

MA BAQUI\textsuperscript{a}, MH RAHMAN\textsuperscript{b}, MT ISLAM\textsuperscript{c}

\section*{Summary:}
Appendiceal anomalies are extremely rare malformations that are found in adult population as an incidental finding during laparotomy due to another reason. Accompanying intestinal or vertebral malformations may be present when appendiceal duplications are detected. Presented here is a case of Acute Appendicitis in a double Vermiform Appendix.

\textit{(J Bangladesh Coll Phys Surg 2013; 31: 45-46)}

\section*{Introduction:}
Duplication of the vermiform appendix is rare with reported incidence of 0.004\%. Less than 100 appendiceal anomalies have been reported in the literature\textsuperscript{1-7}. Most anomalies of the appendix have been observed in adults and most were noticed incidentally during surgery not primarily involving the appendix. Duplication of the vermiform appendix causing small bowel obstruction, mimicking adenocarcinoma of the colon, hypotrophic and duplicated appendix and unusual duplication of appendix and cecum have also been reported. Appendiceal duplication have with colonic duplication and genito-urinary abnormalities, or with gastroschisis can exhibit life-threatening conditions\textsuperscript{1,3}.

\section*{Case Report:}
A 14 year old girl presented with periumbilical pain and anorexia for a duration of 06 hours. Initially the pain was in the umbilical region but later on the pain shifted to the right iliac fossa. There was no vomiting and menstrual complaint. Her bowel and bladder habits were normal. On physical examination the patient was found haemodynamically stable but on local examination the right MC-Burney’s point was tender with positive rebound tenderness. There was leucocytosis with relative neutrophilia. Abdominal ultrasound was normal. Clinically and with relevant investigations the condition was diagnosed as acute Appendicitis. Appendicectomy under general anaesthesia was planned. Laparotomy was performed with a Lanz incision. In the abdominal cavity 02(two) appendices were found in a single caecum (fig: 1). One appendix was found in its normal position and another one 03 cm away from the first one in one of the tinea coli. One of the appendix was found moderately inflamed at its catarrhal stage and other was gangrenous without any evidence of perforation. Appendicectomy was performed without any difficulty.

Postoperative recovery was uneventful. Histopathological examination of excised specimen revealed acute inflammation in one appendix and gangrenous appendicitis in other one.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig-1.png}
\caption{Vermiform appendix marked by arrow (One short with gangrenous tip & another long with inflamed base)}
\end{figure}
Discussion:
Although the range of variation in characters and position is diverse in the experiences of surgeons, the congenital anomalies of appendix are rare in clinical practice. Furthermore, duplication anomaly is so rare that less than 50 cases have been reported in English literature. Appendiceal anomalies include anomalous location of single appendix, horseshoe anomaly of the appendix, agenesis, duplication and triplication. There is single case report of appendicular triplication.

Double appendix is usually asymptomatic, the majority of them are diagnosed on diagnostic laparoscopy or on postmortem examination and some of them can be picked up preoperatively on barium enema or on exploration for appendectomy or for other reason.

The classification of duplication of appendix was first made in 1962 by Cave and Wallbridge and it was finally modified by Bierman in 1993. The classification divides these duplications into the following types (fig. 3).

Type A: It consists of various degrees of partial duplication on a normally localized appendix with a single caecum.

Type B: It includes a single caecum with two completely separated appendices. This type has subgroups.

B1: There are two appendices localized symmetrically on either side of the ileo- Cecal valve; this resembles the normal phylogenetical arrangement in birds, so this group was called the “bird-like or avian” type.

B2: In addition to a normally localized appendix from the caecum at the usual site and a second, separate, rudimentary appendix arising from caecum localized along the taenia line at a varying distance from the first.

B3: The second appendix is located along the taenia of the hepatic flexure of the colon.

B4: The location of the second appendix is along the taenia of the splenic flexure of colon.

Type C: Double caecum, each caecum bears an appendix.

Type D is a horse-shoe appendix with two openings at the common caecum.

This reporting patient had type B2 appendiceal duplication. These two appendices were having two separate bases. Each appendix had its own blood supply. Duplication of the appendix must be distinguished from the solitary diverticulum of the caecum and from appendiceal diverticulosus. This distinction can be best made histopathologically. When appendiceal duplications are detected in childhood, almost all patients have serious associated intestinal, genitourinary or vertebral malformations. These anomalies are mostly associated with type B1 and C duplications.

Conclusion:
Appendicectomy is usually done by junior surgical residents. But they should be aware of and look for the possibility of appendiceal anomalies. In patient with appendiceal duplication both the appendix should be removed so as to avoid the confusion that may arise on removal of single appendix only. Besides, the second untreated appendix or missed appendix may have serious clinical and medicolegal implications.

References:
A Rare Case of Aortico Left Ventricular Tunnel (ALVT)

NNF BEGUM

Summary:
Aortico-Left ventricular tunnel (ALVT) is a rare cardiac malformation with a good post operative long term outcome. The embryological basis for the disease is still unknown. Aortico-left ventricular tunnel can be diagnosed by transthoracic, transoesophageal and fetal echocardiography and by magnetic resonance imaging. A significant amount of aortic regurgitation should raise the possibility of this lesion. Here we report one of such case, which is first ever reported case of AVLT in Bangladesh.

(J Bangladesh Coll Phys Surg 2013; 31: 47-50)

Case Report:
M, a 06 months old baby girl was admitted to Combined Military Hospital Dhaka (CMH Dhaka) in May 2011 with the complaints of feeding difficulty, recurrent respiratory tract infection and failure to thrive. She was 2nd in birth order and born normally to a non-consanguineous parent. She was thoroughly evaluated, CXR showed Cardiomegaly, ECG showed left ventricular hypertrophy and Echocardiography showed an echo drop out in upper end of IVS with severe Aortic regurgitation (AR). Her finding and clinical feature were like ventricular septal defect (VSD), but no VSD was seen in echocardiography, severe AR was noticed and LVEF was 35%. Later cardiac catheterization was performed on 27th September 2011, interventricular septum (IVS) was found intact, ascending aorta was dilated. Severe aortic regurgitation (AR) was noticed and narrowing seen at commencement of ascending aorta. So there was dilemma in diagnosis. We initially diagnosed the case as aneurysm of ascending aorta and recommended Bental procedure. We discussed and reviewed this case with Prof Navin C Nanda of Alabama University,USA during his visit to Bangladesh. Later we referred her to cardiac surgeons of home and abroad. She was accepted by Dr K S Iyer of Escort heart research institute New Delhi, India. She was operated there. Her operative findings were: Aorta to left ventricular tunnel arising between the right coronary cusp and aortic wall. Right coronary ostium was not seen. A tunnel was seen opening in left ventricle below the aortic annulus. Valve was competent. Surgeons had performed Aortico-left
ventricle tunnel repair with gluteraldehyde treated pericardial strip on 9th January 2012. They closed the opening near the valve directly.

Her post operative course was smooth but prolonged due to left ventricular dysfunction. She was electively supported with dobutamine (0-5th POD) in view of LV dysfunction (EF 35%). She had nitroglycerine infusion for high systemic pressure and milrinone infusion (0-6th POD) for persistent tachycardia (HR 160/min).

She was discharged with Enalapril, Lasix and spironolactone. Digoxin was not given as there was history of ventricular ectopics on 1st and 2nd post operative day. She had fever in post operative period and managed accordingly. She was referred back to Bangladesh and got readmission to CMH Dhaka on 28.02.2012 for re-evaluation. Her echocardiography this time showed no AR, LVEF 50%, no pericardial/pleural effusion and no residual shunt seen through LV to AO tunnel. She was discharged after two days with advice to continue Enalapril, Lasix and Spironolactone till next follow up 6 weeks later.

**Fig.-3:** Echocardiography showing aortic regurgitation.

**Fig.-4:** LV Graphy showing no VSD.

**Discussion:**

Aortico Left Ventricular Tunnel (ALVT) is a congenital, extra-cardiac channel which connects the ascending aorta above the sinutubular-junction to the cavity of the left or less commonly right ventricle. This condition presents in early childhood as aortic regurgitation and cardiac failure.

This disease was first described in an adult by Hart in 1902. He described a delayed rupture of a congenital aneurysm of right sinus of valsalva to left ventricle. Levy and his associates first described the entity of the aortico-left ventricular tunnel (AVLT) in three patients. The exact incidence of the disease is unknown, but it may range from 0.5% to less than 0.1% of congenitally malformed hearts in clinicopathological series. The
The embryological basis of ALVT remains uncertain. Speculations have included an anomalous coronary artery, possibly the conal vessel opening in the LV and rupture of a sinus of Valsalva. Another group said it appears to result from a combination of maldevelopment of the cushion which give rise to the pulmonary and aortic root and abnormal septation of the structures.

Among 130 cases reported in the literature, more than 90% of ALVT communicated with the left ventricle. It differs from a ruptured sinus of Valsalva aneurysm in having its vascular orifice in the tubular aorta rather than to a sinus of aortic valve. The ostium of a coronary artery may be within an ALVT and absence of origin of both left or right coronary have been observed. Associated lesion of the aortic valve present in 20% of the cases. Some patient develop aortic incompetence (AR). Stenosis of the pulmonary valve occur less frequently.

Male are predominantly affected by ALVT as found in most of the study though our case was a female. A loud “to and fro” murmur with thrill and bounding pulse indicate rapid runoff of blood. It resembles both aortic stenosis and regurgitation but in ALVT the second heart sound is normal. Most patient develop symptom of heart failure in first year of life like our patient. The onset, severity and progression of heart failure is quite variable and ranges from many years of asymptomatic compensation to rapid decompensation and sudden death.

Echocardiography is the diagnostic investigation of choice. MRI can detect tunnels to left or right ventricle also. Cardiac catheterization is indicated only to see associated lesions or to visualize coronary artery origin. Treatment is always surgical correction. Surgical closure has been recommended at the time of diagnosis, including asymptomatic patients due to inadequacy of medical management, risk of developing severe AR and satisfactory result in neonates and infants from surgery. Small ALVT in asymptomatic patients may closely be followed up because spontaneous closure may occur in some cases.

Conclusion:
ALVT has a good long term outcome after surgery. The diagnosis should be considered in infants with clinical sign of AR. Echocardiography can identify it with associated lesions. Surgery should be done immediately after diagnosis in symptomatic patients. All patients require life long follow up for recurrence of the tunnel, aortic valve incompetence, left ventricular function and aneurismal enlargement of the ascending aorta.

References:


Delayed Diagnosis of Hereditary Hemorrhagic Telangiectasia

A DAS\textsuperscript{a}, MT MIAH\textsuperscript{b}, M JABIN\textsuperscript{c}, AT REZA\textsuperscript{d}

Summary:

Hereditary Hemorrhagic Telangiectasia (HHT), also known as Osler-Weber-Rendu Syndrome, is an autosomal dominant disorder. The typical findings of the disease are telangiectasias in skin and mucous membranes and arteriovenous malformations and aneurysms presenting in the organs like brain, lung, intestine and liver. The most common symptoms are recurrent epistaxis and gastrointestinal bleeding.

We report here a case of 38-year-old male who presented with typical history of recurrent epistaxis, hematemesis and melaena. Although the manifestations occurred since childhood, it took years to reach the diagnosis. Because most of the clinicians thought that upper gastrointestinal bleeding are usually due to peptic ulcer disease and chronic liver disease. The aim of this case report is not only to remind of this rare chronic disease but also to to increase the clinical suspicion for early diagnosis of HHT.

Key words: Epistaxis, Hematemesis, Melaena, Telangiectasia, Hereditary Haemorrhagic Telangiectasia.

(J Bangladesh Coll Phys Surg 2013; 31: 51-53)

Introduction:

The Osler-Weber-Rendu syndrome or Hereditary Haemorrhagic Telangiectasia (HHT) is a rare systemic fibrovascular dysplasia which bears an alteration in the elastic and muscle layers of vessel walls, making them more liable to spontaneous ruptures and injuries\textsuperscript{1,2}. 95% of affected individuals experience recurrent epistaxis, with a mean age of approximately 12 years and a mean frequency of 18 episodes per month.\textsuperscript{3} The prevalence of intestinal telangiectasia varies from 10% to 33%\textsuperscript{4}. They occur anywhere in the gastrointestinal tract, most commonly in the stomach and upper duodenum. Common causes of recurrent upper gastrointestinal bleeding are peptic ulcer disease and oesophageal varices. The aim of this case report is increase the suspicion of the clinician to early diagnosis of HHT which is a rare cause of upper gastrointestinal bleeding.

Case Presentation:

A 38-year-old male patient was admitted into Dhaka Medical College hospital with recurrent epistaxis for 33 years, haematemesis and melaena 1 year. With these complaint, he went to different ENT specialists and underwent cautery twice. He was admitted into several hospitals during each episode of melaena and received total 9 units of blood transfusions during last 4 months in addition to oral iron therapy on discharge each time. His father had similar history of epistaxis and his 9-year-old daughter has been suffering from epistaxis for about 5 years. On examination, patient was anaemic, with telangiectatic spots at oral mucosa of cheek and lower lip (figure 1, 2).

\textbf{Fig.-1: Telangiectatic spot over lower lip (white arrow)}
No purpura, petechiae or ecchymosis were found. Laboratory investigation showed microcytic hypochromic anaemia with haemoglobin 8.8 gm/dl and Platelet count 4,13,000/cubic mm, and coagulation profiles were PT 18.5 seconds, APTT 33.5 seconds with a control of 31 seconds. Other blood biochemistry including liver function tests were within normal limit. Ultrasonogram of whole abdomen shows hepatomegaly with multiple ill-defined space occupying lesion (SOL) of variable sizes suggestive of vascular alterations. These structures correspond to dilated arterial branches and passive venous congestion in the liver. Upper GI Endoscopy showed a telangiectatic spot at pyloric antrum of the stomach and colonoscopy showed a telangiectatic spot in caecum (figure 3). We diagnosed the case as Hereditary Haemorrhagic Telangiectasia.

Discussion:
Diagnosis of Hereditary Hemorrhagic Telangiectasia is based on four main clinical features called Curacao criteria which were established in 1999 to improve and facilitate admission of individuals with Hereditary Hemorrhagic Telangiectasia. These features are as follows: spontaneous recurrent epistaxis (nosebleeds), mucocutaneous telangiectases (abnormal capillary connections that mostly appear on the skin and mucosa), visceral arteriovenous malformations (inadequate connection between arteries and veins in the liver, lungs, digestive system and brain) and an affected first degree relative as indication of autosomal dominant inheritance. Definite diagnosis of HHT is made if three of the four mentioned criteria are present. Hereditary Hemorrhagic Telangiectasia can be suspected if there are two positive criteria and if only one criteria is present, Hereditary Hemorrhagic Telangiectasia is considered to be unlikely.

Almost all the criteria of HHT was present in our patient. But his patient was lately diagnose because of lack of suspicion by the physicians as well as rarity of this disease in our community. Epistaxis is the commonest presentation but commonly overlooked because of so many other common conditions causing epistaxis. Our patient underwent endoscopic examination previously without a definitive diagnosis as endoscopists probably failed to detect telangiectatic spot. It collapsed usually during active gastro intestinal bleeding. After correcting anaemia, telangiectatic spot becomes prominent or overt, so easy to detect during follow up endoscopy, that’s why this case was missed before. Once detected it is better to cauterize in accessible areas.

Catastrophic haemorrhage occurs in the Hereditary Haemorrhagic Telangiectasia population due to pulmonary and cerebral AVMs. Asymptomatic screening for cerebral AVMs remains the subject of debate because of the risks of diagnostic and treatment modalities, and unclear natural history. The prevalence of liver involvement in hereditary hemorrhagic telangiectasia ranges from 8–30%, with more than half the patients being asymptomatic. Doppler color flow study and CT scan of the abdomen are the confirmatory to see the hepatic involvement. Though in our case hepatic involvement is present, we cannot confirm it due to financial support.
Regarding management, treatment of Hereditary Haemorrhagic Telangiectasia is symptomatic (it deals with the symptoms rather than the disease itself), as there is no therapy that stops the development of telangiectasias and AVMs directly. Episodes of severe bleeding are treated with endoscopic argon plasma coagulation (APC) or laser treatment of any lesions identified; this may reduce the need for supportive treatment. During active severe bleeding mainstay of treatment is blood transfusion as happened in our case. After blood transfusion because of severe gastrointestinal bleeding, re-endoscopy was done which detected multiple telangiectatic spots in our patient. He is in need of cauterization of telangiectatic spots.

Conclusion:
Always upper gastrointestinal bleeding is not due to peptic ulcer disease and chronic liver disease. Though HHT is a rare disease, it may be considered if bleeding is recurrent and from different sites. So, any unexplained and recurrent bleeding from a particular site must be taken seriously. Screening is required for the family members in case of HHT. Proper education of patients, family members and more importantly medical practitioners is required in order to diagnose and proper management of the patients with HHT.

References:
Ectopiacordis - A Rare Congenital Anomaly

IP ALAM\textsuperscript{a}, S SHAFIUDDIN\textsuperscript{b}

Summary:
Ectopiacordis is a rare congenital malformation in which the heart is located partially or totally outside the thoracic cavity. It may occur as an isolated malformation or it may be associated with a larger category of ventral body wall defects that affect the thorax, abdomen or both. We present a case of ectopiacordis associated with complete ventral body wall defect.

(J Bangladesh Coll Phys Surg 2013; 31: 54-55)

Case Report:
A 28-year- G3P0 +2 (abortion) patient was admitted at Faridpur Medical College Hospital at her 38 weeks of pregnancy with labour pain. The patient had regular antenatal checkup. The patient did not give any history of medical or surgical illness and no exposure to drugs and toxins. There was no history of congenital anomaly in her family or consanguineal marriage. She had three ultrasonography during pregnancy at her 20 weeks, 28 weeks and at 34 weeks. Her ultrasonogram showing major congenital anomaly of the fetus. The sonologists figured it out to be a probable case of huge sacrococcygeal teratoma. However, each time the patient had antenatal checkup and ultrasonography, she was counseled and advised to get admitted into hospital for termination of pregnancy but she ignored and continued her pregnancy. She came at labour and on examination symphysiofundal height was about 36 weeks pregnant uterus size, presentation could not be definitely identified due to uterine contraction, fetal heart sound was not audible. On per vaginal examination - cervical os was full dilated, membrane ruptured, few intestinal loops were presenting through the os. A dead female baby was delivered spontaneously per vagina by breech. Placenta, cord and membrane were expelled out by controlled cord traction. On examination of the baby, there was complete absence of anterior abdominal wall with evisceration of all the abdominal organs (small and large intestines, liver, spleen, kidneys) along with the heart. There was also abnormal position of the lower limbs with hypoplasia. Other parts of the body (head, face, upper limbs) appeared to be normal. The umbilical cord and placenta were normal in appearance and location. A diagnosis of ectopiacordis associated with ventral body wall defect was made.

Fig: Ectopiacordis with anterior abdominal defect with evisceration of all viscera.

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\textsuperscript{b}. Dr. Sonia Shafiuddin, OSD, Obstetrics & Gynaecology, BSMMU.

Address of correspondence: Dr. Irin Parveen Alam, Assistant Prof Obstetrics & Gynae, Faridpur Medical College Hospital, Faridpur, Mobile- 88-01715348398, E-mail: dririn.alam@yahoo.com
Discussion:
Ectopia cordis is a very rare anomaly with an estimated prevalence of 0.079/10,000 births and may occur more frequently in females. It is a congenital malformation which was observed thousands of years ago. Clinically, ectopia cordis has been classified into four types: cervical, thoracic, abdominal and thoracoabdominal whether the heart is respectively in the neck, anterior to the sternum, within the abdomen or between the thorax and the abdomen. Most common are thoracic and thoracoabdominal. Embryologically, in about the third week, early disturbance in the formation of the cephalic fold will result in defective formation of the thoracic and epigastric walls, finally resulting in ectopia cordis with anterior defect of the sternum and diaphragm and an omphalocele.

To date, the cause of ectopia cordis is still unknown. There have been a number of reports linking it to chromosomal abnormalities. Reported karyotypic abnormalities include trisomy, Turner syndrome, 46,XX,17q+20, various type of congenital anomaly such as central nervous system, cardiac, skeletal, gastrointestinal and other malformation is associated with ectopia cordis, with the advent of ultrasonography it can be diagnose in early pregnancy.

The prognosis of ectopia cordis is generally poor, death commonly occur before or immediately after birth, usually due to associated malformations.

Conclusion:
Ectopia cordis is a rare congenital malformation with a poor prognosis. Ultrasonography is of great value in the prenatal diagnosis. Obstetrical management should include a careful search for associated anomalies, especially cardiac, and assessment of fetal karyotype. Pregnancy termination prior to viability should be considered.

References:
To
Editor-in-Chief
Journal of Bangladesh College of Physicians and Surgeons

Sir,

I had gone through the case report of your valuable journal (Vol 30, No 4, October 2012) title with ‘Oral Histoplasmosis: Report of Two Cases’ by SMA Sadat et al with keen interest and have few observations.

a. Both the cases were well written and the contents and illustrations were nice.

b. Classification of Histoplasmosis was mentioned without any reference in the article. Besides the three types described in this paper, other varieties are primary cutaneous histoplasmosis, African histoplasmosis and progressive disseminated histoplasmosis.1

c. Authors noted the role of itraconazole favorable in local histoplasmosis for which a reference was stated as given by Negroni and colleagues, but there was no mentioning of such names or paper in the reference list. In fact, itraconazole is regarded as first-line therapy for less severe form of disseminated histoplasmosis.2 So, this is a very effective drug in both local and systemic cases.

d. In the first case report, the patient was a painter and was found non-HIV. The other risk factors such as history of exposure to bat/bird droppings, travel history, living conditions, localities etc leading to development of primary histoplasmosis were not discussed.

e. In the second case, patient had past history of pulmonary tuberculosis with irregular treatment. Exclusion of relapse or new infection with TB by proper evaluation was not mentioned.

f. Follow-up plans were not described.

References:

Dr. Rukhsana Parvin
Associate Professor of Medicine
Enam Medical College & Hospital, Savar, Dhaka

Author’s Reply
To
Editor-in-Chief
Journal of Bangladesh College of Physicians and Surgeons

It is my great pleasure that Dr. Rukhsana Parvin, Associate Professor of Medicine, Enam Medical College &Hospital, had gone through the article titled “Oral Histoplasmosis: Report of Two Cases, with much interest and tried to raise the critical comments and queries. I strongly appreciate her effort which can help an author to find out the weakness of his article & thus make it rich in future.


Thank you for adding other three types e.g. Cutaneous Histoplasmosis, African Histoplasmosis and Progressive Disseminated Histoplasmosis.

The reference of Negroni and colleagues was unintentionally missed from the reference cite. The reference was “Negroni R, Taborda A, Robies AM. Itraconazole in the treatment of Histoplasmosis associated with AIDS. Mycoses 1992;35(11-12):281-287.” The drug is effective in both local and systemic forms.

The first reported patient lives in Dhaka city in a densely populated area and occasionally visits his village. Particularly he had no history of exposure to bat or bird droppings.

The second reported patient gave history of pulmonary tuberculosis 25 years back with possible irregular treatment. As the history of TB was long before and
chest radiograph didn’t show any evidence, we avoided other investigations to exclude relapse or new infection with Tuberculosis.

There are some guidelines of follow up of disseminated histoplamosis with maintenance therapy, which are a) Monitoring histoplasma Ag (serum or urine) every 3-6 months during therapy. Rise in level suggestive of relapse. b) Discontinuation of maintenance therapy may be safe if patient is on stable ART >6 months with CD4 >150, serum Ag < 2 units, and have completed induction and minimum of 12 months of maintenance antifungal therapy. C) Serum Itraconazole level should be obtained at least once as absorption can be erratic; should be >1 mcg/ml.

Finally I would like to thank the respected reader for her valuable endeavor in further addition of information in the article and thus to upgrade the quality of Journal of Bangladesh College of Physicians & Surgeons.

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The concept of Continuing Professional Development (CPD) is an emerging issue now a day. It is a multi-professional activity which refers to an educational program that helps professionals to keep their knowledge and skills up-to-date in response to changing demands of the society and of profession.

Present CPD committee, BCPS has organized two CPD programmes, one at BSMMU and another one at Sahid Sohrawardi Medical College and 2nd and 3rd CPD day at BCPS premises.

In CPD program at Sahid Sohrawardi Medical College, two papers were presented. The program was chaired by Prof. Khaja Nazim uddin, Professor of Medicine, BIRDEM and Prof. Maksudul Alam, Professor of Anaesthesiology and Principal, Sahid Sohrawardi Medical College. Prof. Rawshon. Professor of Gastroenterology, SSMC conducted the session as moderator.

Papers presented were:
1. Fantom limb pain and its management. Speaker – Dr. Md. Mainul Hossain, Prof, Anaesthesiology, BSMMU
2. Study habits of post-graduate students and resident. Speaker- Dr. Md. Abdur Rahim, Registrar, Medicine, BIRDEM

2nd CPD day, a day-long programme was organized, on 5th April, 2012 at BCPS premises, where we had 355 post graduate doctors and students as participants. Thirty two papers from different disciplines were presented over the session.

A 3rd CPD day was organized on 24th November, 2012. That was a special day for us because 14 honorable senior teachers of different specialties were with us as speaker of honour. We always gratefully acknowledge their immense contribution to the development of the medical education in this country. Our younger doctors had an opportunity to meet and listen to them, enriched their knowledge and widened their vision by attending the programme. About 300 fellows and post-graduate students were with us as participant.

We had National Professor. Brig.(Retd) Abdul Malik, Professor.Mirza Mazharul Islam , Professor. AKM Anowerul Azim and Professor.Subagata Chowdhury as chairpersons in 3rd CPD day.

Senior teachers who presented their papers over the occasion of 3rd CPD day-
1. Professor. Md. Harun-Ur-Rashid
2. Professor. Md. Abul Faiz
3. Professor. Md. Sanwar Hossain
4. Professor. Mahmud Hasan
5. Professor. Pran Gopal Datta
6. Professor. Hidayutul Islam
7. Professor. Rasiduddin Ahmad
8. Professor. A.H.M. Towhidul Anwar Chowdhury
9. National Professor. Shahla Khatun
10. Professor. Nazmun Nahar
11. National Professor. MR Khan
12. Professor. Md. Abul Kashem Khandaker
13. Professor. Kazi Mezbahuddin Iqbal
14. Professor. Md. Salehuddin

Prof. Mahmud Hasan, President, BCPS, Prof. Kanak Kanti Barua, Honorary Secretary, BCPS, Prof. Nazmun Nahar, Ex. President, BCPS, Prof. A K M Rafique Uddin Ahmed, Chairman and Prof. Tahmina Begum, Member Secretary, CPD committee was present on all the occasions.

Prof. Tahmina Begum
Member Secretary, CPD Committee,
BCPS
FROM THE DESK OF EDITOR in CHIEF

(J Bangladesh Coll Phys Surg 2013; 31: 59)

Dear Fellows

Seasons greeting, this is going to be my and my editorial teams’ last issue. Over the last two years we have tried our level best to improve the quality of our beloved journal and take the task forward left in our hand by our predecessors. First and foremost we have gotten rid of all backlogs alongside the - information for authors section has been updated, a reviewers’ guideline has been developed and a software for up-to-date information and digitalization of articles have been installed. In spite of all these there is one failure we humbly accept that is we have not yet been able to index our journal in the PubMed. I hope that the next editorial team would start from where we have left and fulfill the unfinished task. I on behalf of my editorial team wish to see this journal reach an international height with you fellows by our side.

Thank you all for your support.

Prof. H.A.M. Nazmul Ahasan
Editor-in-Chief
Journal of Bangladesh College of Physicians and Surgeons
**The following Fellows who died December 2012 - January 2013**

<table>
<thead>
<tr>
<th>Name</th>
<th>Date of Death</th>
<th>Details</th>
</tr>
</thead>
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<tr>
<td>Professor Syed Ershad Ali</td>
<td>21st December, 2012</td>
<td>He was awarded fellowship without Examination in Obst. &amp; Gynae, 1974 from Bangladesh College of Physicians and Surgeons (BCPS).</td>
</tr>
<tr>
<td>Professor M. H. Mullick</td>
<td>1st January, 2013</td>
<td>He was awarded fellowship without Examination in Anatomy, 1984 from Bangladesh College of Physicians and Surgeons (BCPS).</td>
</tr>
<tr>
<td>Professor Taimur A.K. Mahmud</td>
<td>11th January, 2013</td>
<td>He was passed fellowship in Medicine in January, 1994 from Bangladesh College of Physicians and Surgeons (BCPS).</td>
</tr>
<tr>
<td>Major General Retd. (Dr.) S. Ameer Ali</td>
<td>22nd January, 2013</td>
<td>He was awarded Honorary fellowship in Surgery, 1997 from Bangladesh College of Physicians and Surgeons (BCPS).</td>
</tr>
<tr>
<td>National Professor Nurul Islam</td>
<td>24th January, 2013</td>
<td>He was the founder fellow of Bangladesh College of Physicians and Surgeons (BCPS).</td>
</tr>
<tr>
<td>Dr. Parveen Shahida Khanum</td>
<td>28th January, 2013</td>
<td>She passed fellowship in Obst. &amp; Gynae in January, 2011 from Bangladesh College of Physicians and Surgeons (BCPS).</td>
</tr>
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