

DCIMC JOURNAL 2018

DHAKA CENTRAL INTERNATIONAL MEDICAL COLLEGE

VOLUME 5 NO 1 JANUARY 2018

ISSN 2410-9282

OFFICIAL PUBLICATION OF
DHAKA CENTRAL INTERNATIONAL MEDICAL COLLEGE

DCIMC

DHAKA CENTRAL INTERNATIONAL MEDICAL COLLEGE JOURNAL (APPROVED BY BMDC)

January 2018, Vol.5 No.1

Contents

From the Desk of Editor-in-Chief 3
Instructions for Authors 4

Editorial

Rituximab in Renal Diseases. 13
Nomany BMS, Chowdhury MAH

Original Articles

Parathyroid Hormone Assay in Total Thyroidectomy - A Predictive Factor for Post Operative Hypocalcaemia. 20
Akram MS, Siddiquee BH, Uddin MM, Kabir ABML, Karim A, Sarker DK

Clinico Haematological Parameters and Evaluation of Risk Factors of Acquired Aplastic Anaemia Patients Admitted in a Tertiary Care Hospital. 31
Kamruzzaman AKM, Nurunnobi AKM, Siraj S, Ali L

Outcome of Lateral Pancreaticojejunostomy in 362 Patients Presenting with Pancreatic Stones, Performed in Tertiary Referral Centres of Dhaka, Bangladesh. 36
Rabbi H, Rashid MM, Hakim HAN, Ahmed AHM T, Chowdhury AQ, Sarder MM, Raihan HM S, Nayeem SR, Ali M

Transabdominal Ultrasonographic Evaluation of Malignant Ovarian Tumors. 47
Shimu F, Jahan I, Farzana T

Effect of Diclofenac on Antihypertensive Efficacy of Amlodipine. 58
Chowdhury RA, Alam I, Farooqui I, Rahman MH

Serum Copper Level in Third trimester of Bangladeshi Pregnant Women with Gestational Diabetes Mellitus. 65
Mishu FA, Yesmin MS

Pattern of Complications and Its Relation with Glycaemic Status in Hospitalized Type 2 Diabetic Patients. 68
Nessa A, Chowdhury RH, Pathan MF

Effect of Aqueous Extract of Aegle Marmelos Fruit and Leaf on Body Weight of Non-Diabetic and Type I Model Diabetic Rats. 77
Debnath R, Ali L, Akhter M, Aziz M

Evaluation of Marker Specific Outcome Study in Patients with Acute Coronary Syndrome. 82
Parvin D, Baul SK, Hossain MSR, Hadiuzzaman M, Fatema K, Chowdhury FA, Hoque MM, Nazneen M

Role of Amnitomy on Duration of Labour in Primigravidae. 89
Khatun J, Siddiqua NM

Review Article

Emergence of Chikungunya in Bangladesh: A Systematic Review. 97
Begum N, Haque SM

Case Reports

A Very Rare Case Report on a 4 Year Old Boy with Crigler-Najjar Syndrome Type-1 in Association with Sinus Venosus Type ASD. 103
Salam W, Nahar K, Rahman MM, Adhikary AB, Hoque R, Islam N, Hossain A, Rahman CMM

Ectopic Parathyroid Adenoma: Surgical Correction and its Complication Management. 106
Basnet N, Singh A, Pradhan R, Sunny SA, Adhikary AB, Islam N

Food Bolus Impaction in a Case of Corkscrew Esophagus: A Rare Case report. 111
Rahman MM, Adhikary AB, Rahman MM, Hoque MR, Ranjan R, Islam MN

DCIMC

Dhaka Central International Medical College Journal

Vol.5 No.1 January 2018

An Official Organ of Dhaka Central International Medical College

CHIEF PATRON

Md. Motazzaroul Islam
Chairman, Governing Body
Dhaka Central International
Medical College

EDITORIAL BOARD

Editor in Chief

Professor Md. Azizul Islam
Principal, Dhaka Central
International Medical College

Executive Editor

Dr. Bakhtiare Md. Shoeb Nomany

Editors

Prof. Zakia Akhter
Dr. Md. Anwarul Alam Chowdhury
Dr. Ahmed Salam Mir

Members

Dr. Md. Abdul Hye Chowdhury
Prof. MafruhaNazneen
Prof. Matira Khanam
Prof. Helena Begum
Dr. Saika Shaheed
Dr. Md. Mahfuzul Islam

ADVISORS

Prof. Md. Anwarul Islam
Prof. Md. Shahid Ullah
Prof. Rashida Begum
Prof. Chowdhury Golam Mahbub-E-Mostafa
Prof. Md. Rafiqul Bari
Prof. Md. Mahbubar Rahaman
Prof. Merina Khanom
Prof. Most. Naznin Nahar

REVIEWERS

Prof. AKM Nazrul Islam
Prof. Mohammad Kamal
Prof. M Fakrul Islam
Prof. Ratu Rumana Binte Rahman
Prof. Selina Ahmed
Prof. Shahanaz Begum
Prof. Shohrab Hossain Sourav
Prof. S M Amjad Hossain
Prof. Rashidul Hassan
Prof. S M Idris Ali

PUBLISHED BY

Dr. Md. Abdul Hye Chowdhury
Dhaka Central International
Medical College
2/1 Ring Road, Shyamoli,
Mohammadpur, Dhaka-1207
Bangladesh

ANNUAL SUBSCRIPTION

Tk. 200/- for local subscribers
US$ 20 for overseas subscribers

ADDRESS OF CORRESPONDENCE

Dr. Bakhtiare Md. Shoeb Nomany

The Dhaka Central International Medical College Journal is a peer reviewed journal. It is published biannually – January and July. It accepts original articles, review articles and case reports.

While every effort is always made by the Editorial Board to avoid any inaccurate or misleading information from appearing in the Dhaka Central International Medical College Journal, information within the individual article is the responsibility of its author(s). The Dhaka Central International Medical College Journal and/or its editorial board accept no liability whatsoever for the consequences of any such inaccurate and misleading information, opinion or statement.

Executive Editor, Dhaka Central International Medical College Journal,
Associate Professor, Department of Medicine, Dhaka Central International Medical College
Tel: +88029124396, Cell No. +8801770008844, Fax: +88029118598
Web: www.dcimch.com, email: jdcimc@yahoo.com
2/1, Ring Road, Shyamoli, Mohammadpur, Dhaka-1207, Bangladesh.

From the Desk of Editor-in-Chief

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

Prof. Md Azizul Islam
Editor-in- Chief

DCIMC

INFORMATION FOR AUTHORS

Manuscript preparation and submission:

Guidelines for the Authors:

The Dhaka Central International Medical College Journal provides publication (six monthly) of articles in all areas of the subject. The Journal welcomes the submission of manuscript that meets the general criteria of significance and scientific excellence.
Papers must be submitted with the understanding that they have not been published elsewhere (except in the form of an abstract or as part of a published lecture, review, or thesis) and are not currently under consideration by another journal published by **INTERNATIONAL RESEARCH JOURNALS** or any other publisher.

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

Editor-in-Chief,
DCIMCJ
2/1, Ring Road, Shyamoli,
Dhaka, Bangladesh.

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

Submit Manuscripts as e-mail attachment to the editorial office at: jdcimc@yahoo.com

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

Article types:

Five types of manuscripts may be submitted:

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 communication 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 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 week. The editorial board will re-review manuscripts that are accepted pending revision. The DCIMCJ editorial board will try to publish the manuscript as early as possible fulfilling all the rigorous journal needs.

I. A. Preparing manuscript for submission to DCIMCJ

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

Condition for submission of manuscripts:

- All manuscripts are subject to peer-review.
- Manuscripts are received with the explicit understanding that they are not under simultaneous consideration that are not under simultaneous by any other publication.
- Submission of a manuscript for publication implies the transfer of the copyright from the author to the publisher of the Dhaka Central International Medical College journal and may not be reproduced by any means in whole or in part without the written consent of the publisher.
- It is 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 has 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 is 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 (29 x 21cm) size white paper.

DCIMC

2. Margin should be 5 cm for the header and 2.5 cm for the remainder.
3. Style should be that of modified Vancouver.
4. Each of the following section should begin separate page :
    - Title page
    - Summary/abstract
    - Text
    - Acknowledgement
    - References
    - Tables and legends

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

I. A. 1.a. General Principles:

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

- 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 coments and queries directly on the paper copy.

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

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

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

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

I. A. 2. Title page:

1. Article title. Concise title is easier to read than long, convoluted ones. Titles that are too short may, however, lack important information, such as study design (which is particularly important in identifying type of trials). Authors should include all information in the title that will make electronic retrieval of the article both sensitive and specific.
2. Authors' names and institutions.
3. The name of the department(s) and institution(s) to which the work should be attributed.
4. Disclaimers, if any.
5. Contact information for corresponding authors. The name, mailing address, telephone and fax numbers, and e-mail address of the authors responsible for correspondence about the manuscript.

DCIMC

6. The name and address of the authors to whom requests for reprints should be address or a Statement that reprints are not available from the authors.
7. Source(s) of support in the form of grants, equipment, drugs, or all of these.
8. A short running head or foot line, of no more than 40 characters (including litters and spaces). Running heads are published and also used within the editorial office for filing and locating manuscript.
9. The number of figures and tables. It is difficult for editorials staff and reviewers to determine whether the figures and tables that should have accompanied a manuscript were actually included unless the numbers of figures and tables are noted on the title page.

I. A. 3. Conflict-of interest notification page:

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

I. A. 4. Abstract:

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

- Should be limited to 250 words

- The abstract should provide the introduction of the study and blinded state and should state the

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

- Because abstracts are the only substantive portion of the article indexed in many electronic

databases, and the only portion many readers read, authors need to be careful that they accurately reflect the content of the article

I. A. 5. Introduction:

- Provide a context or background for the study (that is, the nature of the problems and its significance) It should be very specific, identify the specific knowledge in the aspect, reasoning and what the study aims to answer.

- State the specific purpose or research objective of, or hypothesis tested by, the study or observation; the research objective is often more sharply focused when stated as a question.

- Both the main and secondary objectives should be clear.

- Provide only directly pertinent primary references, and do not include data or conclusions from the work being reported.

I. A. 6. Methods:

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

I. A. 6. a. Selection and description of participants:

- Describe your selection of the observation or experimental participants (patients or laboratory animals, including control) 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 or 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 clear 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.

DCIMC

I. A. 6. b.Technical information:

- Identify the methods, apparatus (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow others to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and briefdescription 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 forlocatin, selection, 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 thereported 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. Result:

- Present results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Please keep 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 then 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 result 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 complete. State new hypotheses when warranted, but label them clearly as such.

DCIMC

I. A 9. References:

I. A. 9. a. General considerations related to References:

- Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible.

- On the other hand, extensive lists of references to original work of a topic can use excessive space on the printed page. Small number of references to key original papers list, is preferable particularly since references can now be added to the electronic version of published papers, and since electronic literature searching allows readers to retrieve published literature efficiently.

- Avoid using abstracts as references. References to papers accepted but not yet published should be designated as "in press" or "forthcoming"; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication.

- Information from manuscripts submitted but not accepted should be cited in the text as "unpublished observations" with written permission from the source.

- Avoid citing a "personal communication" unless it provides essential information not available from a public source, in which case the name of the person and date of communication should be

cited in parentheses in the text. For scientific articles, obtain written permission and confirmation of accuracy from the source of a personal communication. Some but not all journals check the accuracy of all references citations; thus, citation errors sometimes appear in the published version of articles. To minimize such errors, references should be verified using either an electronic bibliographic source such as Pub Med or print copies from original sources.

- Authors are responsible for checking that none of the references cite retracted articles except in the context of referring to the retraction. For articles published in journals indexed in MEDLINE, the ICMJE considers Pub Med the authoritative source for information about retractions.

I. A. 9. b. Reference style and format:

- References should be numbered consecutively in the order in which they are first mentioned in the text.
- Identify references in text, tables, and legends by Arabic numerals in superscript.
- References cited only in tables or figure legends should be numbered in accordance with thesequence 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/figures 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 abbreviation in footnotes, and use the following symbols, in sequence:
*, †, ‡, §, _, ¶, **, ††, ††, §§, _ _, ¶¶, etc.
- Identify statistical measures of variations, such as standard deviation and standard error of the mean.
- Be sure that each table is cited in the text. If you use data from another published or unpublished source, obtain permission and acknowledge that source fully.

I. A. 11. Illustrations (Figures):

- Figures should be either professionally drawn and photographed, or submitted as photographic-

DCIMC

quality digital prints, in addition to requiring a version of the figures suitable for printing, (for example, JPEG/GIF)

- Authors should review the images of such files on a computer screen before submitting them to be sure they meet their own quality standards. For x-ray films, scans, and other diagnostic images, as well as pictures of pathology specimens or photomicrographs, send sharp, glossy, black-and-white or color photographic prints, usually 127 X 173 mm (5 X 7 inches)
- Letters, numbers, and symbols on figures should therefore be clear and consistent throughout, and large enough to remain legible when the figure is reduced for publication.
- Photographs of potentially identifiable people must be accompanied by written permission to use the photograph. Figures should be numbered consecutively according to the order in which they have been cited in the text.
- If a figure has been published previously, acknowledge the original source and submit written permission from the copyright holder to reproduce the figure. Permission is required irrespective of authorship or publisher except for documents in the public domain.
- For illustrations in color, DCIMCJ accept colored illustration only when it seems essential. This Journal publishes illustrations in color only if the author pays the additional cost. Authors should consult the journal about requirements for figures submitted in electronic formats.

I. A. 12. Legends for illustration (Figures):

- Type or print out legends for illustrations using double spacing, starting on a separate page, with Arabic numerals corresponding to the illustrations.

- When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend. Explain the internal scale and identify the method of staining in photomicrographs.

I. A. 13. Units of measurement:

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

- Authors should report laboratory information in both local and International System of Units (SI).

- Drug concentrations may be reported in either SI or mass units, but the alternative should be provided in parentheses where appropriate.

I. A. 14. Abbreviations and symbols:

- Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers.

- Avoid abbreviations in the title of the manuscript.

- The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

I. B. Sending the manuscript to the journal:

- If a paper version of the manuscript is submitted, it should contain print copies of tables and figures; they are all needed for peer review and editing, and the editorial office stall cannot be expected to make the required copies.

- Manuscripts must be accompanied by a cover letter, conflicts of interest form, authorship and declaration, proforma of which is a available in DCIMCJ web site.

Editing and peer review:

All submitted manuscripts are subject to scrutiny by the Editor in-chief or any members of the Editorial Board. Manuscripts containing materials without sufficient scientific value and of a priority issue, or not fulfilling the requirement for publication may be rejected or it may be sent back to the author(s) for resubmission with necessary modifications to suit one of the submission categories. Manuscripts fulfilling the requirements and found suitable for

consideration are sent for peer review. Submissions, found suitable for publication by the reviewer, may need revision/modifications before being finally accepted. Editorial Board finally decides upon the publish ability of the reviewed and revised/modified submission. Proof of accepted manuscript may be sent to the authors, and should be corrected and returned to the editorial office within one week. No addition to the manuscript at this stage will be accepted. All accepted manuscripts are edited according to the Journal's style.

Submission preparation checklist:

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

Check lists:

Final checklists before you submit your revised article for the possible publication in the Journal of Dhaka Central International Medical Collage:

1. Forwarding/Cover letter and declaration form
2. Authorship and conflicts of interest form
3. Manuscript

- Sample of the above document is available in the following links: http://www.dcimc.com

- If you have submitted mentioned 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 underline)
- 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.

Language and grammar:

- Uniformity in the language
- Abbreviations spelt out in full for the first time
- Numbers 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 are 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' privacy maintained (if not, written permission enclosed)
- Credit note for borrowed figures/tables provided
- Each table/figure in separate page

If you have any specific queries please visit our website at www.dcimc .com

Manuscript format for research article:

- **Title**
  - Complete title of your article
  - Complete author information
  - Mention conflict or 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) 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 consent
  - Patient consent
  - Statistical analysis and software used.
- **Result**
  - Clearly present the data
  - Avoid data redundancy
  - Use table information at the end of the sentence before full stop between the small bracket
- **Discussion**
  - Avoid unnecessary explanation of someone else work unless it is very relevant to the study
  - Provide and discuss with literatures to support the study
  - Mention about limitation of your study
- **Conclusion**
  - Give your conclusion
  - Any recommendation
- **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

The editor reserves the right to style and if necessary, shorten the material accepted for publication and to determine the priority and time of publication

---

DCIMC

Updated Treatment of Kidney Transplant (KT) Rejection

Nomany BMS[1], Chowdhury MAH[2]

Introduction:

Transplantation is a recent phenomena. Many of the big developments in this discipline have taken place within the past 40 years. On 1954 Joeseph E. Murray and his colleagues performed the first truly successful kidney transplant from one twin to another at Peter Bent Brigham Hospital in Boston. This was done without any immunosuppressive medicine. Scientists predicted that immune system reactions should be minimal between identical twins. On Late 1950 new approaches were needed to prevent the body from fighting off a 'foreign' donor kidney when an identical twin donor was not available. This fighting off a 'foreign' donor kidney is named rejection. Rejection is defined as the clinical and histopathological responses of the immune system of the body to the transplanted tissue.

Occurrence of rejection:

On 1961 powerful immunosuppressives were available and used in combination to decrease the chance for kidney rejection. On 1980s and 1990s new techniques, new medications and new patient information made kidney transplantation more safer, effective and routine procedure. Thus the occurrence of acute rejection in the first year after transplant has significantly diminished. Previously it was near-universal and now-a-days it is about 10% to 15%. The primary cause is the development of newer immunosuppressive medications.[1] About 25% of acute rejections have a humoral component due to (i) increase in presensitized patients for KT, (ii) patients with donor-specific antibody (DSA) in desensitization protocols, and (iii) ABO-incompatible KT. In acute humoral rejection there may be features of thrombotic microangiopathic anemia (TMA) and thrombocytopenia. If there is immediate cyanosis of the graft on revascularization (hyperacute rejection) or an abrupt decline in urine output and graft tenderness 3 to 14 days after KT (delayed hyperacute or accelerated rejection), donor-specific antibody (DSA) is thought to be responsible. But the management of chronic rejection has remained a challenge, even after having better methods to prevent or reverse the underlying pathology.

1. **Dr. Bakhtiare Mohammad Shoeb Nomany**
Associate Professor, Department of Medicine,
Dhaka Central International Medical College.

2. **Dr. Md. Abdul Hye Chowdhury**
Associate Professor, Department of Surgery,
Dhaka Central International Medical College.

Diagnosis of rejection:

Rejection of kidney was first identified as histopathologic findings following biopsy from transplanted kidney. When biopsy is done to diagnose rejection, two separate cores of tissues should be taken due to patchy distribution of rejection findings. A renal biopsy is considered adequate for analysis if sample contains at least 10 glomeruli and two small arteries. A biopsy with seven to nine glomeruli and one artery is considered as marginally adequate for analysis.

Modified BANFF Classification of Rejection[2]

Antibody Mediated

Acute:

C4d+, presence of circulating antidonor antibodies and acute tissue injury

I. ATN-like (minimal inflammation)

II. Capillary and/or glomerular inflammation and/or thromboses

III. Arterial inflammation

Chronic:

C4d+, presence of circulating antidonor antibodies and chronic tissue injury

I. glomerular double contours,

II. peritubular capillary basement membrane multilayering,

III. tubular atrophy or interstitial fibrosis, and/or

IV. fibrous intimal thickening in arteries

T Cell Mediated

Acute:

Mononuclear cell interstitial inflammation and tubulitis and/or arteritis

IA: More than 25% interstitial infiltration, 4 to 10 mononuclear cells/tubular cross section

IB: More than 25% interstitial infiltration, >10 mononuclear cells/tubular cross section

IIA: Intimal arteritis, mild to moderate (0% to 25% of luminal area)

IIB: Intimal arteritis, severe (>25% of luminal area)

III: Transmural arteritis and/or fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocyte inflammation .

Chronic:

Arterial intimal fibrosis with mononuclear cell infiltration in fibrosis, formation of neointima

Borderline Presence of 10% to 25% interstitial infiltration, <4 mononuclear cells/tubular cross section

Clinical manifestation:

The clinical presentation of T cell and antibody-mediated acute rejection is same. Patients typically present with a rapid rise in serum creatinine, and in severe cases may have fever, decreasing urine output, weight gain, or graft tenderness. Risk factors for acute rejection as well as other causes of graft dysfunction (e.g. cytomegalovirus infection) should be considered during dealing with acute rise in serum creatinine.

Risk Factors for Acute Rejection

High Risk:

Sensitization (high panel reactive antibody percentage),
previous transplantation,
multiple pregnancies, repeated blood transfusion before KT,
delayed graft function (DGF),
deceased donor,
elderly donor,
prolonged ischemic time,
donor brain death,
donor acute kidney injure (AKI),
HLA mismatching,
positive B cell crossmatch,
ABO incompatibility,
low corticosteroid,
infection like bacterial pyelonephritis, cytomegalovirus infection,
adolescent recipient,
previous rejection episode.

Low Risk:

Zero HLA mismatch,
preemptive transplantation,
young donor kidney,
living donor,
first transplant.

Differential Diagnosis of Renal Allograft Dysfunction

First week after KT:

Acute tubular necrosis (ATN)

Hyperacute or accelerated rejection

Urologic complications like obstruction, urine leak

Vascular thrombosis involving renal artery, renal vein

Volume contraction (dehydration)

First to 12 weeks after KT:

Acute rejection

Calcineurin inhibitor (CNI) toxicity

Volume contraction (dehydration)

Urologic complications like obstruction

Infection like bacterial pyelonephriti,s viral infections

Interstitial nephritis (AIN, CIN)

Recurrence of primary disease

After 12 weeks of KT:

Acute rejection

Volume contraction (dehydration)

Calcineurin inhibitor (CNI) toxicity

Urologic complication like obstruction

Infection like bacterial pyelonephritis, viral infections

Chronic allograft nephropathy (CAN)

Recurrence of primary disease

Renal artery stenosis

Post-transplantation lymphoproliferative disorder

Treatment of Acute T Cell–Mediated

Rejection:

Treatment of acute T cell–mediated rejection is often done by the findings on kidney biopsy and the clinical response to pulse methylprednisolone.

For the patient with graft dysfunction and biopsy-proven rejection, treatment with intravenous methylprednisolone 3 to 5 mg/kg (250 to 500 mg/d) for 3 to 5 days is often effective if the histologic injury is tubulointerstitial (Banff class IA or IB). Few studies of the clinical response to corticosteroids in the treatment of acute rejection have been done suggesting that 60% to 70% of patients will respond within 5 days. Response is menifestated by improved urine output and decreasing serum creatinine. If there is inadequate response after pulse therapy or if there is vascular involvement (Banff class IIA, IIB), corticosteroids often must be supplemented with T cell–depleting antibody therapies in a similar dosage of induction therapy.

1. Rabbit antithymocyte globulin (rATG) 1-1.5 mg/kg IV for 7-14 days or
2. Anti-CD52 (injection alemtuzumab-Campath 30mg/ml) 30-60 mg × 1 or 2 doses on days 0 and 2.

For patients who are on a non-tacrolimus based maintenance regimen, tacrolimus conversion may be considered in the rejection with an inadequate response to pulse methylprednisolone,[3] and for patients on a corticosteroid-free regimen, reinstitution of maintenance prednisone should be done.[4]

Recently the use of anti- CD52 (alemtuzumab) has increased in kidney transplantation. This agent binds to CD52, an antigen that is present on B and T cells, and results in depletion of both B and T cell lines. Its ability to induce prolonged, significant lymphopenia for up to 6 to 12 months after administration led to its use in refractory chronic lymphocytic leukemia (CLL). It is a humanized antibody and therefore has fewer infusion-related side effects than either rATG or OKT3. But the long-term impact of prolonged lymphopenia on the risk for opportunistic infection or post-transplant lymphoproliferative disorder (PTLD) has yet to be determined.

Acute Antibody-Mediated Rejection:

Treatment of acute humoral rejection is indicated when the triad of graft injury, C4d staining in peritubular capillaries on biopsy, and circulating donor-specific antibody (DSA) is present, but should also be considered in high-risk circumstances (prior desensitization or known donor-specific antibody) even if all three criteria are not fulfilled. High-quality randomized trials investigating treatment options for acute humoral rejection are lacking[5]. Traditionally, treatment has entailed removal of the pathogenic immunoglobulin(s) with plasma exchange and inhibition or suppression of antibody production with IVIG. In general, at least five plasma exchange treatments should be administered daily or every other day, with 1 to 2 g/kg total dose IVIG. Because IVIG is removed by plasma exchange, a common strategy is to administer IVIG 100 to 200 mg/kg after each exchange. For refractory acute humoral rejection, rituximab may be considered targeting B cells inhibition.[6] Inj. Rituximab 375 mg/m2 with plasma exchange and IVIG.

Moreover, the proteosome inhibitor bortezomib directly inhibits antibody-producing plasma cells is a potential treatment for refractory antibody mediated rejection, in combination plasma exchange and IVIG.[7] Inj. Bortezomib - Bortemib 2 mg or 3.5 mg/vial--1.3 mg/m2 × four doses over 2 weeks.

Eculizumab is a humanized monoclonal antibody that causes terminal complement C5 inhibition and has been shown to significantly reduce the risk of acute humoral rejection as well as subsequent transplant glomerulopathy in patients who have undergone positive crossmatch kidney transplant.[8] For prevention in +XM (positive crossmatch) transplant: 600-1200 mg weekly × 4 then biweekly until successful antibody reduction.

Finally, there are case reports of splenectomy (bulk of B cell removal) for refractory acute humoral rejection.[9] These therapies are typically coupled with targeted T cell therapy such as high-dose corticosteroids and/or depleting antibody therapy, because histologic evidence of mixed T cell rejection is often present and helper T cell function may contribute to an enhanced B cell response.

Chronic Rejection

(T Cell and/or Antibody Mediated)

T cell– or antibody-mediated injury in a graft without features of acute tissue injury remains a therapeutic dilemma in kidney transplantation. No specific intervention has been proven to be effective in reversing the chronic tissue injury; however, consideration should be given to optimizing or enhancing the maintenance immunosuppression by transitioning to tacrolimus-MMF therapy or increasing the dose of these agents if CNI nephrotoxicity is not identified.[10] Any intervention should be weighed against the potential for risk of enhanced immunosuppression and the lack of any long-term data describing the impact of enhancing immunosuppression.

Treatment of Chronic Allograft Injury

Nonimmune:

Treating hypertension with ACE inhibitors or ARBs.

Performing lifestyle modification like stopping smoking, controlling lipids profile in blood.

Controlling diabetes mellitus.

Prevention and treatment of urinary tract infection.

Prevention of CNI toxicity by reducing or replacing CNI but insufficient immunosuppression should be avoided.

Treatment of BK virus nephropathy by reducing immunosuppression with or without antiviral therapy.

Alloimmune:

Diagnosis and treatment of early acute cellular rejection with corticosteroids or antithymocyte globulin.

Diagnosis and treatment of acute antibody-mediated rejection by means such as plasma exchange, or immunoadsorption to eliminate pathogenic antibodies with or without anti-CD20 therapy.

Diagnosis and treatment of chronic antibody-mediated rejection by intravenous immunoglobulins (IVIG) with or without anti-CD20 therapy.

Strategies for the Prevention of Chronic Allograft Injury:

Minimizing sensitization in future organ recipients by avoiding blood transfusions and poor HLA matching during first transplantation.

Obtaining complete donor and recipient typing and knowledge on HLA alloantibodies at time of transplantation.

Minimizing ischemia-reperfusion injury by shortening cold ischemia time.

Avoiding insufficient immunosuppression.

Ensuring prophylaxis for CMV in first 3 to 6 months of transplantation.

Screening for BK virus after transplantation.

Monitoring donor-specific HLA alloantibodies after transplantation (at least in presensitized patients or during drug minimization).

Performing protocol biopsies to detect subclinical rejection (at least in presensitized patients or during drug minimization).

Reviewing for failure by patients to follow any of their medication recommendations.

Prognosis:

Regimen in low immunologic risk with TAC/MMF/Pred, induction with IL-2Ra

(Basiliximab), CNI dose or trough level goal 7-16 ng/ml × 3 months, 5-15 ng/ml, antiproliferative dosing 1 gm bid shows acute rejection at 6 months is only 4%.[4]

Regimen in low immunologic risk with CSA/MMF/Pred, induction with IL-2Ra (Basiliximab), CNI dose or trough level goal 125-400 ng/ml × 3 months, 100-300 ng/ml, antiproliferative dosing 1 gm bid shows acute rejection at 6 months is only 12%.[4]

Drug minimization regimen with CSA(low) /MMF/Pred, induction with IL-2Ra (Basiliximab), CNI dose or trough level goal 50-100 ng/ml, antiproliferative dosing 1 gm bid shows acute rejection at 6 months is 23%.[11]

Drug minimization regimen with TAC(low)/ MMF/Pred, induction with IL-2Ra (Basiliximab), CNI dose or trough level goal 3-7 ng/ml, antiproliferative dosing 1 gm bid shows acute rejection at 6 months is 12%.[11]

Steroid sparing regimen with TAC/MMF, induction with IL-2Ra (Basiliximab), CNI dose or trough level goal 10-20 ng/ml × 3 months, 5-15 ng/ml, antiproliferative dosing 1.5 gm bid × 14 d 1 gm bid shows acute rejection at 6 months is only 9%.[12]

Episodes of acute rejection may predispose to chronic graft dysfunction, with increased histologic findings of chronic rejection and/or interstitial fibrosis and tubular atrophy (IFTA) and clinical findings of reduced graft survival. The clinical response to antirejection therapy appears to be critical in this regard, because the change in renal function from 6 and 12 months after transplant is more predictive of long-term graft survival than the occurrence of prior episodes of acute rejection.[13] Two analyses (one examining the U.S. experience[14] and another examining the Australia–New Zealand experience[15]) have shed light on risk factors for graft loss after episodes of acute rejection. In general, acute T cell–mediated rejection that responds to therapy with return to near-baseline renal function does not portend worse graft survival. However, vascular rejection, late rejection (after 3 months), and rejection that does not respond to within 75% of baseline

serum creatinine are associated with worse graft outcomes. Although acute rejection rates have fallen significantly over the past decade, graft survival rates have not improved in similar fashion; one

explanation for this finding is that the rejection now identified tends to be less responsive to therapy, with fewer patients achieving near-baseline serum creatinine levels. The long-term prognosis after episodes of acute antibody-mediated rejection has not been fully defined in prospective analyses; however, from single-center and retrospective studies it appears that episodes of acute humoral rejection likely affect long-term graft survival. Similarly, the emergence of de novo HLA antibodies at any time after transplant has been shown to be associated with a 5% worse graft survival per year compared with patients who do not form anti-HLA antibodies.[16] For this reason, patients who have experienced episodes of acute rejection must be rigorously monitored with optimization of baseline maintenance immunosuppression. Remaining questions include the value of escalated immunosuppression such as longer-term scheduled antibody therapy, or additional IVIG treatment for those without adequate clinical response or with persistently elevated titers of HLA antibodies.

Summary:

Acute rejection has decreased in incidence over time but remains an important cause of graft dysfunction and progressive graft loss, particularly when antibody-mediated forms of injury are identified. Although many immunosuppressive regimens have been used to minimize both the incidence of rejection and the side effect profile of chronic immunosuppressive agents, the most effective maintenance immunosuppressive regimen for the prevention of rejection is a three-drug regimen consisting of tacrolimus, mycophenolate, and prednisone. Higher-risk patients benefit from induction therapy with lymphocyte depleting agents for the prevention of rejection.

Alternative immunosuppressive strategies may be considered for side effects or toxicities related to immunosuppressive agents, which in clinical practice has led to a myriad of treatment combinations. Until there is an accurate means of determining an individual patient's degree of immune function, suppression, or graft-specific immunity, the clinician must determine the best treatment regimen based on potency (minimizing rejection) and tolerability.

References:

1. Meier-Kriesche HU, Li S, Gruessner RW, et al. Immunosuppression: Evolution in practice and trends, 1994-2004. Am J Transplant. 2006; 6:1111-1131.

2. Solez K, Colvin RB, Racusen LC, et al. Banff 07 classification of renal allograft pathology: Updates and future directions. Am J Transplant. 2008;8:753-760.

3. Jordan ML, Shapiro R, Vivas CA, et al. FK506 "rescue" for resistant rejection of renal allografts under primary cyclosporine immunosuppression. Transplantation. 1994;57:860-865.

4. Humar A, Gillingham K, Kandaswamy R, et al. Steroid avoidance regimens: A comparison of outcomes with maintenance steroids versus continued steroid avoidance in recipients having an acute rejection episode. Am J Transplant. 2007;7:1948-1953.

5. Roberts DM, Jiang SH, Chadban SJ. The treatment of acute antibody-mediated rejection in kidney transplant recipients—a systematic review. Transplantation. 2012;94:775-783.

6. Faguer S, Kamar N, Guilbeaud-Frugier C, et al. Rituximab therapy for acute humoral rejection after kidney transplantation. Transplantation. 2007;83:1277- 1280.

7. Walsh RC, Alloway RR, Girnita AL, Woodle ES. Proteasome inhibitor-based therapy for antibody-mediated rejection. Kidney Int. 2012;81:1067-1074.

8. Stegall MD, Diwan T, Raghavaiah S, et al. Terminal complement inhibition decreases

antibody-mediated rejection in sensitized renal transplant recipients. Am J Transplant. 2011;11:2405-2413.

9. Locke JE, Zachary AA, Haas M, et al. The utility of splenectomy as rescue treatment for severe acute antibody mediated rejection. Am J Transplant. 2007;7:842-846.

10. Theruvath TP, Saidman SL, Mauiyyedi S, et al. Control of antidonor antibody production with tacrolimus and mycophenolate mofetil in renal allograft recipients with chronic rejection. Transplantation. 2001;72:77-83.

11. Matas AJ, Kandaswamy R, Gillingham KJ, et al. Prednisone-free maintenance immunosuppression – a 5- year experience. Am J Transplant. 2005;5:2473- 2478.

12. Bolin P, Tanriover B, Zibari GB, et al. Improvement in 3-month patient-reported gastrointestinal symptoms after conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium in renal transplant patients. Transplantation. 2007;84:1443-1451.

13. Hariharan S, McBride MA, Cherikh WS, et al. Post-transplant renal function in the first year predicts long-term kidney transplant survival. Kidney Int. 2002;62:311-318.

14. Meier-Kriesche HU, Schold JD, Srinivas TR, Kaplan B. Lack of improvement in renal allograft survival despite a marked decrease in acute rejection rates over the most recent era. Am J Transplant. 2004;4:378-383.

15. McDonald S, Russ G, Campbell S, Chadban S. Kidney transplant rejection in Australia and New Zealand: Relationships between rejection and graft outcome. Am J Transplant. 2007;7:1201-1208.

16. Terasaki PI, Ozawa M, Castro R. Four-year follow-up of a prospective trial of HLA and MICA antibodies on kidney graft survival. Am J Transplant. 2007;7:408-415.

Original Article

DCIMCJ 2018 January; 5(1):20-30

Parathyroid Hormone Assay in Total Thyroidectomy - A Predictive Factor for Post Operative Hypocalcaemia

Akram MS[1], Siddiquee BH[2], Uddin MM[3], Kabir ABML[4], Karim A[5], Sarker DK[6]

Abstract:

Objective: To find out PTH as an early predictor for post operative hypocalcaemia following total thyroidectomy by measuring the preoperative PTH value and immediate postoperative PTH value and their percentage decline. Methods: This cross sectional study was carried out in Otolaryngology-Head & Neck Surgery department Bangabandhu Sheikh Mujib Medical University, Dhaka, during the period of January 2013 to March 2014. Patients of both benign and malignant thyroid diseases who underwent total thyroidectomy were enrolled in this study. Pre-operative and 1st hour postoperative PTH levels and Serum calcium (Ca) level of pre operative, after 24 hours and after 48 hours of total thyroidectomy were measured. P-value less than 0.05 were considered statistically significant. To assess the standard value of useful predictive factors, we used receiver operating characteristic (ROC) curves.Results: Most of the patients were in 4th and above decade. Male to female ratio was 1:3.3. Normal (10-65 pg/ml) PTH level was found 100(100.0%) in preoperative patients and below normal (<10 pg/ml) PTH level was found 64(64.0%) in postoperative patients. The mean percentage of decline was found 62.7±24.36. Percentage decline of post operative PTH level area under curve 0.799 with a cut off value ≥70, having 97.4% sensitivity, 73.8% specificity, 83.0% accuracy, 69.6% PPV and 100.0% NPV for prediction of hypocalcaemia at 24 hours post operative day. At 48 hours post operative day area under curve 0.929 with a cut off value ≥70, having 95.7% sensitivity, 81.5% specificity, 90.0% accuracy, 82.1% PPV and 100.0% NPV for prediction of hypocalcaemia. Percentage decline post operative PTH level area under curve 0.582 with a cut off value ≥73.3, having 100.0% sensitivity and 56.1% specificity, 57.0% accuracy, 4.4% PPV and 100% NPV for prediction of symptomatic hypo-calcaemia at 24 hours post operative day. At 48 hours post operative day area under curve 0.936 with a cut off value ≥73, having 88.2% sensitivity and 78.8% specificity, 82.0% accuracy, 68.2% PPV and 92.9% NPV for prediction of symptomatic hypo-calcaemia. Conclusion: Post operative percentage decline of pre-operative PTH can be used as an early predictor for hypocalcaemia following total thyroidectomy because of high sensitivity, specificity, accuracy, positive and negative predictive value.

Keywords: Parathyroid hormone assay, total thyroidectomy, hypocalcaemia

Introduction:

Total thyroidectomy is now the main modality of management for malignant and some benign thyroid common complication after thyroid surgery which may be transient occurring in 10-50% of patients or permanent occurring in 0.5-10.6% of patients.1. The cause of post-operative hypocalcaemia may be due to direct injury to parathyroid glands, haemodilution secondary to surgical stress, urinary calcium excretion, calcitonin release, hungry bone syndrome etc[2].

After thyroid surgery, temporary hypocalcaemia usually develops 24 to 48 hours after surgery which may be symptomatic. Thus, patients have to be observed for this time period prior to discharge in order to prevent development of clinically significant hypocalcaemia[3] and this significantly lengthen hospital stay.

Despite recent development of surgical techniques and every effort of surgeons to preserve as many

1. Dr. Md. Shafiul Akram, Research Officer, National Institute of ENT, Dhaka.
2. Dr. Belayat Hossain Siddiquee, Professor and Chief, Head Neck Surgery Division, Department of Otolaryngology Head & Neck Surgery, BSMMU, Dhaka.
3. Dr. Md. Mosleh Uddin, Associate Professor, Department. of Otolaryngology-Head & Neck Surgery, BSMMU, Dhaka
4. Dr. A.B.M. Luthful Kabir, Research Officer, National institute of ENT, Dhaka.
5. Dr. Abdul Karim, Medical Officer, Sador Hospital, Sherpur.
6. Dr. Dipan Kumar Sarker, Assistent Professor, Department of ENT, Kumudini Women's Medical College.

Correspondence: Dr. Shafiul Akram.
E-mail: akram55.ent@gmail.com

asparathyroid glands as possible, early post-operative hypocalcaemia and hypoparathyroidism still remain a great challenge to surgeons due to lack of reliable parameters to predict the occurrence. So, prediction of hypocalcaemia after total thyroidectomy is important for early treatment in order to avoid troublesome symptoms and to ensure safe discharge.

Measuring of plasma calcium levels just after thyroid surgery is of little value in predicting the onset of subsequent hypocalcaemia or symptoms because of its relative slow decline. But since the half life of the parathyroid hormone in serum is less than 5 minutes, early PTH monitoring after thyroid surgery may be a good predictor to measure post-operative hypocalcaemia, as it identifies the patients at risk for post-operative hypoparathyroidism.

Many studies have tried to predict post-operative hypocalcaemia. Post-operative serum calcium, post-operative intact PTH (iPTH), pre-operative serum calcium, presence of hyperthyroidism, advanced age of the patient, parathyroid preservation, and size of goiter at surgery have all been implicated in the development of post total thyroidectomy hypocalcemia[4]. Measurement of total serum calcium is less expensive but it may be inaccurate because of post-operative haemodilution and it poorly predicts symptomatic hypocalcaemia[5]. In most of the studies, to predict post thyroidectomy hypocalcaemia, the use of post-operative serum PTH was recommended with a sensitivity ranging from 64% to 100% and a specificity ranging from 72% to 100%.6 Few studies reported that percentage decline of the pre-operative PTH level in the immediate post-operative period was useful to predict hypoparathyroidism.In a study it was showed that pre-operative to 10 minutes post-operative PTH percent change, patients with a greater than 75% decrease are likely to have hypocalcemia, with a sensitivity of 100%.[7]

The most common cause of significant hypoparathyroidism is surgical trauma to parathyroid gland. As to the best management of this complication, finding a simple and reliable method to predict which patients may show hypocalcaemia could decrease patients discomfort as well as hospital stay and also treatment cost associated with total thyroidectomy.

The purpose of this study is to evaluate whether PTH percentage decline (the relative difference between PTH values before and after excision) are reliable markers to identify those patients with the risk of developing hypocalcaemia. It may help in identification, prevention and treatment of hypocalcaemia in patients after total thyroidectomy.

Objectives:

General objective:

To find out PTH as an early predictor for post-operative hypocalcaemia following total thyroidectomy.

Specific objectives:

- To observe the demographic characteristics of patients with Thyroid disease.
- To measure pre-operative and post-operative serum PTH level and post-operative serum PTH percentage decline of all the selected patients.
- To measure serum calcium level at pre-operative, after 24 hours & 48 hours for all the selected patients.

Materials and Methods:

Place of the study: Department of Otolaryngology-Head & Neck Surgery, BSMMU, Dhaka.

Period of the study: From January 2013 to March 2014

Study population: Patients of both sexes who underwent total thyroidectomy in the Otolaryngology Department of BSMMU, Dhaka were enrolled in this study.

Study design: Cross sectional study.

Sample size: 100
Sampling technique: Purposive sampling.

Selection criteria:

Inclusion Criteria

Patients of both benign and malignant thyroid disease who underwent total thyroidectomy irrespective of age and sex

Exclusion Criteria:

1. Patients with pre-operative hypocalcaemia.
2. Patient with history of parathyroid disease.
3. Patients with the history of radiation in head-neck region.

Study procedure:

After taking history, study subjects were selected according inclusion criteria and planned for total or completion thyroidectomy. Pre-operatively 5cc blood was taken for serum PTH & serum calcium level measurement. Then post-operatively (1 hour after removal of thyroid gland) 5cc blood was taken for serum PTH level measurement. After 24 hours and 48 hours of total thyroidectomy 3cc blood sample were collected respectively for serum calcium level measurement. All biochemical tests were done in Department of Biochemistry, BSMMU. Post-operative percentage decline of PTH was calculated by using the formula:

$$\frac{PTH_1 - PTH_2}{PTH_1} \times 100$$

PTH1= Pre-operative PTH level

PTH2= Post-operative 1st hour PTH level

Statistical Analysis:

Statistical analysis of the results was obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-20).

The results were presented in tables, figures, diagrams. Unpaired t-test and paired t-test were used to analyze the continuous variable. Receiver-operator characteristic (ROC) analysis and test of validity were performed. P value of <0.05 was considered as significant.

Results:

Table I: Distribution of the study patients by demographic variable (N=100).

Parameter	Number of patients	Percentage
Age (years)		
11 - 20	4	4.0
21 - 30	22	22.0
31 - 40	33	33.0
41 - 50	25	25.0
51 - 60	12	12.0
61 - 70	4	4.0
Mean ± SD	39.5±11.47	
Range (min-max)	(16-65)	
Sex		
Male	23	23.0
Female	77	77.0
Ratio	1:3.3	

In this study population, the mean age of patients was 39.5±11.47 years, with age range from 16 to 65 years and female was predominant with a ratio of Male : Female was 1:3.3

Table II: Mean distribution of PTH level according to pre and post-operative follow up (n=100)

	PTH level (pg/ml)			P value
	Mean	±SD	Range (min, max)	
Preoperative	28.4±14.53		10.6 , 65.3	0.001s
Post operative	10.98±10.52		3.1 , 53.6	

Mean PTH level was significantly higher in pre operative patients.

Table III: Distribution of the patients PTH level according to pre and post-operative follow up

PTH level (pg/ml)	Pre-operative PTH		Post-operative PTH	
	n	%	n	%
Below normal (<10 pg/ml)	0	0.0	64	64.0
Normal (10-65 pg/ml)	100	100.0	36	36.0

Most of patient had below normal (<10 pg/ml) PTH level in post-operative period.

Table IV: Serum calcium level according to pre and 24 hrs post-operative calcium level (n=100)

S. calcium (mg/dl)	Pre-operative calcium		24 hrs Post-operative calcium		P-value
	n	%	n	%	
Hypo-calcaemia	0	0.0	39	39.0	
Normal	100	100.0	61	61.0	
Mean±SD	11.37	±9.49	9.16	±0.99	0.023s
Range (min-max)	9	-10.6	7.9	-11.7	

Serum calcium level was significantly ($p<0.05$) decreased in 24 hrs post-operative calcium level.

Table V: Serum calcium level according to pre and 48 hrs post-operative calcium level (n=100)

S. calcium (mg/dl)	Pre-calcium		48 hrs Post-operative calcium		P-value
	n	%	n	%	
Hypo-calcaemia	0	0.0	46	46.0	
Normal	100	100.0	54	54.0	
Mean±SD	11.37	±9.49	8.74	±1.14	0.007s
Range (min-max)	9	-10.6	6.5	-11.1	

Serum calcium level was significantly ($p<0.05$) decreased in 48 hrs post-operative calcium level.

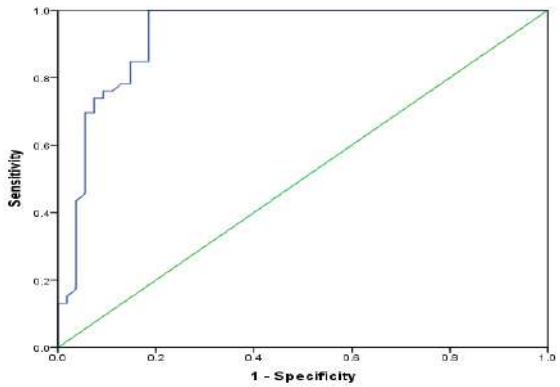


Figure-I: Receiver-operator characteristic (ROC) curve of percentage decline /post-operative PTH level for prediction of hypocalcaemia at 24 hours post-operative day.

Table VI: Receiver-operator characteristic (ROC) curve of percentage decline of post-operative PTH level for prediction of hypocalcaemia at 24 hours post-operative day

	Cut of value	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	Area under the ROC curve	95% Confidence interval (CI)	
								Lower bound	Upper bound
Hypocalcaemia	≥10	100.0	8.2	44.0	41.1	100.0	0.799	0.709	0.890
Hypocalcaemia	≥20	100.0	14.8	48.0	42.9	100.0	0.799	0.709	0.890
Hypocalcaemia	≥30	100.0	21.3	52.0	44.8	100.0	0.799	0.709	0.890
Hypocalcaemia	≥40	100.0	34.4	61.0	50.0	100.0	0.799	0.709	0.890
Hypocalcaemia	≥50	100.0	74.5	69.0	55.7	100.0	0.799	0.709	0.890
Hypocalcaemia	≥60	100.0	59.0	76.0	61.9	100.0	0.799	0.709	0.890
Hypocalcaemia	≥70	97.4	73.8	83.0	69.6	100.0	0.799	0.709	0.890
Hypocalcaemia	≥80	35.9	78.7	62.0	51.9	65.8	0.799	0.709	0.890
Hypocalcaemia	≥90	10.3	99.7	62.0	60.0	62.1	0.799	0.709	0.890

Based on the receiver-operator characteristic (ROC) curves percentage decline of post-operative PTH level had area under curve 0.799.

Table VII: Serum calcium status at 24 hrs post-operative day with percentage of decline (n=100)

Percentage of decline	Hypo-calcaemia (n=39)		Normal calcaemia (n=61)		P-value
	n	%	n	%	
≥70	39	100.0	17	27.9	
<70	0	0.0	44	72.1	
Mean±SD	78.68±7.41		52.48±25.92		0.001s
Range (min, max)	(70.5, 95.3)		(2.6, 92.9)		

Percentage decline of PTH level was significantly ($p<0.05$) lower in normal calcaemia group than hypo-calcaemia group

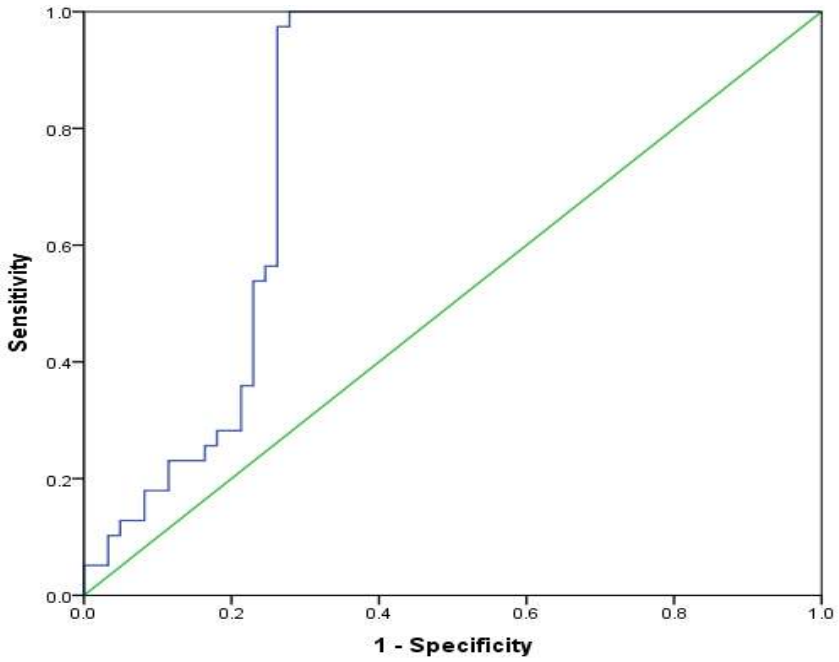


Figure 2: Receiver-operator characteristic (ROC) curve of percentage decline of post-operative PTH level for prediction of hypocalcaemia at 48 hours post-operative day.

Table VIII: Receiver-operator characteristic (ROC) curve of percentage decline of post-operative PTH level for prediction of hypocalcaemia at 48 hours post-operative day

	Cut of value	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	Area under the ROC curve	95% Confidence interval (CI)	
								Lower bound	Upper bound
Hypocalcaemia	≥10	100.0	9.7	51.0	48.4	100.0	0.929	0.877	0.982
Hypocalcaemia	≥20	100.0	16.7	55.0	50.5	100.0	0.929	0.877	0.982
Hypocalcaemia	≥30	100.0	24.1	60.0	53.5	100.0	0.929	0.877	0.982
Hypocalcaemia	≥40	100.0	38.9	68.0	59.0	100.0	0.929	0.877	0.982
Hypocalcaemia	≥50	100.0	53.7	76.0	65.7	100.0	0.929	0.877	0.982
Hypocalcaemia	≥60	100.0	66.7	83.0	73.0	100.0	0.929	0.877	0.982
Hypocalcaemia	≥70	95.7	81.5	90.0	82.1	100.0	0.929	0.877	0.982
Hypocalcaemia	≥80	52.2	99.4	75.0	88.9	69.9	0.929	0.877	0.982
Hypocalcaemia	≥90	13.0	100.0	59.0	100.0	56.8	0.929	0.877	0.982

Based on the receiver-operator characteristic (ROC) curves percentage decline of post- operative PTH level had area under curve 0.929.

Table IX: Serum calcium status at 48 hrs post-operative day with percentage of decline (n=100)

Percentage of decline	Hypo-calcaemia (N=46)		Normal calcaemia (N=54)		P value
	n	%	n	%	
≥70	46	100.0	10	18.5	
<70	0	0.0	44	81.5	
Mean±SD	80.98	±7.58	47.12	±22.85	0.001s
Range (min, max)	(70.5	, 95.3)	(2.6	, 89.7)	

Percentage decline of PTH level was significantly ($p<0.05$) lower in normal calcaemia group than hypo-calcaemia group.

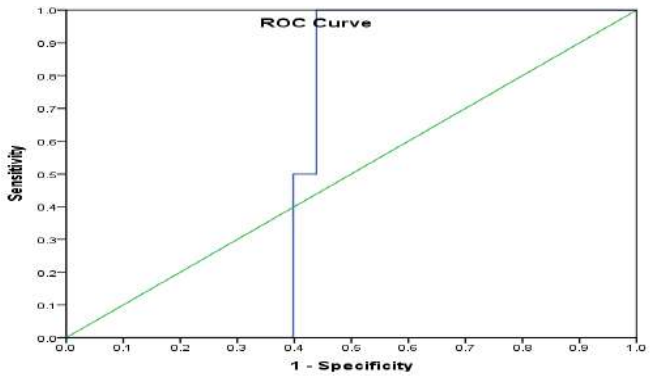


Figure 3: Receiver-operator characteristic (ROC) curve of percentage decline of post-operative PTH level for prediction of symptomatic at 24 hours post-operative day.

Table X: Receiver-operator characteristic (ROC) curve of percentage decline of post-operative PTH level for prediction of symptomatic at 24 hours post-operative day

	Cut of value	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	Area under the ROC curve	95% Confidence interval (CI)	
								Lower bound	Upper bound
Symptomatic	≥70	100.0	44.9	47.0	3.6	100.0	0.582	0.481	0.682
Symptomatic	≥71	100.0	49.0	51.0	3.6	100.0	0.582	0.481	0.682
Symptomatic	≥72	100.0	51.0	52.0	4.0	100.0	0.582	0.481	0.682
Symptomatic	≥73.3	100.0	56.1	57.0	4.4	100.0	0.582	0.481	0.682
Symptomatic	≥74	50.0	60.2	60.0	2.5	98.3	0.582	0.481	0.682
Symptomatic	≥75	00	66.3	66.0	0.0	97.1	0.582	0.481	0.682

Based on the receiver-operator characteristic (ROC) curves percentage decline of post-operative PTH level had area under curve 0.582.

Discussion:

This study was carried out with an aim to measure pre-operative, Post-operative serum PTH level, post-operative serum PTH percentage decline, serum calcium level at pre-operative, 24 hours & 48 hours after thyroidectomy. This study is also to compare the percentage decline of immediate post-operative PTH between the patients of hypocalcaemia and normocalcaemia during 1st post-operative day and 2nd post-operative day and to determine the cutoff value of percentage decline of immediate post-

operative PTH for early prediction of hypocalcaemia following total thyroidectomy.

In this study population of 100 cases, majority (33.3%) of the patients with total thyroidectomy were in 4th decade. The mean age of the patients was 39.5±11.47 years, varied from 16 to 65 years. Similar observation was found in a series with total thyroidectomy ages ranged varied from 15 to 74 years, with an average age of 42 years[2]. In this current study it was observed that male and female patients were 23.0% and 77.0% respectively and male to female ratio was 1:3.3, which indicates that total thyroidectomy is mostly done in female subjects. Similarly, 82.8% females underwent total or near total thyroidectomy were found in another study[8].

In this series, pre-operative mean PTH level was 28.4±14.53 pg/ml and post-operative level was 10.98±10.52 pg/ml. The mean PTH level was significantly (P<0.05) declined in post-operative period with compared to pre-operative period. Another study showed the mean PTH was 96.23 ± 53.54 pg/ml before surgery and 63.82±37.13 pg/ml after surgery,8 difference was statistically significant (p<0.05), which is consistent with the current study.

In this present study it was observed that below normal PTH level was found 64(64.0%) at post-operative period and not found in pre-operative period. Normal PTH level was found 100(100.0%) in pre-operative patients and 36(36.0%) in post-operative period which is comparable to another study[9].

In this series it was observed that hypo-calcaemia was found 39.0% in 24 hrs post-operative calcium level. The mean serum calcium was found 11.37±9.49 mg/dl in pre-operative calcium level and 9.16±0.99 mg/dl in 24 hrs post-operative calcium level. Serum calcium level was significantly (p<0.05) decreased in 24 hrs post-operative period with compared to pre-operative period. Another study revealed that 47.5% developed hypocalcaemia after total thyroidectomy and mean serum calcium level of patients before operation was 9.06±0.47 mg/dl and after operation became 8.35±0.61 mg/dl (p<0.05).8 Calcium level after surgery in hypocalcaemic in comparison to normocalcaemic patients was statistically significant (p<0.05), which is consistent with the current study.

In this present study it was observed that hypo-calcaemia was found 46.0% in 48 hrs post-operative period. The mean serum calcium was found 11.37±9.49 mg/dl in pre-operative calcium level and 8.74±1.14 mg/dl in 48 hrs post-operative calcium level. Serum calcium level was significantly (p<0.05) decreased in 48 hrs post-operative period. The mean serum calcium in post-operative day 2 was 7.8 ± 0.5 mg/dl in hypocalcaemic and 8.8 ± 0.5 mg/dl in normocalcaemic was found in another study, which is comparable with the current study[10].

The percentage of PTH drop is an important predictor for hypocalcaemia. In this current study based on the receiver-operator characteristic (ROC) curves percentage decline of post-operative PTH level had area under curve 0.799 with a cut off value ≥70, having 97.4% sensitivity, 73.8% specificity, 83.0% accuracy, 69.6% PPV and 100.0% NPV for prediction of hypocalcaemia at 24 hours post-operative day which is comparable to another study[11]. Therefore, the percentage of drop can be a more appropriate index for determining the risk of hypocalcaemia.

In this current study it was observed 39(100.0%) patients had hypo-calcaemia and all of them had ≥70 percentage decline of PTH level in 24 hours post-operatively. Normo calcaemia was found in 61 patients among them 44(72.1%) had <70 percentage decline of PTH level. The mean serum percentage decline of PTH level was found 78.68±7.41 in hypo-calcaemia group and 52.48±25.92 in normal calcaemia group. Percentage of decline was significantly (p<0.05) higher in hypo-calcaemic patients with compared to normo-calcaemic patients. On the other hand it was observed 46(100.0%)

patients had hypo-calcaemia at 48 hrs post-operative day and all of them had ≥70 percentage decline of PTH level. Normal calcaemia was found in 54 patients among them 44(81.5%) had <70 percentage decline of PTH level. Mean serum percentage decline of PTH level was found 80.98±7.58% in hypo-calcaemia group and 47.12±22.85% in normal calcaemia group. Percentage decline of PTH level was significantly ($p<0.05$) higheh in hypo-calcaemia group with compared to normal calcaemia group. In a study reported that a >75% decline of iPTH during the operation correlates with the development of post-operative hypocalcemia. However, the overall accuracy of these methods was only 75%, which supports the present study[7].

In this study based on the receiver-operator characteristic (ROC) curves percentage decline post-operative PTH level had area under curve 0.929 with a cut off value ≥70 having 95.7% sensitivity and 81.5% specificity, 90.0% accuracy, 82.1% PPV and 100.0% NPV for prediction of hypocalcaemia at 48 hours post-operative day which is similar to another study[7].

In this series based on the receiver-operator characteristic (ROC) curves percentage decline post-operative PTH level had area under curve 0.582 with a cut off value ≥73.3, having 100.0% sensitivity and 56.1% specificity, 57.0% accuracy, 4.4% PPV and 100% NPV for prediction of symptomatic hypocalcaemia at 24 hours post-operative day. Similarly at 48 hours post-operative day in this series based on the receiver-operator characteristic (ROC) curves percentage decline of post-operative PTH level had area under curve 0. 936 with a cut off value ≥73, having with 88.2% sensitivity and 78.8% specificity, 82.0% accuracy, 68.2% PPV and 92.9% NPV for prediction of symptomatic hypocalcaemia. Another study showed for diagnosis symptomatic hypocalcaemia, 62% PTH drop had sensitivity and specificity is 83.33% and 90.80% respectively and 55.6% PPV and 97.5% negative predictive value (NPV)[8].

Conclusion:

Post-operative hypocalcaemia remains a challenge to surgeons despite advances in surgical techniques and surgeons' efforts to identify and preserve all parathyroid glands during thyroid surgery. A standardized PTH protocol for the prediction of hypocalcemia following total thyroidectomy or completion thyroidectomy is highly efficacious. By using immediate (1 hour) post-operative PTH percentage decline to determine hypocalcaemia, earlier interventions can be made. It will allow us to initiate calcium supplementation instead of waiting for patients to become symptomatic and easy discharge of patients. Because of high sensitivity, specificity, accuracy positive and negative predictive value, the percentage decline of PTH level ≥70% as cut off point from pre-operative to immediate post-operative period can be used as an early predictor for post-operative hypocalcaemia following total thyroidectomy.

References:

1. Le TN, Kerr PD, Sutherland DE, Lambert P. Validation of 1- hour post thyroidectomy parathyroid hormone level in predicting hypocalcaemia. Journal of Otolaryngology-Head and Neck Surgery. 2014; 43: 5.

2. Abboud B, Sargi Z, Akkam M, Sieilary F. Risk factors for postthyroidectomy hypocalcemia. Journal of American College of Surgeons. 2002; 195: 456-61.

3. Sarkar A, Jana S, Basak B, Gayen GC, Sit S, Sarkar A. Evaluation of clinically significant hypocalcaemia after total thyroidectomy: A prospective study. International Journal of Current Research and Review. 2014; 6: 5-8.

4. Pradeep PV, Ramalingam K, Jayashree B. Post total thyroidectomy hypocalcemia: A novel multi-factorial scoring system to enable its prediction to facilitate an early discharge. Journal of Postgraduate Medicine. 2013; 59: 4-8.

5. Lindblom P, Westerdahl J, Bergenfelz A. 'Low parathyroid hormone levels after thyroid surgery: a feasible predictor of hypocalcemia'. Surgery. 2002; 131: 515-20.

6. Kwon YH, Lee KE, Kwon, H Choi JY, Koo DH, Kim E, Youn YK. Pre-operative parathyroid hormone level as a predictive factor for post-thyroidectomy hypoparathyroidism. Korean Journal of Clinical Oncology. 2013; 9: 28-32.

7. Lo CY, Luk JM, Tam SC. Applicability of intraoperative parathyroid hormone assay during thyroidectomy. Annals of Surgery. 2002; 236: 564-9.

8. Mehrvarz S, Mohebbi HA, Motamedi KMH, Khatami SM, Rezaie R, Rasouli HR. Parathyroid hormone Journal of measurement in prediction of hypocalcaemia following thyroidectomy. measurement in prediction of hypocalcaemia following thyroidectomy. the College of Physicians and Surgeons-Pakistan. 2014; 24: 82-7.

9. Islam MS, Sultana T, Paul D, Huq AH, Chowdhury AA, Ferdous C, Ahmed AN. Intraoperative serum parathyroid hormone level is an indicator of hypocalcaemia in total thyroidectomy patients. Bangladesh Medical Research Council Bulletin. 2012; 38: 84-9.

10. Lombardi CP, Raffaelli M, Princi P, Santini S, Boscherini M, De Crea C, Traini E, D'Amore AM. Carrozza C, Zuppi C, Bellantone R. Early prediction of postthyroidectomy hypocalcemia by one single iPTH measurement'. Surgery. 2004;136: 1236-41.

11. Sands N, Young J, MacNamara E, Black MJ, Tamilia M, Hier MP, Payne RJ. Pre-operative Parathyroid Hormone Levels as a Predictor of Postthyroidectomy Hypocalcemia. Otolaryngology - Head and Neck Surgery. 2011; 144: 518.

DCIMC

Original Article

DCIMCJ 2018 January; 5(1):31-35

Clinico Haematological Parameters and Evaluation of Risk Factors of Acquired Aplastic Anaemia Patients Admitted in a Tertiary Care Hospital

Kamruzzaman AKM[1], Nurunnobi AKM [2], Siraj S[3], Ali L[4]

Abstract:

Aplastic anaemia is an often life threatening disorder of multiple etiologies which is characterized by pancytopenia and hypo cellular bone marrow. Acquired aplastic anaemia is the most common variety, probably of an autoimmune etiology. Acquired aplastic anaemia is rare disease which results in morbidity and mortality at a young age. Most cases are classified as idiopathic as no etiological agent can be identified. The incidence of aplastic anaemia shows geographical variability. Incidence varied from 10- 52.7% among patients with pancytopenia. Aim of the study is to find out clinical presentation, hematological parameters, severity and risk factors of aplastic anaemia. Total 50 patients of aplastic anaemia were included in this study. Majority patients (50%) were 15- 30 years age. Male (68%) were more affected than female(32%).Majority patients(90%) exposed to pesticides and insecticides, 50% patients were tobacco users, 06% were Hepatitis B surface antigen positive. Most of the patients were farmer (32%), house wife (30%) and chemical workers (12%). Non severe aplastic anaemia were 50%, severe aplastic anaemia were 40% and very severe aplastic anaemia were 10%. Main clinical findings were weakness (100%), bleeding (64%) and fever (56%). Laboratory findings of the patients were Mean Hb- 7.3gm/dl, Total leukocyte count- 3.7x10^9/L, Absolute Neutrophils count -0.94x10^9/L, Platelet count- 21.9x10^9/L and reticulocyte count- 1%.

Keywords: Aplastic anaemia, hematological parameters, severity, risk factors

Introduction:

Acquired aplastic anaemia is an unusual form of marrow failure with pancytopenia and a hypo cellular bone marrow. The annual incidence of aplastic anaemia in Europe was established in a large international study at 2 to 4 per million. The incidence in Thailand is 4 per million. Men and women are equally affected. At least two thirds of patients, no etiological agent can be identified. The widely accepted criteria for severe aplastic anaemia (SAA) are: absolute Neutrophils count (ANC) below 1.0x10^9/L, platelet count below 20x10^9/L, reticulocyte count below 0.1 percent and less than 20% cellularity of bone marrow[1]. Acquired aplastic anaemia is rare disease which results in morbidity and mortality at a young age. Aplastic anaemia (AA) most commonly presents between 15 – 25 years age but there is a second peak in incidence after 60 years. Most cases are classified as idiopathic as no etiological agent can be identified. Nonetheless, several factors are associated with increased risk. Aplastic anaemia has been etiologically associated with chemicals such as pesticides, benzene and drugs especially choramphenicol. Five to ten percent of cases of aplastic anaemia follow an episode of hepatitis[2].

1. Dr. A.K.M Kamruzzaman**,** Associate Professor & Head, Depertment of Haematology, Rangpur Medical College.

2. Dr. AKM Nurunnobi**,** Professor and Head, Depertment of Dermatology and Venereology, Rangpur Medical College.

3. Dr. Sayada Siraj, Assistant Professor, Depertment of Physiology, Rangpur Medical College.

4. Dr. Md. Liakat Ali, Indoor Medical Officer, Depertment of Medicine, Rangpur Medical College.

Correspondence: Dr. A.K.M Kamruzzaman
E-mail: kamrulrpmc @gmail.com

Acquired aplastic anaemia is classified as

1) Non severe aplastic anaemia-Bone marrow cellularity is <25% plus two out of three of the following:
    - Hemoglobin <10 gm/l
    - Neutrophils count<$1.5x10^9$/L
    - Platelet count<$100x10^9$/L
2) Severe Aplastic anaemia(SAA)- Bone marrow cellularity is <25% plus two out of three of the following:
    - Neutrophil count<$0.5x10^9$/L
    - Platelet count<$20x10^9$/L
    - Absolute reticulocyte count<$20x10^9$/L or below 0.1%.
3) Very severe Aplastic anaemia(VSAA): As for severe aplastic anaemia but Neutrophil count<$0.2x10^9$/L^2.

The incidence of AA is higher in Asia than in West. It appears to be 2 to 3 fold more common in Asia than in Europe[3]. Aplastic anaemia affects people of all ages and all races. Pathogenesis of acquired AA is now believed to be immune mediated, with active destruction of haemopoietic stem cells by lymphocytes, with activated type 1 cytotoxic T cells implicated[4]. Despite the precision of its diagnostic criteria, aplastic anaemia has always been a diagnosis of exclusion. No single test allows us to reliably diagnose idiopathic aplastic anaemia[5]. There is also association of the increased incidence of aplastic anaemia with low socio- economical background[6]. Aplastic anaemia was attributed to an idiosyncratic reaction to drug or chemical exposure[7]. All patients usually present with symptoms of anaemia, petechaie, bruises, mucosal bleeds and fever underwent a detailed clinical examination for the presence of pallor, petechiae, purpura and fever[8]. The treatment of this disease consists of supportive therapy with blood products and finally phases, where there are two possibilities: immunosuppressive therapy and bone marrow transplantation[9]. The study was carried out by clinical history, physical examination and basic laboratory investigations including Hemoglobin%, Total Leucocytes count and differential counts, platelet count, reticulocyte count, peripheral blood film and bone marrow aspiration in all patients. Liver function test and screening for hepatitis B, C was undertaken in every patient.

Objective:

To find out the clinical features, hematological parameters, severity and risk factors of acquired aplastiic anaemia.

Material and Methods:

This cross-sectional, observational study was conducted at the department of Haematology and Medicine in Rangpur Medical College, Bangladesh from July 2016 to June 2017. A total 50 consecutive diagnosed patient were included in the study. Data were collected in a preformed questionnaire. Complete blood counts, reticulocyte count and bone marrow examination were performed. Data were analyzed using SPSS version 20.

Inclusion criteria:

1. Age >10 years
2. Both sexes
3. Who given consent.

Exclusion criteria:

1. Age <10 years
2. Incomplete data
3. Who did not give consent
4. Inherited aplastic anaemia
5. Pregnant women

Results:

Total 50 cases of diagnosed aplastic anaemia patients were included in this study. The youngest patient was 12 and oldest 70 years. In the group upto 30 years there were 25(50%) patients. In the group 31 -45 years there were 14(28%) patients. In the group 46 – 60

years there were 09(18%) patients and in the group 61 -70 years 02(4%). Male (68%) were more than female (32%). M: F ratio 2.1:1.

Out of 50 patients 25(50%) were Non severe aplastic anaemia, 20(40%) were severe aplastic anaemia and 05(10%) were very severe aplastic anaemia. 45(90%) patients were exposed to pesticides and insecticides, 25(50%) were tobacco users, 03(6%) were Hepatitis B surface antigen positive. Occupation of the patients shows farmer 32%, house wife 30%, chemical worker 12%, students 10%, and day labor 10%.

On clinical features weakness was 100%, bleeding 64%, fever 56% and pallor 100%.

Laboratory findings of the patients were Mean Hb-7.3gm/dl, Total leukocyte count- $3.7x10^9$/L, Absolute Neutrophils count -$0.94x10^9$/L, Platelet count-$21.9x10^9$/L and reticulocyte count- 1%

Table 1: Age distribution of the respondents (N=50)

Age group	Number	Percentages
12-30	25	50
31-45	14	28
46-60	09	18
61-75	02	04
Total	50	100

Table 2: Sex distribution of the respondents (N=50)

Variables	Number	Percentages
Male	34	68
Female	16	32
Total	50	100

Table 3: Risk factors of the respondents (N=50)

Risk factors	Number	Percentage
Smoking and smokeless tobacco	25	50
Pesticides	45	90
H/O HBV infection	03	06
Chemical worker	06	12

Table 4: Clinical presentations of the respondents (N=50)

Variables	Numbers	Percentage
Fever	28	56%
Bleeding	32	64%
Weakness	50	100%

Table 5: Severity of aplastic anaemia (N=50)

	Numbers	Percentage
Non severe AA(NSAA)	25	50
Severe AA(SAA)	20	40
Very severe AA(VSAA)	05	10
Total	50	100

Table 6: Haematological parameters of respondents (N=50)

Variables	Mean
Hb conc.(gm/dl)	7.3 gm/dl
Total Leukocyte count	$3.7x10^9$ /L
Absolute Neutrophils count	$0.94x10^9$ /L
Platelet count	$21.9x10^9$ /L
Reticulocyte count	1%

Discussion:

In many parts of the world increasing number of aplastic anaemia had been reported. This may be due to more accurate diagnosis or may be true increase in the incidence of aplastic anaemia.

In this study 50 cases of aplastic anaemia were included. Majority of the patients (50%) were 12- 30 years age, 28% were 31- 45 years, 18% were 46 -60 years, 4% were 61 -70 years. This is not similar to the study done by Milosevic et al who showed 48% were 12- 30 years, 12% were 31- 45 years, 12% were 46-60 years and 28% were 61- 70 years [9].

Male were 68% and female were 32%. M: F 2.1:1. This is almost similar to the study carried out by Ehsan et al[2] who showed male 59.8%, female 40.2% and M:F 1.48:1.

Our study shows 90% patient had history of exposure to pesticides and insecticides which was higher than the study done by Ehsan et al[2] who showed 12.1% and Issaragrisil et al[10] who showed 12%.

12% patients were exposed to chemicals in this study which was lower than the study done by Issaragrisil, Kaufman and Young who showed 70%[10].

06% patients were Hepatitis B surface antigen positive in our study which is similar to the study done by Ehsan et al who found 06%[2].

On severity this study shows 50% were non severe aplastic anaemia (NSAA), 40% severe aplastic anaemia (SAA) and 10% very severe aplastic anaemia (VSAA) which was reversed than the study done by Milosevic et al[9] who showed 14.3% NSAA, 64.3% SAA, 21.4% VSAA and Mahapatra et al[3] Singh, Mishra, Saxena who showed 10% NSAA, 75% SAA, 15% VSAA.

Clinical features of the patients in this study shows weakness 100%, bleeding 64%, fever 56% which was almost similar to the study done by Milosevic et al[9] who found weakness 100%, bleeding 79%, fever 36% and Mahapatra et al[3] who showed weakness 97%, bleeding 69.6%, fever 54%. Laboratory findings of the patients were Mean Hb- 7.3gm/dl, Total leukocyte count- $3.7x10^9$/L, Absolute Neutrophils count -$0.94x10^9$/L, Platelet count- $21.9x10^9$/L and reticulocyte count- 1% which was almost similar to the study done by Shetty et al[8] who found Hb-5.1gm/dl, Total leukocyte count- $3.2x10^9$/L, Absolute Neutrophils count -$1.06x10^9$/L, Platelet count- $23.2x10^9$/L and reticulocyte count- 0.5%.

Conclusion:

Aplastic anaemia is a serious, relatively rare illness, has a high morbidity and is associated with significant mortality. Majority of the patients were 12- 30 years age. Male were more affected than female. Most of the patients exposed to pesticides, insecticides and 50% were tobacco users. Hepatitis B surface antigen was positive in 6% patients. Non severe aplastic anaemia (NSAA) was predominant type. Pallor and bleeding were more common clinical features. Despite many studies conducted on aplastic anaemia, the causative factors of aplastic anaemia remain unclear. So in conclusion our study shows that patients with more exposed to pesticides, insecticides and tobacco users may be at high risk of developing aplastic anaemia.

Recommendation:

In this study as work was carried out in a short period of time with a small number of cases, a long term comprehensive study with a large number of cases should be carried out to identify the true incidence of aplastic anaemia and the etiologic factors.

Reference:

1. Lee HK. Aplastic Anaemia. The HONG KONG Medical Diary 2011; 16(3):15- 17.

2. Ehsan A, Riaz Shah S A, Ibrahim T. Epidemiology of acquired aplastic anaemia in Pakistan. J Ayub Med Coll Abbottabad 2011; 23(1):102- 105.

3. Mahapatra M, Singh PK, Mishra P, Saxena R. Epidemiology, Clinico-Haematological profile and management of aplastic anaemia: AIIMS experience. Supplement to Journal of the association of Physicians of INDIA 2015: 30-35.

4. Melinkeri SR. Epidemiology, pathogenesis and diagnosis of aplastic anaemia. Supplement to Journal of the association of Physicians of India 2015: 8- 12.

5. Guinan EC. Diagnosis and management of aplastic anaemia. American Society of Haematology 2011:76- 81.

6. Yong ASM, Goh AS, Menon J. Epidemiology of Aplastic anaemia in the state of Sabah, Malaysia. Med J Malaysia 1998; 53(1):59- 62.

7. Young NS, Scheinberg P, Cal ado RT. Aplastic anaemia. Curr Opin Hematol. 2008; 15(3):162-168.

8. Shetty M, Adiraju KP, Modugu N R. Study of Aplastic anaemia with Cyclosporine in resource poor setting. Journal of clinical and diagnostic research 2016; 10(6):15- 18.

9. Milosevic R, Jankovic G, Colovic M. Aplastic anaemia–clinical characteristics and survival analysis. Srp Arh Celok Lek.1998;126(7-8):234-8.

10. Issaragrisil S, Kaufman DW, Young NS. The epidemiology of aplastic anaemia in Thailand. Blood 2006; 107(4):1299- 1307.

Original Article

DCIMCJ 2018 January; 5(1):36-46

Outcome of Lateral Pancreaticojejunostomy in 362 Patients Presenting with Pancreatic Stones, Performed in Tertiary Referral Centres of Dhaka, Bangladesh

Rabbi H[1], Rashid MM[2], Hakim HAN[3], Ahmed AHMT[4], Chowdhury AQ[5], Sarder MM[6], Raihan HMS[7], Nayeem SR[8], Ali M[9]

Abstract:

Background: Chronic pancreatitis is a persistently occurring inflammatory disease that causes pancreatic duct stones or calcification, stricture, dilatation of pancreatic duct and irreversible morphological changes resulting intractable pain and losses of exocrine and endocrine function. Appropriate management protocol recognizing underlying pathology, can prevent complications and improves the quality of life. Methods: The retrospective observational study was carried out on 362 patients of pancreatic stone diseases, surgically treated by Lateral Pancreaticojejunostomy following Pancreatolithotomy. Result: Most of our patients were in 3rd decade of life 163 (45.02%), 91 patients (25.13%) between 21-30 yrs age group and 156 male and 206 female. 281 (77.62%) patients presented with diabetes. Steatorrhoea was noted in 126 patients (34.80%), Malnutrition in 199 patients (54.97%) and jaundice in 08 patients (2.20%). Pancreatolithotomy with standard Roux-en-Y Longitudinal/ lateral Pancreaticojejunostomy was the procedure of choice for ductal decompression. Visual Analog Scale (VAS) was used for scoring pain. In our series we found that good pain relief was achieved only in 196 cases (54.14%) and 69 patients (19.06%) with moderate pain control. Postoperative morbidity was noted in 20.24 % cases, but there was no anastomotic leakage or mortality in the immediate postoperative period in our series. Conclusion: Pain is the predominant clinical feature in chronic pancreatitis sometimes difficult to control. Correction of diabetes, malnutrition & weight gain is a major challenge. This study revealed, adequate ductal clearance with wide pancreato-jejunal anastomosis is key to better pain control, improves quality of life and prevents recurrence.

Keywords: Pancreatolithiasis, Lateral Pancreaticojejunostomy

Introduction:

Chronic Pancreatitis is a disease of remission and relapse. It is a persistently occurring inflammatory disease that causes pancreatic duct stones or calcification, stricture, dilatation of pancreatic duct and irreversible morphological changes resulting endocrine function. Most patients suffer for years, has high burden of morbidity due to prolong duration of disease with recurrent attacks. Pancreatolithiasis is most prevalent and almost exclusively occurs in the developing countries of the tropical world, with younger age at onset. It is associated with multiple intraductal calculi, accelerated course of disease leading to varying degrees of malnutrition and uncontrolled glycemic status[1–4]. Incidence of pancreatolithiasis is less than 1% and 90% patients of chronic pancreatitis has pancreatic stones[5]. The condition is more common in females. There is wide variation in incidence and presentation between European, North American, USA, South African and Asian countries [6,7]. Pain was the predominant clinical feature followed by steatorrhoea and malnutrition.

Pancreatic ductal and parenchymal changes on imaging, calcification and endosonographic

1. *Dr. Hashim Rabbi, Assistant Professor, Department of Hepato-biliary-Pancreatic Surgery, BIRDEM General Hospital.
2. *Dr. Md. Mamunur Rashid, Associate Professor, Department of Hepato-biliary-Pancreatic Surgery, BIRDEM General Hospital.
3. Dr. H A Nazmul Hakim, Assistant Professor, Department of Surgery, Dhaka Medical College.
4. Dr. A H M Tanvir Ahmed, Registrar, Department of Hepato biliary-Pancreatic Surgery, BIRDEM General Hospital.
5. Dr. Ajmal Quader Chowdhury, Registrar, Department of Surgery, Dhaka Medical College.
6. Dr. Mahmud Mohammad Sarder, Medical Officer, Dhaka Medical College.
7. Dr. HM Sabbir Raihan, Resident Medical Officer.
8. Dr. Sarder Rizwan Nayeem, Resident Medical Officer.BIRDEM
9. Dr. Mohammad Ali, Professor.BIRDEM

*Bearing authors share equal responsibility as first authorship

Correspondence: Dr. Hashim Rabbi
E-mail:hrabbi72@gmail.com

abnormalities suggestive of CP. Pancreatic enzymes and analgesics are considered as initial medical therapy. Endotherapy was preferred if medical therapy fails. Surgery was offered after failure to both medical, endotherapy and in suspected malignancy[8]. It is subdivided into tropical calcific pancreatitis (TCP), when associated with diabetes mellitus it is, Fibrocalculus pancreatic diabetes (FCPD) when both the exocrine and endocrine pancreatic insufficiency occurs.

Aim of the study:

Understanding of the disease spectrum helps in proper evaluation and treatment of patients with pancreatic stone disease. The objective of the study was to assess the mode of presentation, determine the effect of different surgical treatment strategies related to pancreatic stone disease and their outcome.

Inclusion criteria:

All 362 patients with pancreatic stone diseases, surgically treated by Lateral Pancreaticojejunostomy following Pancreatolithotomy in pancreatic stone disease were included in this study. They were included randomly irrespective of their mode of presentation and diabetes status. They were operated by the same surgical team and followed up regularly.

Exclusion Criteria:

Non-surgically treated patients like endoscopic (ERCP) removal, extracorporeal shockwave lithotripsy (ESWL) etc. are excluded from the study. Patients with severe chronic pancreatitis who required head coring operation or pancreatic resections and patients with portal hypertension due to splenic vein encasement were also excluded from this study.

Materials and methods:

This retrospective observational study was performed in BIRDEM General Hospital, Dhaka Medical College Hospital and other hospitals of Dhaka by team of surgeons follow the same surgical principle between the periods from January 2000 to July 2017.

It includes, on 362 patients of pancreatic stone diseases irrespective of their age, sex, mode of presentation and diabetes status.

They were surgically treated by Lateral Pancreaticojejunostomy following Pancreatolithotomy. They were thoroughly evaluated by detailed clinical history, physical examination, investigations and standard criteria of Visual Analogue Scale for pain scoring. Imaging studies that includes plain x-ray of abdomen (anterior-posterior & lateral view), Ultrasound scan, Magnetic Resonance Cholangiopancreatogram (MRCP), Endoscopic Retrograde Cholangiopancreatogram (ERCP) and Computed Tomography scan (CT-scan) was done. Initially ERCP was done routinely but the later it was done only in selected cases. Imaging was done to assess pancreatolithiasis, stricture and dilatation of MPD, parenchymal changes like fibrosis, atrophy and mass lesions. Tumor marker Carbohydrate Antigen (CA-19.9) was done in suspected cases of malignancy.



Figure 1: Plain X-ray Abdomen & Pancreatic stones after removal

Original Article

DCIMCJ 2018 January; 5(1):47-57

Transabdominal Ultrasonographic Evaluation of Malignant Ovarian Tumors

Shimu F[1], Jahan I[2], Farzana T[3]

Abstract:

The purpose of this article is ultrasound characteristics of ovarian and adnexal masses and to discuss the prediction of the likelihood of ovarian cancer based on these characteristics and clinical parameters. After introduction of ultrasound this modality remain the basic scanner and most of the times the only modality prior to surgery in our country. After satisfactory clinical examination by a reasonably real time scanner a surgeon can confidently go for operative management. Transabdominal sonogram is most reliable predicting that an ovarian lesion is benign or malignant; and malignant ovarian tumors are of clinical importance and deserve considerable emphasis. Ultrasound characteristics can be used to diagnose the classic appearing non neoplastic entities, benign neoplasms and malignancies. In cases in which the appearance of an ovarian mass is not classic, assignment of relative risk of malignancy using a multiparametric model is appropriate and beneficial for patient management.

Keywords: Malignancy, ovarian cancer, ovary, risk prediction, ultrasound

Introduction:

Tumor of the ovary is a common form of neoplasm in women. They may be benign or malignant. Every year malignant ovarian cancer kills more women than does cancer of the uterine cervix and body combined.

Patients may present with a palpable mass or a mass suspected clinically. Often an ovarian mass is detected incidentally while an abdominal ultrasound scan is performed for other indications. Ovarian mass can occurs at any age. In the general population, the lifetime risk of ovarian cancer is 1.8%. The risk of malignancy increases 12 fold from 20-29 to 60-69 years of age. Determination of early stage of malignant ovarian mass is essential in planning appropriate management.

1. Dr. Farhana Shimu, Assistant professor, Deprtment of Radiology & Imaging, Dhaka Central International Medical College.

2. Dr. Ismat Jahan, Assistant Professor, Deprtment of Radiology & Imaging , Marks Medical College, Dhaka.

3. Dr. Tayseer Farzana, Consultant, Deprtment of Radiology & Imaging, Popular Diagnostics Center, Dhaka.

Correspondence: Dr. Farhana Shimu
E-mail: shimu.farhana2015@gmail.com

Ultrasound remains the study of choice in the initial evaluation of suspected ovarian masses because it is relatively inexpensive, noninvasive and widely available. Soft tissue images are obtained without the need for contrast agents and do not cause damage to tissue. Additionally the ultrasound examination is a dynamic process. The bladder can be filled or emptied to enhance imaging, the patient can be repositioned to allow for better visualization of particular area and the transducer itself can help to localize pain and therefore direct screutinization.

A lot of information can be gained from a scan in case of ovarian masses. We can say whether it is unilateral or bilateral, solid or cystic, unilocular or multilocular, thick or thin walled. Septa if present whether are thick or thin, complete or incomplete etc. Simple cysts are probably benign, where as cysts with thick septa & solid elements are frequently malignant (Meire et al., 1978).

Several characteristics features on ultrasound imaging can aid in diagnosed malignant neoplasm including bilaterality, thick walled cysts, thick septa particularly if they are incomplete, solid areas within the mass, presence of excrescences, presence of ascites, extension to adjacent organs, lymphadenopathy.

Diagnosis by ultrasound feature analysis is 80 to 90 percent accurate in distinguishing benign from malignant (Lees and Highmen, 1998).

However, ultrasound may be limited by obesity, acoustic shadowing from bowel gas previous surgery and small field of view. Transvaginal ultrasonography overcomes some of these limitations. Accordingly to Noor et al., (2002) transabdominal scan demonstrate more information than transvaginal in 25.5% of cases of ovarian masses, particularly when the mass is larger and crosses the pelvic brim. In addition, the availability of special transvaginal probe as well as trained and experienced operators are very limited in our country. Now transvaginal ultrasound is more commonly used as means of screening for ovarian cancer in postmenopausal ovaries (Elischer 1988).

Color Doppler US of ovarian mass helps identify vascularized tissue and can assists in differentiating solid tumor tissue from nonvascularized structures but problems associated with Doppler with US include operator dependences & lack of standard criteria in distinguishing benign from malignant waveforms. Doppler indexes can be misleading in premenopausal women. In a study by Reles et al., 1997, the sensitivity of Color Doppler US was 80% & the specificity only 67% in premenopausal patients, where as postmenopausal patients the sensitivity of Color Doppler US was 93% & the specificity 83%.

Other diagnostic aids, such as CT and MRI are usually performed in the assessment and staging of neoplasm of pelvic organs. CT is accurate in assessing local tumor invasion and provides accurate localization for both biopsy and radiotherapy. The multiplanar imaging facility, the lack of irradiation, the high degree of soft tissue contrast provided by MRI are considerable advantage in the evaluation of benign and malignant pelvic disease. But in our country these modalities are expensive and are less available. So transabdominal sonography remains as widely available, basic imaging method.

The use of transabdominal USG associated with plasmatic dosages of Ca 125, Ca 19-9, and CEA, represents an excellent method of preoperative screening for the evaluation of malignant ovarian tumefactions and for directing the surgeon toward the best therapy [Piccioni et al., (2003)].

Rapidity of examination, lack of irradiation, cost-effectiveness and ready availability of high-resolution transabdominal ultrasound provides an initial means of confirming and localizing malignant ovarian mass and frequently a definitive diagnosis.

Materials and methods:

Research Approach:

This cross sectional study attempted on 48 patients aged from 13-65 years, admitted in Gynaecology & Obstetrics Department of MMC, H having complaints suggestive of malignant ovarian tumor. They were referred to the radiology & Imaging Department of MMC, H to diagnosis by ultrasonography (TAS) and the study was carried out from January 2007 to December 2007.At first all these patients were evaluated by detail history, clinical examination with special emphasis on lower abdomen.

Sonographic examinations were then performed for the diagnosis of malignant ovarian tumor and an expert opinion was taken in each case.

The subjects were observed and out of 48 patients, five cases were found in operable and were excluded from the study group. Another three cases excluded as histopathology report was not obtained. Finally 40 patients were included in the study.

Sample size:

Total 40 patients were included in this study. The sample size was determined by the following formula-

$$n=z^2pq/ d^2$$

according to this formula the estimated final sample size was 48. However 8 cases were excluded due to previously mentioned causes. Therefore final sample size was 40.

Sampling Method:
Consecutive cases diagnosed clinically and who were referred to the radiology and imaging department of MMCH for ultrasonographic diagnosis of malignant ovarian tumors.

Diagnostic Criteria:
Criteria for diagnosis of malignant ovarian tumors (Carol M Rumack, p.553-578)

1. Tumor with thick regular/irregular wall with septation.
2. Tumor with multiloculation.
3. Cystic, solid or complex area within mass.
4. Local extension, lymphadenopathy present or not.
5. Distant metastases to other organs.
6. Ascites-present or not.

Confirmation of Diagnosis:
The findings of Transbdominal sonography were confirmed byHistopathological examination done in the department of Pathology, Mymensingh Medical College Hospital, Mymensingh.

Analysis of Results:
The result of this study was calculated by statistical formula. Percentage was calculated to find out the disease pattern among the total. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value calculated after confirmation of diagnosis and calculated by using the standard formula shown in (Appendix iii) Level of significance was expressed as 'P' value.

Observation and Results:
Age group of patients:
This study included 40 women having palpable or clinically suspected ovarian carcinoma.

The age range was 13-65 years. They are divided into six age groups. The average age was 36.4 ± 11.7. Highest incidence was found in 30-39 years age group.

Table- I: Age group of patients

Age groups (Years)	Numbers of patients	Percentage (%)
<20	5	12.5%
20-29	6	15%
30-39	12	30%
40-49	9	22.5%
50-59	7	17.5%
>60	1	2.5%
Total	40	100%

Incidence of Clinical Feature:
The most common symptom associated with malignant ovarian tumor had lower abdominal pain in 34%, 23.4% presented with palpable pelvic mass and another 23.4% was menstrual irregularity. Other 10% presented with vaginal bleeding, 5.3% were asymptomatic and 3.2% had infertility.

Table II: Distribution of Clinical Feature

Clinical Feature	Numbers of patients	Percentage (%)
Lower abdominal pain	32	34.04
Palpable Pelvic mass	22	23.4
Menstrual irregularity	22	23.4
PV bleeding	10	10.6
Asymptomatic	5	5.3
Infertility	3	3.2

Distribution of Sonographic Findings:

Among 40 cases, 27 (67.5%) cases were diagnosed as malignant ovarian tumor and 13 (32.5%) cases were non malignant condition on USG. Results shown in table III.

Table III – Distribution of the Sonographic findings

Sonographic findings	Number of patients	Percentage
Malignant ovarian tumor	27	67.5%
Non malignant condition	13	32.5%
Total	40	100%

Site of Distribution according to USG findings:

Among 40 patients, Bi-lateral malignant ovarian tumor was diagnosed in 18 patients and unilateral in 9 patients. In non malignant condition most of are unilateral in location (10cases) Table IV shows site of distribution according to USG findings.

Table IV – Site od distribution according to USG findings

Tumor type	Unilateral		Bilateral		Total	
	no	%	no	%	no	%
Malignant Tumor	14	34.5%	13	32%	27	67.5%
Non-malignant condition	10	25%	3	7.5%	13	32.5%

Tumor wall as per USG findings:

Out of 27 malignant ovarian tumor thick, irregular was in 19 patients, thick regular wall in 8 patients. All 13 in malignant cases were thin regular wall. Table V shows the tumor walls according to USG findings.

Table V - Tumor wall as per USG findings:

Tumor type	Thin regular wall		Thick regular wall		Thick irregular wall		Total	
	no	%	no	%	no	%	no	%
Malignant	0		8	20%	19	47.5%	27	6.75%
Non- malignant	13	32.5%	0		0		13	32.5%

Loculation within tumor wall as per USG findings:

Out of the 27 patients of malignant ovarian tumor 21 cases showed multiloculation and 6 cases showed no loculation. 11 non-malignant cases were unilocular and cases were multilocular in USG findings.

Table VI - Loculation within tumor as per USG findings:

Tumor type	Unilocular		Multilocular		Total	
	no	%	no	%	no	%
Malignant Tumor	6	15%	21	52.5%	27	67.5%
Non-malignant condition	11	27.5%	2	5%	13	32.5%

Distribution of cystic, solid or complex mass observed on USG:

Among 27 patients of malignant ovarian tumors cystic areas were present within tumors in 5 cases, solid areas were present in 9 cases and complex areas were present in 13 cases. All 13 cases of non-malignant condition showed cystic mass. Distribution of cystic., solid or complex mass according to USG findings have been shown in Table VII.

Table VII - Distribution of cystic, solid or complex mass observed on USG:

Tumor type	Present		Absent		Total	
	no.	%	no.	%	no.	%
Malignant	3	7.5%	24	60%	27	67.5%
Non-malignant	0		13	32.5%	13	32.5%

Local Extension of tumor observed on USG:

Among 27 patients of malignant ovarian tumors 10 local extensions of tumors observed in 9 cases and in 18 cases was no local extension of tumor presence or absence of local extension observed on USG is shown on Table VIII

Table VIII - Local Extension of tumor observed on USG:

Tumor type	Present		Absent		Total N=40	
	no.	%	no.	%	no.	%
Malignant	9	22.5%	18	45%	40	67.5%
Non-malignant	0		13	32.5%	13	32.5%

Among 27 cases of malignant ovarian tumors distant metastasis was observed in 3 cases and not found in 24 cases. Remaining 13 cases, out of 40 were non-malignant. Presence or absence of distant metastasis observed on USG is shown on Table IX.

Table IX - Distant Metastasis of Tumor observed on USG:

Tumor type	Cystic mass		Solid mass		Complex mass		Total	
	no	%	no	%	no	%	no	%
Malignant	5	12.5%	9	22.5%	13	32.5%	27	67.5%
Non- malignant	13	32.5%	0		0		13	32.5%

Ascites observed on USG:

Among 27 cases of malignant ovarian tumor Ascites present on USG in 4 cases and absent in 23 cases. Presence or absence of ascites observed on USG is shown on Table X

Table X - Ascites observed on USG:

Tumor type	Present		Absent		Total	
	no.	%	no.	%	no.	%
Malignant	4	10%	23	57.5%	27	67.5%
Non-malignant	0		13	32.5%	13	32.5%

5.11 Distribution of the Histopathological findings:

Out of 40 cases malignant ovarian tumor were diagnosed in 28 cases (70%) and non malignant condition were 12 cases (30%). Table XI shows distribution of the histopathological findings.

Histopathological findings	Number of patients	Percentage
Malignant ovarian tumor	28	70%
Non malignant condition	12	30%
Total	40	100%

5.12. Comparison between Histopathology and Sonographic finding of Ovarian Tumor:

Among 40 cases, 26 cases were true positive and 4 were false positive. As 8 patients with lower abdominal pain and menstrual irregularity were proved to have no malignant lesion, they were considered as true negative, 2 cases were false negative.

Comparison of Transbdominal Sonographic finding with Histopathology

TAS	Histopathology		Total
	Malignant	Non – malignant	
Malignant	25 (True Positive)	2 (False Positive)	27
Non – malignant	3 (False Negetive)	10 (True Negative)	13
Total	28	12	40

5.13. Sensitivity, Specificity, Accuracy, Positive Predictive value and Negative predictive value of TAS:

Transabdominal sonography in evaluation of malignant ovarian tumor had sensitivity 92%, specificity 66%, accuracy 85%, positive predictive value 86% and negative predictive value 80%.

Table XIII - Sensitivity, Specificity, Accuracy, Positive Predictive value and Negative predictive value

Diagnostic Accuracy	Percentage
Sensitivity	92%
Specificity	66%
Accuracy	85%
Positive Predictive value	86%
Negative predictive value	80%

Discussion:

During the past two decades, there have been significant technological advancements of diagnostic imaging. Ultrasonography started its modest beginning over 50 years ago. The recent years have witnessed an expansion of indication for sonographic examination; this is uniquely true in the evaluation of the female pelvic. Ultrasound of female pelvic permits the rapid, confident and cost effective diagnosis of a full spectrum of pathology in patients of all ages. It has been shown to have excellent correlation with histologic characteristic of ovarian masses. Diagnosis by ultrasound feature analysis is 80 to 90 percent accurate in distinguishing benign from malignant (Less and Highmen, 1998)

In this study 40 patients of clinically suspected ovarian cancer were included. The age range was 13-60 years. It was found that majority (30%) belonged to the group between 30-39 years closely followed by the group belonging to that between 40-49 years (22.5%). This was close to the observation of Huda (1997), who showed highest incidence (33.33%) of pelvic mass in the age group between 33-37 years.

Analysis of clinical features reveals that most common presenting complaints were lower abdominal pain (34.04%). 22 patients (23.4%) each presented with menstrual irregularity and palpable abdominal mass and 10 patients (10.6%) presented with per vaginal bleeding respectively. Some of the patients (5.32%) were asymptomatic and the ovarian malignancy was detected incidentally while an abdominal ultrasound scan was performed for other indications.

A knowledge about the pathologic and clinical basis of the lesion greatly aids radiologist in coming to a diagnosis. Simple cyst are probably benign, where as cysts with thick septa and solid elements are frequently malignant (Meire et at, 1978).

In this study among 40 cases, malignant ovarian tumors were diagnosed in 27 cases (67.5%). Ultrasound examination was contributory in all cases. Out of 27 cases of malignant ovarian tumor 13 cases (32%) were found bilateral, thick irregular wall mass were found in 19 cases (47.5%), multilocular mass were seen in 21 cases (52.5%). Malignant ovarian tumor with cystic pattern found in 5 cases (12.5%) , solid pattern found in 9 cases (22.5%) and complex pattern found in 13 cases (32.5%). Extension to adjacent organs, hepatic metastases and ascites present in 9 (22.5%), 3 (7.5%), 4 (10%) cases of malignant ovarian tumor. Ultrasonography can detect ovarian cancers by finding semi-solid, semi cystic masses with septa, papillary growth on the surface, bilateral lesions with ascites which, however may be the characteristics of advanced ovarian cancers (Moyl et al 1973, Herrmann et al 1987).

In this present series sensitivity of ultrasonography was 92% and specificity was 66%. Similarly Voss et al., (1983) showed sensitivity and specificity of ultrasound 79% and 86% respectively and the study was done on patients who underwent exploratory laparotomy for a pelvic mass diagnosed by ultrasonography preoperatively. A retrospective study conducted on 78 patients. These patients underwent both a transabdominal and biochemical examination of serum levels of Ca- 125, CEA. Subsequently these patients underwent surgery or medical therapy according to the suspected diagnosis. So, ultrasound examination is on its own an excellent method for preoperative screening in case of adnexal tumefactions(Piccioni et al, 2003)

In this study transabdominal sonography were used only. Transabdminal ultrasound examination is a good and economic method for evaluation of different malignant ovarian cancer. Considering its ready availability, cost-effective and lack of irradiation, transabdominal ultrasonography examination can be regarded as a best method for evaluating ovarian cancer. (Chadha et al., 1994) showed that a diagnostic accuracy of clinical examination alone was 68% compared to 76% of ultrasound examination in diagnosing ovarian mass. In this study diagnostic accuracy of malignant ovarian tumor was 85%.

Transvaginal sonography is relatively a new technique in pelvic imaging that can provide more diagnostic information in some cases. It can define the internal architecture of the mass better than transabdominal scan did. However, the transvaginal technique is limited in some circumstances because of the smaller field of view of the transvaginal probe. It cannot be helpful in larger masses, because it is difficult to image. Fleischer et al, (1989) showed in their study that Tranvaginal scan is particularly helpful in pelvic masses less than 5cm in size. They showed in their study that transvaginal sonography can miss some obvious lesion above pelvic brim and it is used best as an adjunct to transabdominal sonography.

Transabdominal sonography is still required to gain to overall assessment of large pelvic masses. However, the limited field of view with transvaginal ultrasonography permits adequate visualization of only the true pelvis. According to Ahmed (1999) in case of ovarian mass USG findings were correlated with operative findings and found to be more than 95% correction. So, conventional transabdominal sonography has been one of the best methods for evaluating the malignant ovarian cancer.

Summary and Conlusion:

This cross-sectional study was designed to observe the accuracy, sensitivity and specificity of transabdominal ultrasonography in the diagnosis of malignant ovarian tumor. 40 cases having clinical manifestation of ovarian tumor were studied in the Department of Radiology & Imaging MMCH with the cooperation of the Department of Obstetrics & Gynaecology, MMCH during the period from January 2007 to December 2007.

The age range of the patients was 13 to 65 years. The peak incidence was found in the age group between 30 to 39 years. Most common presenting complaints were lower abdominal pain, that was present in 32 (34.04%). Rest of the patients had palpable lower abdominal mass (23.4%) menstrual irregularity (23.4%), PV bleeding (10.6%) and some patients were asymptomatic (5.32%).

Out of 40 cases, 27 cases (67.5%) were diagnosed by USG as malignant ovarian tumor. Histopathological study revealed malignant ovarian tumor in 28 cases (70%).

In this study, thick regular to irregular wall with thick septations, multiloculations, mostly solid to complex masses were noted sonographically.

In this study transabdominal sonography had sensitivity 92%,specificity 66%, positive predictive value 86% and negative predictive value 80%.

Conclusion:

The study was limited to patients who underwent transabdominal ultrasonography with subsequent histopathological confirmation. During this study it was found that appropriate clinical data could raise the specificity of transabdominal ultrasonography. The advent of relatively inexpensive and easy use real time machines has made it possible to obtain information without spending time. Transabdominal ultrasonography of female pelvic permits the rapid, confident and cost effective diagnosis of malignant ovarian tumor in patients of all ages. In my study diagnostic accuracy of malignant ovarian tumor was 85%, so my hypothesis is accepted.

References:

1. Patel MD. Pitfalls in the sonographic evaluation of adnexal masses. Ultrasound Q. 2012;28:29–40.[PubMed]

2. Valentin L, Ameye L, Franchi D, et al. Risk of malignancy in unilocular cysts: a study of 1148 adnexal masses classified as unilocular cysts at transvaginal ultrasound and review of the literature. Ultrasound Obstet Gynecol. 2013;41:80–89. [PubMed]

3. Ekerhovd E, Wienerroith H, Staudach A, Granberg S. Preoperative assessment of unilocular adnexal cysts by transvaginal ultrasonography: a comparison between ultrasonographic morphologic imaging and histopathologic diagnosis. Am J Obstet Gynecol. 2001;184:48–54. [PubMed]

4. Jain KA. Sonographic spectrum of hemorrhagic ovarian cysts. J Ultrasound Med. 2002;21:879–886.[PubMed]

5. Patel MD, Feldstein VA, Filly RA. The likelihood ratio of sonographic findings for the diagnosis of hemorrhagic ovarian cysts. J Ultrasound Med. 2005;24:607–614. [PubMed]

6. Outwater EK, Siegelman ES, Hunt JL. Ovarian teratomas: tumor types and imaging characteristics. Radiographics. 2001;21:475–490. [PubMed]

7. Mais V, Guerriero S, Ajossa S, Angiolucci M, Paoletti AM, Melis GB. Transvaginal ultrasonography in the diagnosis of cystic teratoma. Obstet Gynecol. 1995;85:48–52. [PubMed]

8. Brown DL. A practical approach to the ultrasound characterization of adnexal masses. Ultrasound Q. 2007;23:87 05. [PubMed]

9. Park JY, Kim DY, Kim JH, Kim YM, Kim YT, Nam JH. Malignant transformation of mature cystic teratoma of the ovary: experience at a single institution. Eur J Obstet Gynecol Reprod Biol. 2008;141:173–178. [PubMed]

10. Patel MD, Acord DL, Young SW. Likelihood ratio of sonographic findings in discriminating hydrosalpinx from other adnexal masses. AJR Am J Roentgenol. 2006;186:1033–1038. [PubMed]

11. Guerriero S, Ajossa S, Lai MP, et al. Transvaginal ultrasonography associated with colour Doppler energy in the diagnosis of hydrosalpinx. Hum Reprod. 2000;15:1568–1572. [PubMed]

12. Savelli L, Ghi T, De Iaco P, Ceccaroni M, Venturoli S, Cacciatore B. Paraovarian/paratubal cysts: comparison of transvaginal sonographic and pathological findings to establish diagnostic criteria. UltrasoundObstet Gynecol. 2006;28:330–334. [PubMed]

13. Vaysse C, Capdet J, Mery E, Querleu D. Paratubal endometrioid cystadenocarcinoma: case report and review. Eur J Gynaecol Oncol. 2009;30:443–445. [PubMed]

14. Smorgick N, Herman A, Schneider D, Halperin R, Pansky M. Paraovarian cysts of neoplastic origin are underreported. JSLS. 2009;13:22–26. [PMC free article] [PubMed]

15. Thakore SS, Chun MJ, Fitzpatrick K. Recurrent ovarian torsion due to paratubal cysts in an adolescent female. J Pediatr Adolesc Gynecol. 2012;25:e85–e87. [PubMed]

16. Asch E, Levine D. Variations in appearance of endometriomas. J Ultrasound ed. 2007;26:993–1002.[PubMed]

17. Alcázar JL, Laparte C, Jurado M, López-García G. The role of transvaginal ultrasonography combined with color velocity imaging and pulsed Doppler in the diagnosis of endometrioma. Fertil Steril. 1997;67:487–491. [PubMed]

18. Varras M, Polyzos D, Perouli E, Noti P, Pantazis I, Akrivis Ch. Tubo-ovarian abscesses: spectrum of sonographic findings with surgical and pathological correlations. Clin Exp Obstet Gynecol. 2003;30:117–121. [PubMed]

19. Guerriero S, Ajossa S, Mais V, Angiolucci M, Paoletti AM, Melis GB. Role of transvaginal sonography in the diagnosis of peritoneal inclusion cysts. J Ultrasound Med. 2004;23:1193–1200. [PubMed]

20. Smorgick N, Maymon R, Mendelovic S, Herman A, Pansky M. Torsion of normal adnexa in postmenarcheal women: can ultrasound indicate an ischemic process? Ultrasound Obstet Gynecol. 2008; 31:338–341. [PubMed]

21. van Nagell J, DePriest P, Reedy M, et al. The efficacy of transvaginal sonographic screening in asymptomatic women at risk for ovarian cancer. Gynecol Oncol. 2000;77: 350Y356. [PubMed]

22. Varras M. Benefits and limitations of ultrasonographic evaluation of uterine adnexal lesions in early detection of ovarian cancer. Clin Exp Obstet Gynecol. 2004;31:85–98. [PubMed]

23. Geomini PM, Kluivers KB, Moret E, Bremer GL, Kruitwagen RF, Mol BW. Evaluation of adnexal masses with three-dimensional ultrasonography. Obstet Gynecol. 2006; 108:1167–1175. [PubMed]

24. Alcázar JL, Castillo G. Comparison of 2-dimensional and 3-dimensional power-Doppler imaging in complex adnexal masses for the prediction of ovarian cancer. Am J Obstet Gynecol. 2005;192:807–812.[PubMed]

25. Kaijser J, Sayasneh A, Van Hoorde K, et al. Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: a systematic review and meta-analysis. Hum Reprod Update. 2014;20:449–462. [PubMed]

26. Valentin L, Hagen B, Tingulstad S, Eik-Nes S. Comparison of 'pattern recognition' and logistic regression models for discrimination between benign and malignant pelvic masses: a prospective cross validation. Ultrasound Obstet Gynecol. 2001;18:357–365. [PubMed]

27. Dodge JE, Covens AL, Lacchetti C, et al. Preoperative identification of a suspicious adnexal mass: a systematic review and meta-analysis. Gynecol Oncol. 2012;126(1):157–166. [PubMed]

28. Sokalska A, Timmerman D, Testa AC, et al. Diagnostic accuracy of transvaginal ultrasound examination for assigning a specific diagnosis to adnexal masses. Ultrasound Obstet Gynecol. 2009;34:462–470.[PubMed]

DCIMC

Original Article

DCIMCJ 2018 January; 5(1):58-64

Effect of Diclofenac on Antihypertensive Efficacy of Amlodipine

Chowdhury RA[1], Alam I[2], Farooqui I[3], Rahman MH[4]

Abstract:

Objective: To clarify effect of Diclofenac on antihypertensive effect of Amlodipine. Method: It was a prospective observational study which was carried out in the outpatient department of Medicine of MAG Osmani Medical College Hospital, Sylhet from 2011 to 2012. Diagnosed hypertensive patients with osteoarthritis were the study subjects. Thirty patients were included in the study. Each patient was studied through 3 study periods (phases) of one month duration each. Before administration of NSAIDs when only antihypertensives were being taken, this period was phase 0. In the first month (phase 1) they was treated by Amlodipine and Diclofenac, In second month (phase 2) NSAID of first month were replaced by Paracetamol and in third month (phase 3) NSAID of first month were resumed by replacing Paracetamol. Blood pressure was measured in the supine, sitting and standing position with standard mercury sphygmomanometer, at the inception (phase 0; baseline), and at the end of the first month (phase1) , of the second (phase2), and of the third study month (phase 3). Mean blood pressure was calculated. Results: There were 30 study subjects, 16 females (53.3%) and 14 males (46.%). They aged 52.8±9.5 years with body weight 61.7±6 kg, and their lying mean BP at the inception of this study was 107.7±6.6 mm of HG). There were no significant differences (p>0.05) in patients weight status Combination of Diclofenac with Amlodipine resulted in an increase of mean baseline BP by 0.64% (0.7 mm Hg) after phase-1 which was not significant. In phase-2 BP was decreased by 6.82% (7.5 mm Hg) from Phase-1 which was significant (p=0.001). In phase-3 BP increased by 4.3% (4.4mm Hg) relative to phase-2 which was not significant. Conclusion: Diclofenac attenuates the BP lowering efficacy of antihypertensive Amlodipine. Though the results are statistically not significant it may be an alarming concern for the treating physician to balance between risk and benefit.

Keywords: Non-steroidal anti-inflammatory drugs, antihypertensive drags, Diclofenac, Amlodipine

Introduction:

Arterial hypertension is the most important preventable cause of premature death and disability. Although its treatment is very effective and well tolerated, sometimes, the practical achievements are not satisfactory for two main reasons: inadequate medication (noncompliance, inappropriate prescription) and interferences (untoward life style, co-medication with prohypertensive agents, pharmacokinetic and/ or pharmacodynamic drug interactions)[1]. In Bangladesh, prevalence of hypertension with systolic blood pressure (sBP) >140 mmHg was 10.5% and with diastolic blood pressure (dBP) > was 9.0%[2]. Age and sex-specific prevalence hypertension showed progressive rise of systolic and diastolic tension in females as compared to males. Studies from India and Bangladesh have shown upward trend in the prevalence of hypertension[3].

Rheumatic disorders are common causes of morbidity, disability, and work loss in rural and urban communities of Bangladesh[4]. Females are at higher risk of developing osteoarthritis than elderly male[5]. It is uncommon in adults under age 40 and highly prevalent in those over age 60[6].

The prevalence of osteoarthritis is higher in the urban affluent community than in the rural and urban slum[4]. Antihypertensive drugs appear to be affected to variable degrees by NSAIDs. Diuretics, angiotensin-converting enzyme inhibitors (ACEIs), beta-blockers, and angiotensin II receptor blockers (ARBs) are most susceptible to the hypotensive nullifying effects of

1. Dr. Rahat Amin Chowdhury, Honorary Medical Officer, Department of Medicine, MAG Osmani Medical College, Sylhet.

2. Dr. Iftikher Alam, Junior Consultant, Department of Neurology, Dhaka Medical College, Dhaka.

3. Dr. Iffath Farooqui, Lecturer, Department of Biochemistry, Sylhet Womens Medical College.

4. Dr. Md Habibur Rahman, Indoormedical Officer, Department of Medicine, MAG Osmani Medical College, Sylhet.

Correspondence: Dr. Rahat Amin Chowdhury
E-mail: @.....gmail.com

NSAIDs. Calcium channel blockers and centrally acting antihypertensives are less affected[7-9]. The hypertensive effect of NSAIDs varies depending on the specific NSAID used and the type of antihypertensive agent, if they are taken concurrently[10]. More than five days of treatment with either drugs are normally required for the interaction to manifest[11].

Almost all antihypertensive drugs lose some of their efficacy when combined with NSAIDs. Calcium channel blockers are an exception, drugs of choice for the subset of hypertensive population concomitant analgesic/anti-inflammatory treatment[1].

Some NSAIDs are more prone to elevate blood pressure than others. On the other hand some antihypertensive drugs are more susceptible and others are more resistant to the interaction with NSAIDs. There are considerable number of patients with coexisting hypertension and osteoarthritis. Among NSAIDs, Diclofenac is mostly used in due to their low incidence of gastrointestinal ADRs and short half lives. On the other hand, calcium channel blockers are commonly used antihypertensive drugs, particularly in elderly people. In this perspective, we selected Diclofenac and Amlodipine to assess their interaction and subsequent effect of NSAIDs on BP lowering effects. This might be helpful for the physicians to rationally prescribe concurrent antihypertensive and NSAIDs in patients suffering from hypertension with concomitant osteoarthritis.

Materials and methods:

It was a prospective observational study which was carried out in the outpatient department of Medicine of MAG Osmani Medical College Hospital, Sylhet From 1st July 2011 to 30in June 2012.

Study population:

Diagnosed hypertensive patients with osteoarthritis attending at the medicine outdoor of MAG Osmani Medical College Hospital were the study subjects. Patients who fulfilled the inclusion and exclusion criteria were enrolled in the study. Inclusion criteria were: hypertensive persons with concomitant osteoarthritis; requiring regular intake of NSAIDs; age 40 years or more. The patients excluded were: unable to tolerate withdrawal of their osteoarthritis therapy; those unwilling to participate and uncooperative; patients with HTN taking NSAIDs due to other arthritis other than OA; organ dysfunction (bronchial Asthma, COPD, renal failure, liver failure etc.) and other co-morbid condition as DM; hypersensitivity to tolerate to any of the drugs studied. Ultimately 30 patients were included in the study.

Study Procedures:

A structured questionnaire was used as research instrument. Outcome variables were as follows: age, sex, occupation, social background, economic background, smoking, family history, physical activity, weight were demographic variables. Blood pressure (systolic, diastolic & mean) was the clinical variable.

After selection of the subjects, the objectives, nature, purpose and potential risk and benefits of all procedures used for the study was explained in details to the patients. For any condition (sitting, lying or standing) mean blood pressure of a patient was defined by the following formula:

Mean blood pressure = Diastolic pressure + one third of pulse Pressure.
Where Pulse pressure = Systolic pressure - Diastolic pressure.

Ethical consideration:

Informed verbal and written consent was taken from each of the patients before taking any interviews. The attendant was the witness of taking verbal informed consent. The consent form clearly described the purpose and methods of the study, confidentiality of the interviews, risks and benefits of participating in the study, their rights to participate voluntarily and to refuse at any point in time without consequences. Name of the participants were excluded from interviews, and were intentionally excluded during analysis and report writing considering the research ethics. All informations were collected confidentially with complete respect to the patient wish and without

any force or pressure. Patient's rights were preserved according to Helsinki declaration and informed written consent was taken from agreed patients.

Each patient was studied through 3 study periods (phases) of one month duration each. Before administration of NSAIDs when only antihypertensives were being taken, this period was phase 0. In the first month (phase-1) they was treated by Amlodipine and Diclofenac,

In second month (phase-2) NSAID of first month was replaced by Paracetamol and in third month (phase-3) NSAID of first month was resumed by replacing Paracetamol.

Blood pressure was measured in the supine, sitting and standing position with standard mercury sphygmomanometer, at the inception (phase-0; baseline), and at the end of the first month (phase-1), of the second (phase-2), and of the third study month (phase-3). Mean blood pressure was calculated.

The dose of the drugs:

The patients were advised to continue the dose of standard Amlodipine and Losartan on which they were on. The dose of the both drugs were not modified further during the study.
NSAID - Diclofenac 50 mg twice daily[12]
Paracetamol- 1000 mg three times daily[13].

Monitoring:

Patients were monitored at the inception, at the end of each phase for hypersensitivity, side effects and any type of morbidity.

Statistical analysis:

The result was presented as means ± standard deviation (SD) and 95% confidence limit *($CI_{Q,95}$)* and p value < 0.05 was taken as level of significance. Statistical significance was assessed using paired and unpaired t test (Microsoft Excel), analysis of variance (ANOVA) was done by employing web service http:// www.physics.csbsju.edu/stats/anova.html to test the difference between means. A "p" value less than 0.05 was regarded as significant.

Results:

There were 30 study subjects, 16 females (53.3%) and 14 males (46.7%). Patients were treated with Amlodipine, aged 52.8±9.5 years with body weight 61.7±6 kg, and there lying mean BP at the inception of this study was 107.7±6.6 mm of Hg). Table II represents the change in weight for different phases during the study period. There were no significant differences ($p>0.05$) in patients weight status.

Table III represents the change in mean BP of the study subjects in different phases during the study period. Group-1 exhibits insignificant change of mean BP. There was no significant change of BP.

Comparison of BP changes between the phases was presented in table IV (paired t-test).

Combination of Diclofenac with Amlodipine results in an increase of mean baseline BP by 0.64% (0.7 mm Hg) after phase-1. The increase in BP was not significant in phase-1, whereas after phase-2 replacing Diclofenac by Paracetamol BP was decreased by 6.82% (7.5 mm Hg) from Phase-1. The change in BP with respect to baseline BP was significant ($p=0.001$). After phase-3 where Diclofenac was reintroduced in place of Paracetamol the BP increases by 4.3% (4.4mm Hg) relative to phase-2 and the change in BP with respect to baseline was not significant. The relative changes were insignificant.

Table I: Baseline Characteristics of the study subjects

Study Group Parameter	(AM+D)
Randomized (N)	30
Male/Female (n)	14/16
Age (Years: Mean ± SD)	57.9 ±11. 5
Weight (kg: Mean ± SD)	66.5 ± 7
Lying Mean BP (mm Hg : Mean ± SD)	109.2 ±7.4

SD= Standard deviation; BP= Blood pressure; AM= Amlodipine; D= Diclofenac

During phase-1 all the patients of both groups were treated with Diclofenac.

Table II: Weight Change in phases during study period

	Phases					
Patients	Phase-0	Phase-1	Phase-2	Phase-3	ANOVA	
					F	p
(AM+D)	66.462±7.04	67.086±7.16	66.562±7.07	66.892±6.95	0.002	1.00

AM= Amlodipine; D= Diclofenac

Table III: (Lying Mean) Blood Pressure Change in different phases

	Phases					
Patients	Phase-0	Phase-1	Phase-2	Phase-3	ANOVA	
					F	p
(AM+D)	109.23±7.4	109.87±9.7	102.38±6.51	106.85±6.26	2.589	0.064

AM= Amlodipine; D= Diclofenac; BP= blood pressure.

Table IV : Comparison of paired Observations

Patients	**Mean BP(±SD) in different phases**			**t value**	**p values**
	Phase 0	Compared Phases	Mean BP		
(AM+D)	109.2 ±7.4	PI	109.9 ±9.7	0.265	0.79
		P2	102.4 ± 6.5	3.95	0.001
		P3	106.8 ±6.3	1.39	0.18
		P2	105.4 ±6.3	4.91	0.0003
		P3	115.6 ±6.7	3.28	0.006

SD= Standard deviation; BP= Blood pressure; AM= Amlodipine; D= Diclofenac ; P= phase.

Paired t test done. $p < 0.05$ was considered as significant.

Discussion:

Non-steroidal anti-inflammatory drugs are blamed to attenuate the efficacy of some antihypertensive drugs. They may increase BP of normotensive osteoarthritis patients on prolonged use or they may have negative influence on BP lowering effects of some antihypertensive drugs.

Osteoarthritis and primary hypertension are two diseases that are common in old age. In a substantial number of patients both co-exist and both demand long term treatment for symptomatic well being and to avoid morbid consequences. We studied one mostly prescribed NSAID for its effects on efficacy of two popular groups of drugs for treatment of hypertension. Diclofenac is mostly prescribed NSAIDs for long term use. Amlodipine (calcium channel blocker) is commonly prescribed antihypertensive drugs.

The aim of our study was to evaluate the influence of Diclofenac on BP lowering effect of Amlodipine for

co-existent osteoarthritis and hypertensive patients. It was a prospective observational study. Randomly selected 30 patients with co-existent OA and HTN were given combinations-Amlodipine+Diclofenac.

Age distribution of all study subjects were consistent with similar studies[3,6]. Mean baseline BP of all study subjects were measured and BP changes observed after the end of different study phases (1 month for each phase: Phase-1, NSAID combined with antihypertensives, Phase-2, NSAIDs were replaced by Paracetamol, Phase-3, reintroduction of NSAIDs combined with antihypertensive drugs).

The decrease of BP for both groups were consistent with the influence of NSAID on BP lowering effects of antihypertensive drugs. For diclofenac combined with amlodipine, BP increased 0.6% from baseline. There was 6.8% decrease in BP when diclofenac was replaced by paracetamol as rescue agent (p=0.001). Again BP was increased by 4.3% with reintroduction of Diclofenac replacing the rescue agent (shown in table-II, IV).

The prohypertensive effects of NSAIDs presumably depend on several mechanisms[1]. Their analgesic and anti-inflammatory effects are mostly derived from cyclooxygenase (COX) inhibition and consequent decrease in prostaglandin synthesis. COX inhibition leads to decreased PGI_2 production in the vascular endothelium, with no change in TxA_2 synthesis in the platelets, predisposing to vasoconstriction, thrombosis and endothelial lesions. Moreover all NSAIDs impede physiological prostaglandin synthesis in the kidneys resulting in fluid retention and local vasoconstriction[1].

Almost similar BP changes were observed during different phases[1,9,14], though some antihypertensives and NSAIDs were not similar (antihypertensives were Lisinopril/Hydrochlorthiazide combination, amlodipine, valsartan and Lisinopril; NSAIDs were Ibuprofen, Acetaminophen, Piroxicam and Indomethacin). In our study, there was BP elevation with introduction of NSAID, reduction of BP when NSAIDs were replaced with Paracetamol (predominant analgesic action), and again BP elevation after reintroduction of NSAIDs. This observation is indicative of interaction of NSAIDs with antihypertensive, blunting their BP lowering effects. At the end of the study after 3 months (end of phase-3). To assess the probable mechanism of NSAIDs on BP elevating influence, we measured weight changes of study subjects in different phases. Though we did not measure serum electrolytes, it is supposed that fluid retention usually follows electrolytes. There was no significant weight change in our study in any phase (shown in table-III), implicating that, probably the NSAIDs do not influence on BP elevation by fluid and salt retention. This finding was also consistent with other studies[1]. In one study it was found that there was significant weight gain when NSAID Naproxen combined with Calcium channel blocker Nicardipine[7]. Despite the significant increase in body weight, the antihypertensive action of the Ca channel blocker nicardipine was not significantly affected by co-treatment with naproxen. In another study to see the influence of Ibuprofen, Diclofenac and Sulindac on BP lowering effect of Hydrochlorothiazide, there were no significant change in biochemical parameters like plasma electrolytes, plasma renin activity, aldosterone, albumin and creatinine or 24 hour urinary excretion of sodium and potassium[15]. Since we did not observe a significant increase in body weight during intake of NSAIDs combined with antihypertensive drugs, probably the observed BP elevation was largely due to vasoconstriction might be related to inhibition of vasodilatory prostaglandin synthesis by COX- inhibition of NSAID and less so to volume expansion.

There was some studies where no significant influence of NSAIDs seen on BP[16]. Though there was significant influence of NSAID in our study on BP lowering efficacy of antihypertensives, it is not certain about its significance about decision taking for its discontinuation. It is also not certain about the magnitude of BP change by NSAID that might be harmful to continue the combined therapy. It was estimated that a 5 to 6 mmHg increase in diastolic BP maintained over a few years may be associated with a 67% increase in total stroke occurrence and a 15%

increase in events associated with coronary heart disease[14]. It has been estimated that the avoidance of minor change in systolic BP in patients with osteoarthritis, subjected to treatment with NSAIDs would avoid over 30000 deaths due to MI in United States alone[11].

Conclusion:

Non-steroidal anti-inflammatory drugs are widely prescribed and are associated with blood pressure elevation. They may actually or potentially reduce the efficacy of several antihypertensive drags and may have important public health implications for the management of hypertension in the elderly persons taking NSAIDs. The hypertensive effect of NSAIDs varies depending on the specific NSAID used and the type of antihypertensive agent, if they are taken concurrently. From our study NSAID Diclofenac attenuate the BP lowering efficacy of antihypertensive Amlodipine. Though the results are statistically not significant it may be an alarming concern for the treating physician to balance between risk and benefit.

Recommendation:

Further studies with different commonly prescribed antihypertensive drugs and NSAIDs and with a larger sample size are recommended that might be helpful for the physicians to select better combinations of NSAIDs with antihypertensive drugs.

References:

1. Pavlicevic I, Kuzmanic M, Rumboldt M, Rumboldt Z. Interaction between antihypertensives and NSAIDs in primary care:a controlled trial. J Clin Pharmacol. 2008;15(3):372-382.

2. Sayeed MA, Banu A, Khan AR, Hussain MZ. Prevalence of diabetes and hypertension in a rural population of Bangladesh. Diabetes Care. 1995; 18(4): 555-558.

3. Das SK, Sanyal K, Basu A. Study of urban community survey in India: growing trend of high prevalence of hypertension in a developing country. Int J Med Sci. 2005; 2(2):70-78.

4. Haq SA, Darmawan J, Islam MN, Uddin MZ, Das BB, Rahman F et al. Prevalence of rheumatic diseases and associated outcomes in rural and urban communities in Bangladesh: a COPCORD study. J Rheumatol. 2005; 32(2):348-353.

5. Issa MM, Fenter TC, Black L, Grog AL, Crouep EJ. An Assessment of the Diagnosed prevalence of Diseases in Men 50 Years of Age or Older. AMJ Manag Care. 2006; 12(4):83-89.

6. Felson DT. Osteoarthritis. In: Harrison's Principles of Internal Medicine,17th edn. Vol II. The McGraw Hill companies. United States of America, 2008: 2158-2165.

7. Klassen DK, Jane LH, Young DY, Peterson CA. Assessment of Blood Pressure During Naproxen Therapy in Hypertensive Patients Treated with Nicardipine. Am J Hypertens. 1995; 8(2):146-153.

8. Monson K. Dosing With Diclofenac Sodium. (Accepted, October 12, 2009) at http://pain.emedtv.com/diclofenac-sodium/ dosing-with-diclofenac-sodium.html. Date of access 11/04/2012.

9. Horn JR, Hansten PD. NSAIDs and antihypertensive agents. (accepted, JulyS, 2010) at http://www.pharmacytimes.com /issue/ pharmacy/2006/2006-04/2006-04-5484(access date 15/06/2012).

10. Johnson AGI. NSAIDs and Blood Pressure: Clinical Importance for Older Patients. Drugs & Aging, Adis international. 1998; 12(1):7-27.

11. Salort-Llorca C, Minguez-Serra MP, Silvestre-Donat FJ. Interaction between Ibuprofen and antihypertensive drugs: Incidence and clinical relevance in dental practice. Med Oral Patol Oral Cir Bucal. 2008; 13(11):717-721.

12. Sayeed MA, Mahtab H, Khanam PA, Begum R, Banu A, Khan AKA. Diabetes and hypertension in pregnancy in a rural community of Bangladesh: a population based study. Diabet Med. 2005; 22(9):1267-1271.

13. Boureau F, Schneid H, Zeghari N, Wall R, Bourgeois P. The IPSO study: Ibuprofen, Paracetamol study in osteoarthritis. A randomised comparative clinical study comparing the efficacy and safety of Ibuprofen and Paracetamol analgesic treatment of osteoarthritis of the knee or hip. Ann Rheum Dis. 2004; 63(9):1028-1034.

14. Johnson J, Weinryb J. Safe pharmacologic treatment strategies for osteoarthritis pain in African Americans with hypertension, and renal and cardiac disease. J Natl Med Asso. 2006; 98(7):1126-1135.

15. Koopmans PP, Thien TH, Gribnau FWJ. The influence of Ibuprofen, Diclofenac and sulindac on the blood pressure lowering effect of hydrochlorothiazide. Eur J Clin Pharmacol. 1987; 31:553-557.

16. Thakur V, Cook ME, Wallin D. Antihypertensive effect of the combination of Fosinopril and HCTZ is resistant to interference by NSAIDs. American Journal of Hypertension. 1999; 12(9):925-928.

.....

Original Article

DCIMCJ 2018 January; 5(1):65-67

Serum Copper Level in Third trimester of Bangladeshi Pregnant Women with Gestational Diabetes Mellitus

Mishu FA[1], Yesmin MS[2]

Abstract:

Background: The term Gestational Diabetes Mellitus (GDM) is becoming a major health problem in developing countries undergoing rapid changes in lifestyle, dietary habits and body mass index. . GDM is associated with an increase incidence of congenital abnormalities which is also aggravated by mother's some trace elements deficiency such as zinc, copper, magnesium. Copper is one of the essential trace element for normal embryogenesis and fetal growth and its deficiency increase mortality and morbidity rate of mothers, embryos and neonates. Objective: To evaluate the association of serum copper with GDM in their third trimester. Methods: It was a case control study. This study was conducted in Mymensingh Medical College Hospital during the period from July 2013 to June 2014 to evaluate the association of Copper levels of Healthy pregnant women with GDM. A total number of 172 subjects were participated in this study; among them eighty six women diagnosed with GDM were selected as case (Group-I) and eighty six healthy pregnant women were control (Group-II). Student's unpaired t test was used to analyse the data between groups. For analytical purpose 95% confidence limit ($p<0.05$) was taken as level of significance. Results: We found very significant difference ($p<0.01$) in serum copper level when GDM compared to normoglycemic pregnant women in third trimester. Conclusion: Estimation of serum copper level should be incorporated in every GDM cases for prevention of complications.

Keywords: Diabetes mellitus, GDM, OGTT, Trace elements

Introduction:

Gestational diabetes mellitus is defined as glucose intolerance resulting in hyperglycemia, with first onset or detection during pregnancy[1,2]. Usually initiation of GDM is in middle and late gestational period and continues to term.Glucose intolerance usually returns to normal range within 6weeks after delivery[3]. Approximately 1-14 % of all pregnancies are complicated by GDM [4]. The incidence of GDM in Bangladesh is 6.7% among all Bangladeshi pregnant mothers[5]. Frequency of congenital malformation in infants of diabetic mothers is estimated to be 6-10%[6]. Pregnancy is associated with physiological changes that result in increased plasma volume and red blood cells and decreased concentrations of plasma proteins and micronutrients[7]. It is a time of increased nutritional needs, both to support the rapidly growing fetus and to allow for the changes occurring in the pregnant[8].Gestational diabetes is associated with excessive nutrient losses due to glycosuria[9]. Different researchers demonstrated that micro and macro nutrients are essential for the development of fetus. With the progress of pregnancy, the level of plasma copper increased and it was high in all trimesters[10]. Serum copper is significantly increased in GDM patients as compared with healthy pregnant women (Hussein, 2005) [11].

1. Dr. Farzana Akonjee Mishu, Assistant Professor & Senior Research Officer, Institutional Affiliation: Department of Physiology and Molecular Biology, Bangladesh Institute of Research & Rehabilitation In Diabetes, Endocrine & Metabolic Disorders (BIRDEM) Dhaka.

2. Dr. Mst. Shaila Yesmin, Assistant Professor, Department of Heamatology and Clinical Pathology, Bangladesh Institute of Research & Rehabilitation In Diabetes, Endocrine & Metabolic Disorders (BIRDEM) Dhaka.

Correspondence: Dr. Farzana Akonjee Mishu
E-mail: farzanamishu@yahoo.co.uk

Aim of the Study:

We aimed to see whether the changes in serum copper could help in better understanding of the biochemical and metabolic abnormalities in GDM.

Materials and Methods:

This case control study was carried out from July 2013 to June 2014 in the biochemistry department of

Mymensingh Medical College. Total 172 subjects were selected by purposive sampling technique from the outpatient department of Obstetrics and Gynaecology and department of Endocrinology in Mymensingh Medical College Hospital. Clinically diagnosed GDM (n=86) was in the case group as Gr-I and it was done on the basis of OGTT by WHO criteria 2013[12]. The normoglycemic pregnant women at second were taken as control group (n=86) as Gr-II. All those pregnant women with the previous history of diabetes, hypertension, and other endocrine disorders were excluded from this study. This study protocol was approved by the institutional review committee. Data were collected through a preformed data collection sheet (questionnaire).The variables were age, education, occupation, socioeconomic status, residential address, dietary habit, height, weight, family history of diabetes, previous pregnancy history and previous history of gestational diabetes mellitus. Written informed consent was obtained from all the participants of the study groups prior to their enrolment into this study. Blood samples, from pregnant women, which was withdrawn for OGTT during screening for GDM was used for this study. In this study serum glucose was determined by Enzymatic method with GOD-PAP serum, Serum copper was determined by colorimetric method with the 3,5-DiBr-PAESA stain. The results were analyzed statistically and values were expressed as mean ± SD. The level of significance was determined by employing Student's unpaired t test. Only when the p value was less than 0.05; the difference between two groups and subgroups were considered as statistically significant.

Result:

In this study, 58 out of 86 GDM patients had family history of diabetes mellitus. The present study showed that serum Copper level was very significantly ($p<0.01$) increased in the GDM women in second trimester as Gr-I group compared to healthy controls in the second trimester Gr-II group.

Table:I Clinical and Biochemical Characteristics of the study subjects

Variables	Mean ± SD (cases Gr-I)	Mean ± SD (controls Gr-II)	P value
Age	28.6±3.23	27.3±3.13	0.778
BMI	26.4±1.49	26.3±1.27	0.774
Copper(µg/dl)	240.09± 7.618	234.33± 3.809	0.002

(Student's t test was used to analyses the data between groups)

Discussion:

Copper are important trace element in metabolism, growth, development and reproduction. In this study, the values of copper in GDM subjects were significantly higher ($p<0.05$) when compared to the control. Our finding is supported by the studies of Yinsong Wang (2002) [8]. Copper in the blood also depends on the time of gestation. The possible causes of the changes are due to the hormonal, metabolic and enzymatic changes in pregnancy. The increase in serum copper may be due to the increase in the inflammatory response especially in copper containing enzyme (ceruloplasmin)[13]. In diabetes mellitus, oxidative stress seems primarily due to both increased plasma free radical concentrations and a sharp reduction in antioxidant defense. Loven et al (1992) found that there is no statistically significant difference in serum copper concentrations between healthy pregnant women and women with GDM[14].

Conclusion:

Analyzing the finding of the present study, significant alteration in Serum Copper levels were observed in GDM Patients. This study was done within the context of the facilities available to us, it has got some limitation. As the study was case-control the population size was small. Further studies with large number of subjects and with the application of modern sophisticated technology was required to give a conclusive decision.

Therefore it might be recommended that estimation of this biochemical parameter in GDM patients should be carried out for earlier detection and management the complications of GDM.

References:

1. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: a World Health Organization Guideline. Diabetes Res Clin Pract. 2014;103:341–3632.

2. Buckl, Dunne F. and on behalf of the DALI Core Investigator Group.2012. Gestational diabetes mellitus in Europe: ey, B. S, Harreiter, J , Damm P, Corcoy, R , Chico, A, Simmons, D, Vellinga, Aprevalence, current screening practice and barrier to screening. A review. Diabet. Med. 844–854.

3. Kim, C, Newton, KM. & Knopp, RH. 2002. Gestational diabetes and the incidence of type 2 diabetes. Diabetes Care .25,1862–8.

4. Gokcel,A.,Bagis,T.,Killicadag, E.B.,Tarim, E. & Guvener,N. 2002.Comparison of the criteria for gestational diabetes mellitus by NDDG and Carpenter and Coustan, and the outcomes of pregnancy. J Endocrinol Invest ,25,357-61.

5. Alam, M.R. 2006.Gross and Histomorphologic study of Umbilical cord in pre-gestational diabetes mellitus (thesis). BSMMU; Bangladesh.

6. Reece, EA, Wu,YK.& Wiznitzer. A.1998 role of free radical in membrane lipid induced congenitalmalformation. J Soc Gynaecol Invest. 5(9),178-187.

7. Jovanovic P. and Peterson.1996.Vitamin and mineral deficiency which may predispose to glucose intolerance of pregnancy. J.Am,coll,Nutr.15(1),14-20.

8. Wang,Y., Tan, M., Huang, Z., Sheng, L., Ge, Y., Zhang, H., Jiang, M. et al. 2002.Elemental contents in serum of pregnant women with gestational diabetes mellitus. Biol Trace Elem Res. 88(2):113-118.

9. Ajose,A., Fasubaa, B., Anetor, J.I., Adelekan, D.A. and Makinde, N.O. 2001. Serum zinc and copper concentrations in Nigerian women with normal pregnancy. Niger Postgrad Med ,J; 8: 161-164.

10. Khadam H. Level of serum Copper and Zinc in pregnant Women with Gestational Diabetes Mellitus. J Fac Med Bagdad. 2005’ 17 (3):287-289.

11. Fox, P, Mukhopadhyay, C. and Ehrenwald, E. 1995. Structure, oxidantactivity and cardiovascular mechanisms of human ceruloplasmin. Life Sci.56:1749-1758.

12. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia. Geneva: World Health Organization; 2013.

13. Black, R.E. 2001. Micronutrients in pregnancy. British Journal of Nutrition. 85: 193-S7.

14. Loven A, Romem Y, Pelly IZ, Holeberg G and Agam G.1992. Copper metabolism--a factor in gestational diabetes? Clin chim Acta.31:213(1-3):51-9.

DCIMC

Original Article

DCIMCJ 2018 January; 5(1):68-76

Pattern of Complications and Its Relation with Glycaemic Status in Hospitalized Type 2 Diabetic Patients

Nessa A[1], Chowdhury RH[2], Pathan MF[3]

Abstract:

Objective: To find out pattern (Macrovascular and microvascular) of complications in hospitalized subjects with type 2 diabetes mellitus. Methodology: This cross sectional study was carried out enrolling 2000 hospitalized subjects with type 2 diabetes, in the BIRDEM General Hospital, Dhaka, over a period of six months. Results: Among 2000 subjects, mean age was 50.86±14.46 years and male were 64.85% and rests 35.15% were female. The study subjects had hypertension (65.95%), dyslipidaemia (84.5%), Alcoholism (0.6%) and history of smoking (35.5%) as pre-existing risk factors. Majority of the subjects (62%) had BMI between 23.01 to 24.99 kg/m^2 with mean BMI 24.83(±3.27) kg/m^2. Among 2000 diabetic subjects, 19% (380) had no complication. Remaining 81% (1620) patients had diabetic complications. Acute complications of the study subjects were DKA (0.04%), HHS (0.07%) and hypoglycemia (1.41%). Among the microvascular complications nephropathy, neuroparhy and retinopathy were found respectively in 37.4%, 43.51% and 50.18% cases of study subjects. IHD, stroke and PVD as Macrovascular complications were found in 35%, 24.24% and 18.64% cases respectively. It was revealed, all the subjects with diabetic complications had uncontrolled blood glucose (Mean FBG- 9.2±2.02 mmol/L, mean PPBG- 11.8±2.15 mmol/L and mean Hb A_{1C}- 9.7±2.05%. Majority (52.6%) of the subjects with diabetic complications had suffered from diabetes for 5 to 10 years. Conclusion: From the study result it was concluded that type 2 diabetic subjects presented with both microvascular and macrovascular complication along with acute major complications like DKA, HONK and hypoglycemia. So, from the gathered information from the present study, it could be noted that in case of patients with type 2 diabetes, these common complications should be kept in mind along with their relation with glycaemic status of the patients and duration of diabetes to provide better management.

Keywords: Type 2 diabetes mellitus, glycaemic status, macrovascular complications, microvascular complications

Introduction:

Diabetes mellitus (DM) is a metabolic disorder that is characterized by persistently high blood glucose in the context of insulin resistance and relative insulin deficiency[1, 2]. Diabetes requires long-term medical attention to limit the development of its devastating complications and to manage them when they do occur.

1. Dr Azimun Nessa, Senior Medical Officer, Department of Endocrinology, BIRDEM General Hospital.

2. Dr Rubyat Hasan Chowdhury, Senior Medical Officer, Department of Cardiology & CCU, BIRDEM General Hospital.

3. Prof Md Faruque Pathan, Professor & Head, Department of Endocrinology, BIRDEM General Hospital.

Correspondence: Dr Azimun Nessa
E-mail: sheuly_39@yahoo.com

It is a disproportionately expensive disease; in the United States in 2007, the direct medical costs of diabetes were $116 billion, and the total costs were $174 billion; people with diabetes had average medical expenditures 2.3 times those of people without diabetes. The emergency department utilization rate by people with diabetes is twice that of the unaffected population[3,4].

Diabetes affects 8.3% of Americans of all ages, 11.3% of adults aged 20 years and older, and 25% of persons age 65 and older, according to the National Diabetes Fact Sheet for 2011[5]. About 27% of those with diabetes-7 million Americans-do not know that they have the disease. About 215,000 people younger than 20 years had diabetes (type 1 or type 2) in the United States in 2010[1,5]. Data from different surveys in USA showed that in 2010, total

20,676,427 patients were suffering from diabetes, with prevalence of different complications per 10,000 population being 45.5 for MI, 52.9 for stroke, 28.4 for amputation, 20.0 for ESRD and 1.5 for death from hyperglycemic crisis[6]. Despite the advent of novel methods for diagnosis and management, incidence of Diabetes is increasing.

Diabetic retinopathy may be the most common microvascular complication of diabetes. It is responsible for ~ 10,000 new cases of blindness every year in the United States alone. Development of diabetic retinopathy in patients with type 2 diabetes was found to be related to both severity of hyperglycemia and presence of hypertension in the U.K. Prospective Diabetes Study (UKPDS)[3,7,8].

Diabetic neuropathy may manifest in several different forms, including sensory, focal/multifocal, and autonomic neuropathies. More than 80% of amputations occur after foot ulceration or injury, which can result from diabetic neuropathy. Because of the considerable morbidity and mortality that can result from diabetic neuropathy, it is important for clinicians to understand its manifestations, prevention, and treatment[4].

Diabetic nephropathy is a chronic condition developing over many years, characterized by gradually increasing urinary albumin excretion (UAE) and blood pressure (BP). The risk of cardiovascular disease (CVD) increases dramatically as renal disease progresses. Diabetic kidney disease occurs in 20–40% of patients with diabetes and is a leading cause of ESRD[9].

There is little data regarding the pattern of complications of type 2 DM in recent years in Bangladesh. In this background this study was performed to find out pattern of complications of type 2 DM in BIRDEM General Hospital. The study will help in planning better management strategies to prevent development of complications and minimize the total treatment cost.

Materials and methods:

This cross sectional descriptive study was carried out on 2000 subjects aged 30-66 years in BIRDEM General Hospital, Dhaka, from July 2013 to December 2013. Study subjects were collected from in-patient departments of BIRDEM General Hospital using stratified random sampling. Each day two wards (One male ward and one female ward) were selected by lottery from in-patient department. Data was collected from every even number patient from their guide books and hospital records. The selection criteria included all adult type 2 diabetic subjects of both sexes willing to participate in the study. Those having Type-1 diabetes or unwilling to participate were excluded.

Patients were thoroughly informed about the aims, objectives and detail procedure of the study before examination. He/She was encouraged for voluntary participation and allowed freedom to withdraw from the study whenever she liked even after participation. From all eligible subjects after getting consent clinical history was taken and clinical examination was done. Reports of relevant investigations were recorded, and no investigation was advised by the investigator. Serum creatinine level was recorded to assess nephropathy along with ultrasonographic findings. To assess the presence of diabetic retinopathy, findings of fundus examination performed by an ophthalmologist following mydriasis of both eyes with tropicamide and phenylephrine eye drops were recorded. Retinopathy was grouped into proliferative and non-proliferative. Patients filled up a questionnaire about their symptoms such as a feeling of pins and needles, abnormal cold or warm sensations in their feet, sharp pain, aching pain, or irritation to feet or legs by bedclothes at night. Stroke was diagnosed by clinical and imaging records where available. CVD was diagnosed by ECG and echocardiograpgy reports. Related investigation reports of RBS, lipid profile and serum creatinine were also collected. Clinical examination and laboratory tests were done and data collected.

Demographic information was prospectively recorded and substantiated by means of inspection of medical record.

Ethical considerations:

Prior to the commencement of this study the research protocol was approved by Ethical Review Committee, Diabetes Association of Bangladesh. The objectives of this study along with risks and benefit were fully explained to the subjects in easily understandable local language and then informed written consent was taken from each patient.

Results:

A total of 2000 cases were included in the study. The mean age was 50.86±14.46 years. Majority (43.6%) of the respondents were found in the age group of 41-50 years. Among the study subjects, 64.85% (1297) were male and rest 35.15% (703) were female (Fig-1).

Majority of the subjects [1240 (62%)] had BMI between 23.01 to 24,99 kg/m^2, and 420 (21%) had BMI above 25 kg/m^2. Hypertension (65.95%), dyslipidemia (84.5%) and smoking (35.5%) were found as pre-existing risk factors.

Among the study subjects, 19% (380) had no chronic diabetic complication. Of the remaining subjects, 557(27.85%) had only micrvascular complications, 268(13.4%) had only macrovascular and 795(39.75%) had both micro and macrovascular complications. Retinopathy (50.18%) was the most prevalent microvascular complication, followed by neuropathy (43.51%) and nephropathy (37.4%). Regarding macrovascular complications, IHD (35%) was most common, followed by stroke (25.24%) and peripheral vascular disease (18.64%). Acute complications of the study subjects were DKA (Diabetic ketoacidosis) (0.04%), HHS (Hyperglycemic Hyperosmolar State) (0.07%) and Hypoglycemia (1.41%).

Regarding biochemical profiles, there was no significant difference between microvascular and macrovascular complication groups. Mean serum creatinine level was 1.80±0.4 mg/dl in microvascular and 1.70±0.7 mg/dl among subjects with macrovascular complications. Post prandial blood sugar was 14.5±1.81 and 15.1±2.5 mmol/l in microvascular and macrovascular group respectively. HbA_{1C} was 9.6±2.8% and 9.5±1.3% respectively in microvascular and macrovascular groups. Serum triglyceride was 285±152 mg/dl in microvascular and 298±163 mg/dl in macrovascular groups. HDL levels were 39.73±13.23 mg/dl and 35.15±12.94 mg/dl in two groups respectively. Mean LDL levels were 130±53.7 mg/dl and 126±43.7 mg/dl in macrovascular and microvascular group respectively. Mean serum creatinine was 0.7±0.3 mg/dl, fasting blood sugar 7.2±0.5 mmol/l, post prandial blood sugar 12.2±1.8 mmol/l, Hb A_{1C} was 7.5±0.5%, cholesterol 198±15.5 mg/dl, HDL 40±5 mg/dl and LDL was 100±10 mg/dl in diabetic subjects without complication (Table-I).

Among the study subjects, those having uncontrolled (more than 10 mmol/l) fasting and peak postprandial blood glucose and high HbA_{1c} (>9%) were prone to develop complications. The chance of complications were also highest (52.6%) in patients with duration of diabetes 5-10 years.

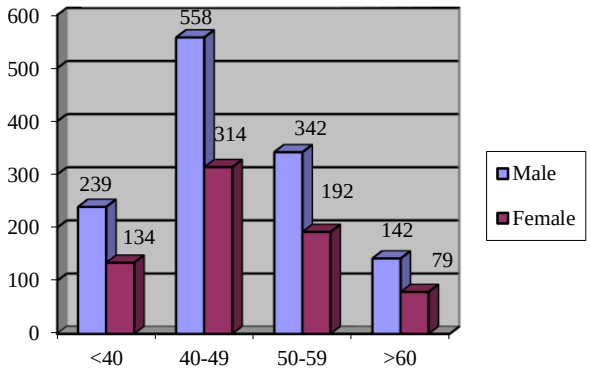


Figure 1: Age and gender distribution of the study subjects (N=2000)

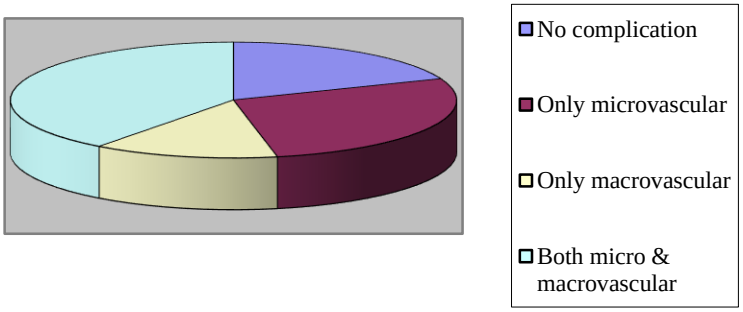


Figure-2: Distribution of study subjects according to complications (N=2000)

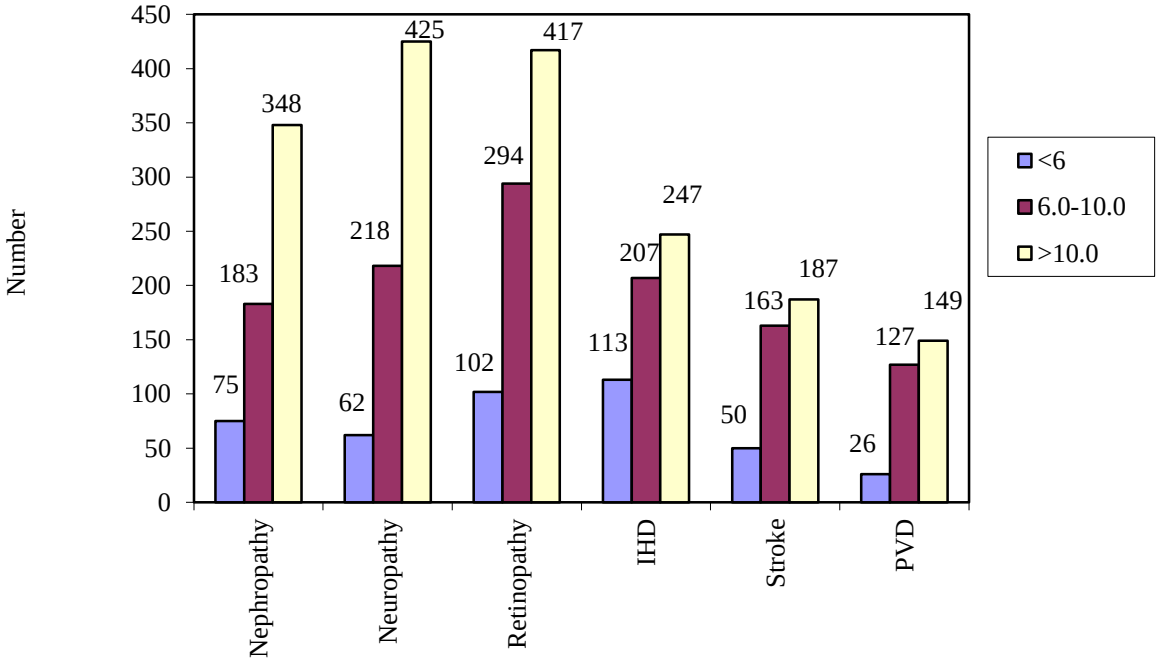


Figure 3: Distribution of different complications according to different values of fasting blood glucose (mmol/L) (N=1620)

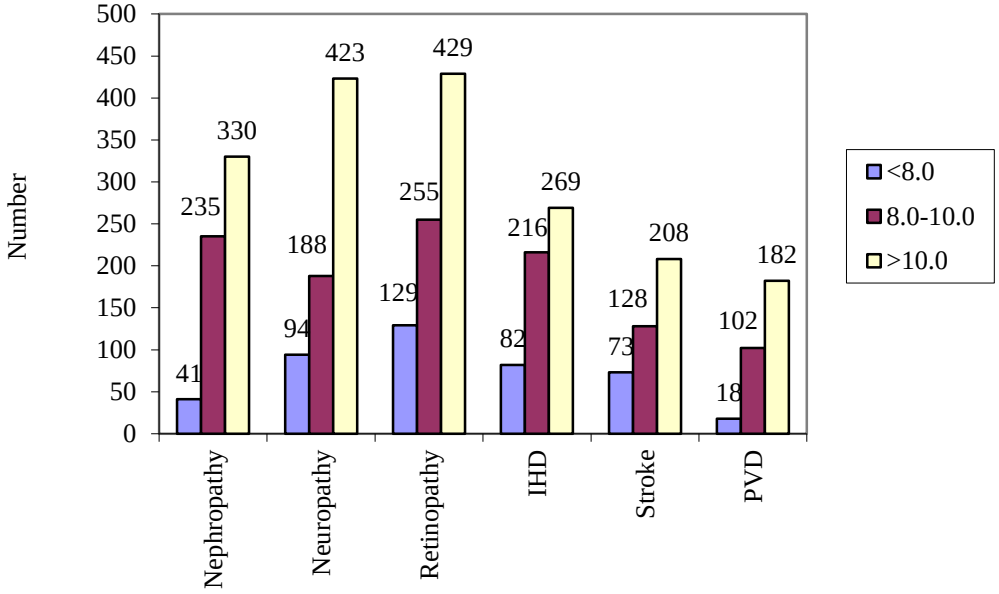


Figure 4: Distribution of different complications according to different values of postprandial blood glucose (mmol/L) (N=1620)

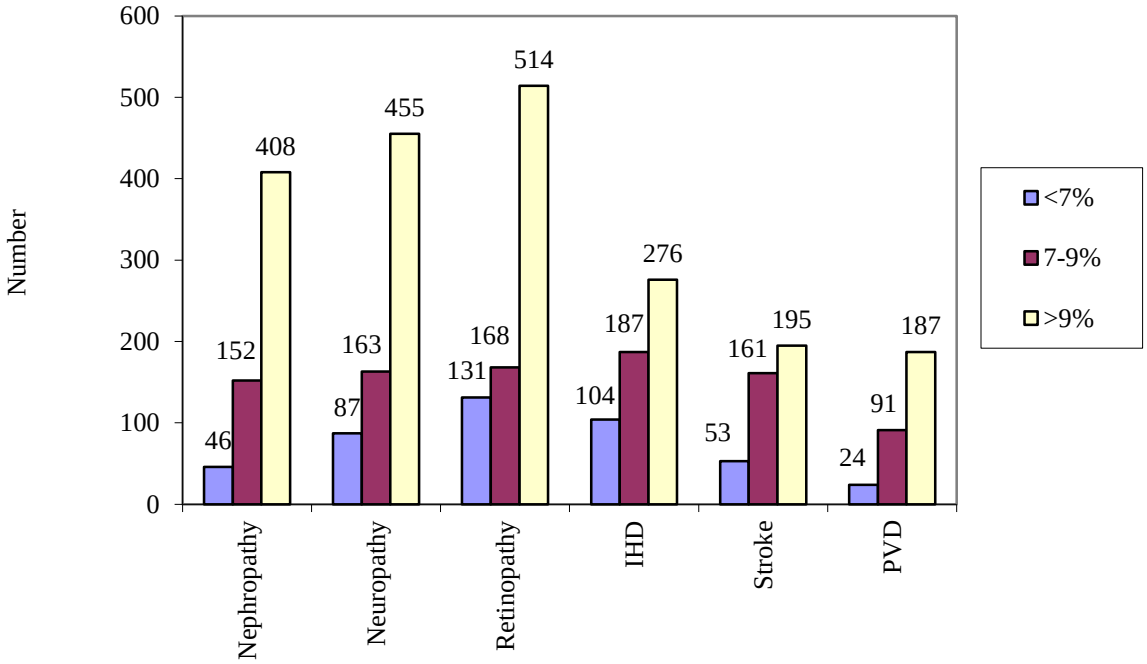


Figure 5: Distribution of different complications according to different values of HbA_{1c} (N=1620)

Table I: Laboratory findings of the study subjects (N=2000)

Laboratory parameters	Subjects without complications	Subjects with complications	
		Macrovascular group	Microvascular group
Serum Creatinine (mg/dl)	0.7±0.3	1.70±0.7	1.80±0.4
Fasting blood sugar (mmol/l)	7.2±0.5	10.3±2.81	10.8±1.24
Post prandial blood sugar (mmol/l)	12.2±1.8	15.1±2.5	14.5±1.81
Hb A_1C%	7.5±0.5	9.5±1.3	9.6±2.8
Cholesterol (mg/dl)	198±15.5	246±61.4	255±81.9
Triglyceride (mg/dl)	160±17	298±163	285±152
HDL (mg/dl)	40±5	35.15±12.94	39.73±13.23
LDL (mg/dl)	100±10	126±43.7	130±53.7

Table II: Microvascular complications of hospitalized type 2 diabetic subjects (N=1620)

Microvascular complications	n	%
Nephropathy	606	37.40
Neuropathy	705	43.51
Retinopathy	813	50.18

Table III: Macrovascular complications of hospitalized type 2 diabetic subjects (N=1620)

Macrovascular complications	n	%
IHD	567	35.00
Stroke	409	25.24
PVD	302	18.64

Table IV: Distribution of the subjects with complications according to duration of diabetes (N=2000)

Complications	Duration of diabetes in years N(%)		
	≤5	5-10	≥10
Microvascular			
Nephropathy (n=606)	49(8%)	272(44.8%)	285(47%)
Retinopathy (n=813)	73(8.9%)	429(52.7%)	311(38.2%)
Neuropathy (n=705)	55(7.8%)	394(55.8%)	256(36.3%)
Macrovascular			
IHD (n=567)	72(12.6%)	404(71.2%)	91(16%)
Stroke (n=409)	49(11.9%)	242(59.1%)	118(28.8%)
PVD (n=302)	54(17.8%)	217(71.8%)	31(10.2%)
Total (2000)	**609(30%)**	**1053(52.6%)**	**338(16.9%)**

Discussion:

The objective of this study was to describe the pattern of complications in hospitalized subjects with type 2 diabetes mellitus. Two-thousand diabetic patients were included in the study, having mean age of 50.86±14.46 years. Majority (43.6%) of the respondents were found in the age group of 41-50 years. Among the patietnts, 64.85% (1297) were male and rests 35.15% (703) were female. This is the common epidemiological feature regarding age-gender distribution of type 2 DM[1,2,5].

The present study revealed that the study subjects had hypertension (65.95%), dyslipidaemia (84.5%) and smoking (35.5%) as pre-existing risk factors. It is a well known fact that sedentary life style, obesity, hypertension, tobacco or alcohol intake, positive family history had relation with DM[1,2,5,10,11].

Glycemic status was unsatisfactory in most of the patients, documented by HbA1c levels 7.5±0.5%, 9.6±2.8% and 9.5±1.3% in patients without complications, with macrovascular complications and with microvascular complications respectively. Theer was also raised Triglycerides, total and LDL cholesterol and low HDL cholesterol levels in all groups. A comparable study in Bangladesh showed deteriorating glycaemic control with mean HbAlc of 8.6 ± 2.0%. 70.8% of patients had LDL levels >2.6 mmol/L; 43.8% had triglycerides >2.2 mmol/L; 44.1% had HDL<1 mmol/L despite 48% of the patients being on lipid lowering agents[12].

Among the study subjects, 19% (360) had no complication, and remaining 81% (1620) subjects had diabetic complications. Diabetic retinopathy (50.18%) and IHD (35%) were the commonest microvascular and macrovascular complications. Both micro and macrovascular complications were associated with duration of diabetes and poor glycaemic control. These findings are consistent with the previous studies. A cross sectional study revealed that 45.7% of type 2 diabetic subjects had nephropathy and 29.5% had peripheral neuropathy[13].

In a comparable study the overall prevalence of retinopathy was 37.8%[14]. Retinopathy and peripheral neuropathy were seen in 31.4% and 35.2% of the subjects in another study [15].

Harrzallah et al. found neuropathy in 24%, nephropathy in 13%, retinopathy 8% and hypertension in 22% of diabetic patients[16]. In another study conducted by Weerasuriya in Sri Lanakan diabetic patients, neuropathy was present in 25.1 %, nephropathy in 29%, retinopathy in 15% and hypertension in 23%[17]. Another study showed that the frequency of positive screening tests for hyperlipidemia, hypertension, neuropathy, nephropathy and retinopathy was found to be 73.5%, 58.5%, 52%, 10%, and 6% respectively in diabetic subjects[18]. A similar study in Bangladesh showed microvascular, macrovascular and severe late complications were present in 39.2%, 9.9% and 12.1% patients respectively[12]. It was observed that incidence of clinical complications was significantly associated with glycaemia and in patients with type 2 diabetes the risk of diabetic complications was strongly associated with previous hyperglycaemia as well as any reduction in HbA_{1c} was likely to reduce the risk of complications, with the lowest risk being in those with HbA_{1c} values in the normal range (<6.0%)[19].

Limitations:

The study had several limitations. The original sample size was relatively small in relation to huge number of diabetic population in our country. As the study period was only six months, large sample could not be included and follow up could not be done. Data was collected from only one center, which may not represent the picture of whole country.

Conclusion:

From the study result it is evident that a significant proportion of the type 2 diabetic subjects in our country are suffering from microvascular and macrovascular complications along with acute major complications like DKA, HHS and hypoglycemia. Poor glycemic control and long duration of diabetes are important risk factors for the development of these complications. Therefore, physicians should try to prevent the occurrence of complications by optimum control of diabetes, and routinely screen for the detection of complications at the earliest possible time.

References:

1. Sayeed MA, Mahtab H, Khanam PA, Latif ZA, Ali SMK, Banu A, Ahren B, Khan AKA. Diabetes and impaired fasting glycemia in a rural population of Bangladesh. Diabetes Care. 2003; 26:1034–1039.

2. Hussain A, Rahim MA, Khan AKA, Ali SM, Vaaler S. Type 2 diabetes in rural and urban population: diverse prevalence and associated risk factors in Bangladesh. Diabet Med. 2005; 22:931–936.

3. Watkins PJ. Retinopathy. BMJ. 2003; 326:924 - 926.

4. American Diabetes Association. Standards of medical care in diabetes--2012. Diabetes Care. 2012; 35: 11-63.

5. Rahim MA, Hussain A, Khan AKA, Sayeed MA, Ali SMK, Vaaler S. Rising prevalence of type 2 diabetes in rural Bangladesh: a population based study. Diabetes Res Clin Pract. 2007; 77:300–305.

6. Gregg EW, Li Y, Wang J, Burrows NR, Ali MK, Rolka D, Williams DE, Geiss L. Changes in Diabetes-Related Complications. in the United States, 1990–2010. N Engl J Med. 2014;370:1514-23.

7. Fong DS, Aiello LP, Ferris FL 3rd, Klein R. Diabetic retinopathy. Diabetes Care. 2004; 27:2540 -2553.

8. Keenan HA, Costacou T, Sun JK, Doria A, Cavellerano J, Coney J, Orchard TJ, Aiello LP, King GL. Clinical factors associated with resistance to microvascular complications in diabetic patients of extreme disease duration: the 50-year medalist study. Diabetes Care. 2007; 30: 1995-1997.

9. Tuttle KR, Bakris GL, Bilous RW. Diabetic kidney disease: a report from an ADA Consensus Conference. Diabetes Care. 2014;37: 2864–83.

10. Hoque MA, Islam MS, Khan MAM, Nazmul HAM. Knowledge of diabetic complications in a Diabetic population. J Medicine. 2009; 10: 90-93.

11. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004; 27:1047–1053.

12. Latif ZA, Jain A, Rahman MM. Evaluation of management, control, complications and psychosocial aspects of diabetics in Bangladesh: DiabCare Bangladesh 2008. Bangladesh Med Res Counc Bull. 2011; 37(1):11-6.

13. Seyum B, Mengistu Z, Berhanu P, Abdulkadir J, Feleke Y, Worku Y, Ayana G. Retinopathy in Tikur Anbessa hospital diabetic clinic. Ethiop Med J. 2001; 39(2):123–131.

14. Worku D, Hamza L, Woldemichael K. Patterns of Diabetic Complications at Jimma University Specialized Hospital, Southwest Ethiopia. Ethop J Health Sci. 2010; 20: 33-39.

15. Ejigu A. Patterns of chronic complications of diabetic patients in Menelik II Hospital, Ethiopia. Ethiopian Journal of Health Development. 2000; 14: 113-116.

16. Harzallah F, Ncibi N, Alberti H, Brahim AB, Smadhi H, Kanoun F et al. Clinical and metabolic characteristics of newly diagnosed diabetes patients: experience of a university hospital in Tunis. Diabetes Metab. 2006; 32 (6): 632–635.

17. Weerasuriya N, Siribaddana S, Dissanayake A, Subasinghe S, Wariyapola D, Fernando DJ. Long-term complications in newly diagnosed Sri Lankan patients with type 2 diabetes mellitus. QJM. 1998; 91 (6) 439–443.

18. Heydari I, Radi V, Razmjou S, Amiri A. Chronic complications of diabetes mellitus in newly diagnosed patients. Int Jour of DM. 2010; 2: 1-70.

19. Stratton IM, Adler AI, Neil HWN, Matthews DR et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000; 321(7258): 405–412.

Original Article

DCIMCJ 2018 January; 5(1):89-96

Role of Amnitomy on Duration of Labour in Primigravidae

Khatun J[1], Siddiqua NM[2]

Abstract:

Objective: To see the effects of amniotomy and spontaneous rupture of membrane on duration of labour in primigravidae. Study design: Observational Cross-sectional study. Study setting and period: Department of Obstetrics and Gynaecology, Sylhet MAG Osmani Medical College Hospital, Sylhet, between December 2014 to May 2015. Study population: All term primigravidae in active labour admitted in the Dept of obstetrics and Gynecology. Methods: Women in active phase of labour and having cervical dilatation > 4 cm were enrolled for the study. Women in whose ARM done were included in amniotomy group and whose membrane were allowed to rupture spontaneously were included in non-amniotomy group. Progress of labour was monitored by partograph. Time taken from the enrollment to full dilatation of cervix was noted. Mode of delivery, post delivery complications, foetal outcome and APGAR score of the baby at 1 and 5 minutes were recorded and documented. Relevant data from history, physical examination and investigations were recorded in predesigned questionnaire. Result: There was a significant decreased in duration labour both 1st and 2nd stage in amniotomy group. The mean duration of 1st stage was 3.52± 1.27 hr in amniotomy group and 7.36±2.19 hr in non-amniotomy group. The mean duration of 2nd stage was 1.04± 0.51 hr in amniotomy group and 1.64± 0.55 hr in non-amniotomy group and the differences were statistically significant (p<0.05) between two groups. Most of the patients were delivered by normal vaginal delivery and LUCS was done in 18% patients of amniotomy group and 22 % in non-amniotomy group, the difference were not statistically significant (p>0.05) between two groups. Conclusion: Amniotomy significantly reduces the duration of labour when compared with the leaving the membranes intact until second stage without any effect on delivery outcome in the newborn or mother.

Keywords: Amniotomy, Labour

Introduction:

Labour has been termed the most dangerous journey a human ever under takes. The reason being that although it is a natural process but complications can arise at any time during its course[1]. Normal labour is a continuous process that has been divided into three stages[2]. First stage duration is 12 hours in primigravidae and 6hours in mutiparae, second stage duration is 2 hours in primigravidae and 30 minutes in multiparae, third stage duration is about 15 minutes in both primigravidae and in multiparae[3]. Amniotomy also called artificial rupture of membranes (ARM) is an intervention to induce or augment the labour[4]. Amniotomy was first introduced by Thomas Denman of Middlesex hospital in 1756[5]. It has long been in obstetric practice because of general belief that it reduces the duration of labourr[6-8]. When tension is by spontaneous or artificial rupture of membrane the presenting part directly press the cervix and force of distension of the cervix increased after rupture of membrane[9]. Amniotomy reduces length of labour. Amniotomy also detects meconium staining of amniotic fluid during foetal distress by direct examination of liqour where modern facilities of fetal monitoring is not easily available[10].

Amniotomy is a common obstetrical procedure with both benefits and risks. It has been associated with a 60-120 min reduction in labour duration mainly in nulliparae with no evidence of increased likelihood of fetal heart rate abnormalities or adverse neonatal outcomes[11]. Several studies in this regard revealed amniotomy to be effective in shortening delivery and decreasing variability of 5th minute Apgar score and that is why it is used extensively[12].

Materials and methods:

This study was a hospital based Observational cross sectional study, carried out in IPD (inpatient

1. Dr. Jamila Khatun, Associate Professor, Department of Obstetrics and Gynecology, Sylhet M.A.G Osmani Medical College, Sylhet.

2. Dr. Noor Mahal Siddiqua, Honorary Medical Officer, Department of Obstetrics and Gynecology, Sylhet M.A.G Osmani Medical College and Hospital, Sylhet.

Correspondence: Dr. Jamila Khatun
E-mail: mirshah1962@gmail.com.

Materials and methods:

This study was a hospital based Observational cross sectional study, carried out in IPD (inpatient department) of Obstetrics and Gynecology of Sylhet M.A.G Osmani Medical College and Hospital, Sylhet in between December 2014 to May 2015. Total 100 pregnant women in active labour (50 cases of amniotomy group and another 50 women were spontaneous rupture of membrane) were enrolled in this study. Data was collected by using a preformed questionnaire and check list. Cases were selected according to inclusion and exclusion criteria. Relevant infromations (according to questionnaire) were taken from patients. Women in whose ARM done were included in amniotomy group and whose membrane were allowed to rupture spontaneously were included in non-amniotomy group. Foetal heart rate was monitored by intermittent auscultation and progress of labour was monitored by partograph. Time taken from the enrollment to full dilatation of cervix was noted. Data was processed manually and analyzed with the help of SPSS (Statistical package for social sciences) Version 16.0.

Results:-

Total 100 primigravida in active labour were included in this study. There was a significant decrease in duration of labour (both 1st and 2nd stage) in amniotomy group. The mean duration of 1st stage was 3.52± 1.27 hour in amniotomy group and 7.36±2.19 hour in non-amniotomy group. The mean duration of 2nd stage was 1.04± 0.51 hr in amniotomy group and 1.64± 0.55 hr in non-amniotomy group. The differences were statistically significant ($p<0.05$) between two groups. Most of the patients were delivered by normal vaginal delivery. LUCS was done in only 18% patients of amniotomy group and 22% of non-amniotomy group, with no statistically significant difference between two groups($p>0.05$).

Table-I: Distribution of study patients according to age, height, weight, occupation and socio-economic condition:

Parameter	Amniotomy group (N= 50)		Non-amniotomy group (N= 50)		P-value
	n	%	n	%	
Age in year					
<20	9	18.0	7	14.0	0.59
20 – 25	36	72.0	39	78.0	0.49
>25	5	10	4	8.0	0.73
Mean ±SD	22.06±2.43		22.12±2.24		0.90
Height in cm					
< 150	13	26.0	15	30.0	0.66
150 – 155	29	58.0	28	56.0	0.84
>155	8	16.0	7	14.0	0.78
Mean ±SD	150.86±4.83		150.68±4.51		0.85

Parameter	Amniotomy group (N=50)		Non-amniotomy group (N= 50)		P-value
	n	(%)	n	(%)	
Weight in kg					
<55	9	18.0	11	22.0	0.62
55-65	35	70.0	34	68.0	0.83
>65	6	12.0	5	10.0	0.75
Mean ±SD	58.78±5.27		58.66±5.32		0.91
Occupation					
House wife	41	82.0	39	78.0	0.62
Teacher	4	8.0	5	10.0	0.73
Others	5	10.0	6	12.0	0.75
Socio-economic condition					
Lower class	23	46.0	26	52.0	0.55
Middle class	24	48.0	22	44.0	0.69
Upper class	3	6.0	2	4.0	0.65

Table-II: Distribution of study patients according to gestational age:

Gestational age(Wks)	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	n (%)	n (%)	
37- 38	8(16)	11(22)	0.44
39-40	37(74)	35(70)	0.66
41-42	5(10)	4(8)	0.73
Mean ±SD	39.16±1.71	39.24±1.13	0.78

The mean gestational age was 39.16±1.71 in amniotomy group and 39.24±1.13 in non-amniotomy group, but the difference was not statistically significant (p>0.05) between two groups.

Table-III: Duration of labour after enrollment:

Stage of labour	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	Mean±SD(Range)	Mean±SD(Range)	
Duration of 1st stage(hr)	3.52± 1.27(2, 6)	7.36±2.19(4, 11)	<0.00001
Duration of 2nd stage(hr)	1.04± 0.51 (0.5, 2)	1.64± 0.55 (0.7,2.5)	<0.00001

The mean duration of 1st stage was 3.52± 1.27 hr in amniotomy group and 7.36±2.19 hr in nonamniotomy group. The mean duration of 2nd stage was 1.04± 0.51 hr in amniotomy group and 1.64± 0.55 hr in non-amniotomy group and the difference was statistically significant ($p<0.05$) between two groups.

Table-IV: Distribution of study patients according to Mode of delivery:

Mode of delivery	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	n(%)	n(%)	
Normal vaginal delivery	38(76)	37(74)	0.82
Instrumental delivery	3(6)	2(4)	0.65
LUCS	9(18)	11(22)	0.62

76% had normal vaginal delivery, 6% had instrumental delivery and 18% had LUCS . In non-amniotomy group 74% had normal vaginal delivery, 4% had instrumental delivery and 22 % had LUCS, and the difference were not statistically significant ($p>0.05$) between two groups.

Table-V: Maternal complications during labour:

Complications	Amniotomy group (N= 11)	Non-amniotomy group (N= 16)	P-value
	n(%)	n(%)	
Cervical dystocia	2(4)	3(6)	0.65
Uterine inertia	1(2)	2(4)	0.56
Intrapartum eclampsia	1(2)	2(4)	0.56
Prolonged 2nd stage	4(8)	5(10)	0.73
Maternal distress	3(6)	4(8)	0.70

The difference of all maternal complications during labour were not statistically significant ($p>0.05$) between two groups.

Table-VI: Maternal complications after labour:

Complications	Amniotomy group (N= 11)	Non-amniotomy group (N= 16)	P-value
	n(%)	n(%)	
Perineal Tear	1(2)	1(2)	-
Post-partum haemorrhage	4(8)	5(10)	0.73
Cervical tear	2(4)	3(6)	0.65
Vaginal laceration	1(2)	1(2)	-
Uterine atony	1(2)	1(2)	-
Manual removal of placenta	1(2)	2(4)	0.56
Blood transfusion needed	1(2)	2(4)	0.56
Puerperial pyrexia	1(2)	1(2)	-

The difference of all maternal complications after labour were not statistically significant ($p>0.05$) between two groups.

Table-Vll: Distribution of study patients according to foetal out come:

Foetal out come	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	n(%)	n(%)	
Healthy baby	46(92)	44(88)	0.50
Asphyxiated	4(8)	5(10)	0.73
Still born	0(0)	1(2)	0.31
Admission to Neonatal ward	4(8)	5(10)	0.73

The difference was not statistically significant ($p>0.05$) between two groups.

Table-Vlll: Apgar score of the babies:

	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	n(%)	n(%)	
Apgar score at 1 minute			
<3	3(6)	4(8)	0.70
4 – 6	7(14)	9(18)	0.59
>7	40(80)	38(76)	0.63
Mean±SD	8.08±2.12	7.42± 2.25	0.13
Apgar score at 5 minute			
<3	1(2)	2(4)	0.56
4 – 6	3(6)	3(6)	-
>7	46(92)	45(90)	0.73
Mean±SD	8.94±1.38	8.64±1.87	0.63

The difference of Apgar score at 1 minute and 5 minute were not statistically significant (p>0.05) between two groups.

Discussion:

In this study it was observed that majority of the patients (72% in amniotomy group and 78% in non-amniotomy group) belonged to age group 20 to 25 years and the mean age was 22.06±2.43 in amniotomy group and 22.12±2.24 in non-amniotomy group. Which is comparable with the study of Mikki et al.[11] Abdullah et al.[13] and Rasheed et al[14].

In this study it was observed that more than half of women the mean height was 150.86±4.83 in amniotomy group and 150.68±4.51 in nonamniotomy group. It is consistent with the study by Ghani et al[9]. The mean weight was 58.78±5.27 in amniotomy group and 58.66±5.32 in non-amniotomy group. In a study by Mikki et al. found mean weight 75.6+10.8 kg in the intervention group and 73.8+10.7 kg in the controlled group which is higher than the present study[11]. It may be due to geographical variation of weight of the women.

In this present study it was observed that majority of the patients (74% in amniotomy group and 70% in non-amniotomy group) belong to 39 to 40 weeks of gestation and the mean gestational age was 39.16±1.71 in amniotomy group and 39.24±1.13 in nonamniotomy group. Abdullah et al.[13] found mean gestational age 38.41±1.03 weeks.

Amniotomy is associated with a reduction in labour duration of between 60 and 120 minutes[7]. In this present study the mean duration of 1st stage was 3.52 ± 1.27 hr in amniotomy group and 7.36± 2.19 hr in non-amniotomy group/ the mean duration of 2nd stage was 1.04± 0.51 hr in amniotomy group and 1.64± 0.55 hr in non-amniotomy group and the difference was

statistically significant ($p<0.05$) between two groups. This indicates that amniotomy significantly reduced the duration of both 1st and 2nd stage of labour. In a study by Abdullah et a1.[13] mean duration of labour was 6.66±1.41 in amniotomy group and 7.60±1.75 in spontaneous rupture of membrane group. It was significantly low in amniotomy group than in spontaneous rupture of membrane group. Another study by Bellad et al. found mean duration of 1st stage of labour 4.76±1.64 hours in amniotomy group and 5.66±1.85 hours in non-amniotomy group[15]. The duration labour was significantly lower in amniotomy group. Similar findings regarding duration of labour were also observed by Mikki et al.[11] and Ghani et al.[9] which are consistent with the present study.

There was no significant difference in the mode of delivery beween two group. It was observed that in amniotomy group 76% had normal vaginal delivery, 6% had instrumental delivery and 18% had LUCS . In non-amniotomy group 74% had normal vaginal delivery, 4% had instrumental delivery and 22 % had LUCS, and the difference were not statistically significant ($p>0.05$) between two groups. Similar findings regarding mode of delivery were also observed by Ghani et al.[9] Bellal et al[15] and Naseer et al[16].

It was observed that the difference of all maternal complications during and after labour were not statistically significant ($p>0.05$) between two groups. It is similar to study by Ghani et al[9]

Majority of the newborn were healthy (92% in amniotomy group and 88% in non-amniotomy group). apgar score at 1 minute and 5 minute were not statistically significant ($p>0.05$) between two groups.

Conclusion:

It is concluded from the study that, amniotomy significantly reduces the duration of labour when compared with the leaving the membranes intact until second stage without any effect in cesarean section rates or rate of operative vaginal delivery. It does not increase the risk of any adverse outcome in the newborn or mother.

References:

1. Javed I, Bhutta S, Shoaib T. Role of partogram in preventing prolonged labour. J Pak Med Assoc 2007; 57(8) :408-411.

2. Archie CL. The Course and Conduct of Normal Labor and Delivery. In: DeCherney AH, Nathan L, Goodwin TM, Laufer N, editors. Current Diagnosis and Treatment Obstetrics and Gynecology.10th ed. New York: McGraw-Hill; 2007. p. 203 211.

3. Normal Labour. In: Koner H, editors. D.0 Dutta's Text Book of Obstetrics. 17th ed. Kolkata: New Central Book Agency(P)Ltd; 2011. p. 113-143.

4. Wolomly JJ, Tozin RR. Amniotomy for shortening Spontaneous labour: RHL Commentary [last revised:5 Jan 2009]. The WHO Reproductive Health Liabrary; Geneva:WHO.

5. Calder AA. Induction and augmentation of labour: In: Edmonds DK, editor Dewhurst's textbook of obstetrics and gynaecology for postgraduates 6th edition. London: Blackwell Science; 1999. 255.

6. Ajadi MA, Kuti 0, Oriji EO, Ogunnivi SO, Sule SS. The effect of amniotomy on the outcome of spontaneous labour in uncomplicated pregnancy. J of Obstet Gynaecol 2006;26(7):631. 631-634.

7. Fraser WD, Turkot L, Krauss I, Carrol G. Amniotomy for shortening spontaneous labour Conchrane data base systemic reviews 2006; issue Art No.: CD000015.

8. Incerti M, Locatelli A,Ghidini A, Civiello E, Malberti S, Consonni S, et al. Prediction of duration of active labour in nulliparous women at term. Am J Perinat 2008;25:859.

9. Ghani T , Rahim A, Begum F, Mahmuda B. Amniotomy shortens the induction delivery interval CBMJ 2013 July; 02(02):67- 70.

10. Majeed N, Tariq S. Comparison of Artificial Rupture of Membranes with Intact Membrane in Labouring Multigravidae. JRMC 2013;17(2):234-237.

11. Mikki N, Wick L, Asab NA, Rmeileh NMEA . A trial of amniotomy in a Palestinian hospital. Journal of Obstetrics and Gynaecology, May 2007; 27(4): 368 — 373.

12. Olfati F, laluha F. Effect of amniotomy in latent phase and active phase on rate of cesarean section. Academia Journal of Medicine November 2012; 1: 5- 8.

13. Abdullah A, Saboohi S, Hashami U. Effects of Amniotomy versus Spontaneous Rupture of Membrane on Progress of Labour and Foetal Outcome in Primigravidae. JLUMHS January-April 2010; 09 (1): 33-36.

14. Rasheed FA, Ahmed AA, Hussain SA. The Impact of Early Versus Late Amniotomy on Duration of Labor, Maternal and Neonatal Outcomes in Iraqi Primigravida with Spontaneous Labor. Medscience, 2014; 3:8132.

15. Bellad MB, Kamal P, Rajeshwar P. Does Artificial Rupture of Membranes (ARM) Reduce Duration of Labor in Primigravidae: A Randomized Controlled Trial. South Asian Federation of Obstetrics and Gynecology, January-April 2010;2(1):37-39.

16. Naseer N, Hag G, Soomro N. Active Versus Expectant Management of Labour Study of 100 Cases. Pakistan Journal of Surgery; 25(4): 274-278.

Original Artical

DCIMCJ 2018 January; 5(1):82-88

Evaluation of Marker Specific Outcome Study in Patients with Acute Coronary Syndrome

Parvin D[1], Baul SK[2], Hossain MSR[3], Hadiuzzaman M[4], Fatema K[5], Chowdhury FA[6], Nazneen M[7], Hoque MM[8]

Abstract:

Background: A life-threatening manifestation of coronary artery disease is acute coronary syndrome (ACS) that ranges from unstable angina (UA) to acute myocardial infarction (AMI). A prognostic indicator should be available at the time of initial patient's evaluation in order to maximize the potential benefits of early risk assessment. Objectives: This study was designed to evaluate plasma BNP as a prognostic tool in patients with ACS. Methodology: A prognostic cohort study was carried out to evaluate the plasma BNP as a prognostic tool in acute coronary syndrome. In this study, 90 ACS cases were enrolled from the cardiology emergency department. Plasma BNP concentrations were measured on enrollment and then grouping of the study subjects were done on the basis of their empirical cut off value of plasma BNP concentration 640pg/ml. Results: Group I includes 57 (63.3%) subjects with plasma BNP concentration less than 640pg/ml and group II includes 33 (36.7%) subjects with plasma BNP concentration above 640pg/ml. After conventional treatment and periodical follow up patients were assessed clinically for any kind of clinical outcomes. Patients clinical outcome were evaluated on the perspective of their baseline plasma BNP concentration. In group II patients having high baseline plasma BNP concentration significantly less good outcome but significantly high bad outcome found compared to those in group I patients having low plasma BNP concentration (p-0.000).Conclusion: Higher bad clinical outcomes in group II compared to group I indicates that the increasing baseline plasma BNP concentration is associated with worsening clinical outcome.

Keywords: BNP, Acute coronary syndrome, unstable angina, acute myocardial infarction

Introduction:

In both developed and developing countries, coronary heart disease (CHD) is the leading cause of mortality and morbidity worldwide affecting millions of peoples.Cardiovascular disease continues to be the major cause of death in USA, Europe, and part of Asia[1]. About 80% of the deaths due to ischemic heart disease (IHD) occurred in the developing world mostly in South Asia. It has been observed that prevalence of CHD is higher in South Asians, with the highest rates among Bangladeshi and Pakistani origins[2]. Acute coronary syndrome (ACS) encompass a continuum of cardiac ischemic event ranging from unstable angina (UA) with no evidence of biochemical necrosis to non ST- elevation myocardial infarction (NSTEMI) and ST- elevation myocardial infarction (STEMI)[3]. Acute coronary syndrome is a common presentation of ischemic heart disease (IHD). The South Asian countries like India, Pakistan, Bangladesh, Sri Lanka and Nepal accounts for about a quarter of the world's population and contribute to the highest proportion of cardiovascular disease burden compared with any other region globally[4]. Following recovery from an acute episode of ACS, patients continue to be at heightened risk of heart attack and stroke for which a range of secondary preventive treatment are available[5].

1. Dr. Dilshad Parvin, Assistant Professor, Department of Clinical Biochemistry, NICVD & H, Dhaka.
2. Dr. Sunil Krishna Baul, Associate Professor, Department of Biochemistry, Satkhira Medical College.
3. Dr. S. M Rahat Hossain, Assistant Professor, Department of Microbiology, Sheikh Hasina Medical College, Tangail.
4. Dr. Md. Hadiuzzaman, Assistant Professor, Department of Biochemistry, Sheikh Shayera Khatun Medical College, Gopalgonj.
5. Dr. Kaniz Fatema, Medical Officer, NICVD & H, Dhaka.
6. Dr. Farzana Ahmed Chowdhury, Biochemist, NICVD & H, Dhaka.
7. Prof. Mafruha Nazneen, Head, Department of Biochemistry, Dhaka Central International Medical College.
8. Prof. Md. Mozammel Hoque, Professor and Chairman, Department of Biochemistry, BSMMU, Dhaka.

Correspondence: Dr. Dilshad Parvin
E-mail: drsdilshad72@gmail.com

Because atherosclerotic plaque is often present throughout the arterial tree, patients who survive after an episode of ACS live with an ongoing risk of recurrent acute cardiovascular event, AMI, sudden cardiac death or stroke[6]. In contrast to the injury markers, newly identified serum substances have drawn attention for their ability to portend acute coronary events and their outcomes. Now biomarkers like natriuretic peptide may provide additional pathophysiological insight and add to the strategy for comprehensive assessment[7]. B-type natriuretic peptide (BNP) is a 32 amino acid neurohormone (peptide) released from ventricular myocardium predominantly in response to increased ventricular wall stress, ventricular dilatation, and pressure overload[8]. Along with atrial natriuretic peptide (ANP), BNP has effects on natriuresis, diuresis, vasodilatation and inhibition of rennin-angiotensin-aldosterone system and sympathetic nervous system; all of which contribute to the modulation and control of cardiovascular hemodynamics[9,10]. Plasma BNP concentration increases in patients with CCF in proportion to the degree of left ventricular dysfunction and the severity of heart failure[11]. BNP have been shown to aid in the diagnosis of heart failure and to correlate with left ventricular dilatation, remodeling, dysfunction and the mortality among patients presenting with AMI[12,13]. After AMI, BNP concentration rises rapidly during the first 24 hours and then tends to stabilize[14] There is an association between BNP and the short and long term risk of death across the spectrum of ACS including patients without myocardial necrosis or clinical evidence of heart failure[15,16]. Plasma BNP concentration measured between one to four days after a transmural infarction provides prognostic information that is independent of the left ventricular ejection fraction and other important baseline variables[17]. The association between BNP and long term risk of death in ACS is independent of cardiac function, renal function, the troponin I level, electrocardiographic changes and other known risk predictors[18]. BNP is an independent marker for risk stratification in ACS patients. So, elevated level of plasma BNP in ACS patient is serious enough to warrant the follow up examination. Studies evaluating the prognostic implications of BNP have been limited to patients with myocardial infarction with ST segment elevation and few data are available on patients who have ACS without ST segment elevation.

Material & Method:

The present cohort study was conducted in the Dept. of Biochemistry, BSMMU, NICVD & BIRDEM Dhaka, Bangladesh during the period from January 2009 to December 2009.

A total of 90 diagnosed acute coronary syndrome (ACS) patients free from heart failure, renal disease, thyroid disorder and hepatic disorder were enrolled from the cardiology emergency department of BSMMU, NICVD and BIRDEM. After measurement of plasma BNP concentration, subjects were categorized into two groups. Those having BNP concentration <640 pg/ml were included in Group-I and those having plasma BNP concentration >640pg/ml were included in Group II. All patients were treated and managed identically by conventional standard management protocol during their hospital stay and even after their discharge. After discharge all patients were followed up periodically in every month up to 6 months. During hospital stay and their follow up period patients were assessed clinically for any kind of clinical outcomes (good recovery, recurrent ACS, heart failure, cardiogenic shock, stroke, and cardiovascular death.) In every visit patient was evaluated on the basis of clinical assessment, ECG, Echocardiogram, CAG, cardiac markers according to the merit individual case. At the end of follow up patients clinical outcome were evaluated on the perspective of their baseline plasma BNP concentration.

Result and Esult and Observations:

In a prognostic cohort study, 90 diagnosed ACS patients were enrolled in the study on the basis of their clinical and laboratory diagnostic criteria.

At the outset, plasma BNP concentration of all patients was measured and then followed up. Out of 90 ACS patients 74 (82.2%) were male and 16 (17.8%) were female with the mean age of 51.8 years and the age range of 30 to 90 years (Table- I). Among the enrolled patients, 24 (26.7%) were non ST-elevation myocardial infarction (NSTEMI) and 66 (73.3%) were ST-elevation myocardial infarction (STEMI). STEMI includes 29 (32.2%) anterior MI, 21(23.3%) inferior MI, and 16 (17.8%) other varieties of MI e.g. anterior-inferior MI, posterior MI, right ventricular MI. Group I includes 57 (63.3%) subjects with plasma BNP concentration less than 640 pg/ml and group II includes 33 (36.7%) subjects with plasma BNP concentration above 640pg/ml.

With respect to hypertension, diabetes and smoking status two groups found identical but with respect to types of ACS, STEMI found to be more in group II and NSTEMI were more in group I (Table-1I).

Baseline plasma BNP concentration was associated with the clinical outcome of study subjects. In group I (n=57), good recovery, morbidity and mortality found to be in 41 (71.9%), 15 (26.3%) and 1 (1.8%) patients and those in group II (n=33) found in 6 (18.2%), 19 (57.6%) and 8 (24.2%) patients respectively. Chi-square test was done to assess the association of baseline plasma BNP concentration with the clinical outcome of the study subjects. In group II patients having high baseline plasma BNP concentration; significantly low good recovery but significantly high morbidity and mortality found compared to those in group I patients having low plasma BNP concentration (Table III).

Baseline plasma BNP concentration was also associated with the dichotomous clinical outcome (good outcome and bad outcome) of study subjects. In group I (n=57) good outcome and bad outcome found in 41 (71.9%) and 16 (28.1%) patients and those in group II (n=33) found in 6 (18.2%) and 27 (81.8%) patients respectively. Chi- square test was done to assess the association of baseline plasma BNP concentration with the clinical outcome of the study subjects.

In group II patients having high baseline plasma BNP concentration significantly less good outcome but significantly high bad outcome found compared to those in group I patients having low plasma BNP concentration (Figure I).

Table I: Age and Sex distribution of Study subjects (n=90):

Total	Male	Female	Age (yrs)	
			Mean age	Age range
90	74 (82.2%)	16 (17.8%)	51.8	30-90

Table-II: Distribution of baseline characteristics and clinical types of ACS between two groups:

Characteristics	Group I (n=57)		Group II (n=33)		x^2	P
	Frequency	Percentage	Frequency	Percentage	Value	Value
NSTEMI	22	38.6	2	6.0	11.314	0.001
STEMI	35	61.4	31	94.0		
Hypertensive	24	42.1	15	45.5	0.095	0.757
Normotensive	33	57.9	18	54.5		
Diabetic	20	35.1	13	39.4	0.167	0.683
Nondiabetic	37	65.9	20	60.6		
Smokers	39	68.4	22	66.7	0.029	0.864
Nonsmokers	18	31.6	11	33.3		

In group I, among the 22 NSTEMI, good outcome and bad outcome found in 19 (86.4%) and 3 (13.6%) patients whereas among the 35 STEMI good outcome and bad outcome found in 22 (62.8%) and 13

(37.2%) patients respectively. In group II, among 2 NSTEMI, good outcome and bad outcome found in 1 (50%) and 1 (50%) patients whereas among the 31 STEMI, good outcome and bad outcome found in 5 (16.1%) and 26 (83.95) patients respectively. Fisher exact test done in each group to evaluate statistically the association between the types of ACS and clinical outcome but no significant association found (Table-IV).

Table III: Association of plasma BNP concentration with the clinical outcome of the study subjects:

Group	Good Recovery		Morbidity		Mortality		X^2 Value	P Value
	(n)	(%)	(n)	(%)	(n)	(%)		
Group I (57) (BNP<640)	41	71.9	15	26.3	1	1.8	27.537	0.000
Group II (33) (BNP>640)	6	18.2	19	57.6	8	24.2		

χ^2 Value: 24.199; p-Value: 0.000

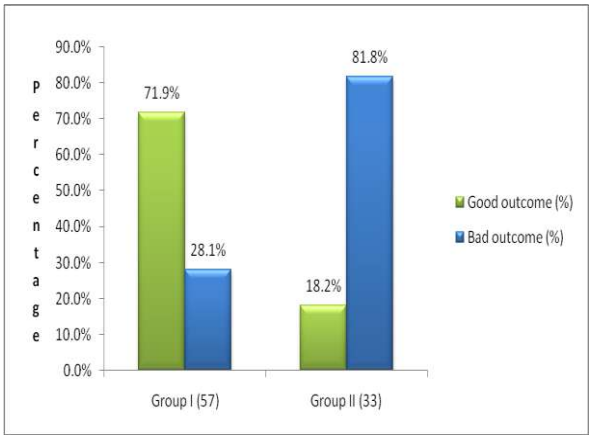


Figure I: Clinical outcomes (good and bad) of study subjects (ACS) in group I and group II showing percentage.

Keeping the group I in reference category, it is found significant for group II (p- 0.000) with the odds ratio 11.5. The odds ratio of 11.5 indicates that there is 11.5 times higher chance of getting bad outcome in ACS subjects having higher plasma BNP concentration (group II) than those having low baseline plasma BNP concentration (group I) (Table-V).

Table IV: Association of the clinical types MI (STEMI & NSTEMI) with clinical outcome in relation to plasma concentration of BNP.

Groups	Parameter	Good Outcome		Bad Outcome		Exact Sig.
		(n)	(%)	(n)	(%)	
Group I (57)	NSTEMI (22)	19	86.4	3	13.6	.073
	STEMI (35)	22	62.8	13	37.2	
Group II (33)	NSTEMI (2)	1	50	1	50	.335
	STEMI (31)	5	16.1	26	83.9	

P-value reached by Fisher's exact test.

Table V: Logistic regression analysis of plasma BNP concentration with respect to clinical outcomes of study subjects:

Parameter	Regression Coefficient	Standard Error	P value	Odds ratio Exp (B)
Group II/Outcome	2.4	0.5	0.000	11.5
Group I/Outcome	Reference Category			1

Discussion:

In line with this study, many studies abroad have demonstrated BNP as a predictor of adverse outcome in ACS while others have refuted an association. In the present study, Group I includes 57 (63.3%) subjects with plasma BNP concentration less than 640pg/ml and group II includes 33 (36.7%) subjects with plasma BNP concentration above 640pg/ml.

In group II patients having high baseline plasma BNP concentration significantly less good outcome but significantly high bad outcome found compared to those in group I patients having low plasma BNP concentration (p-0.000). Higher bad clinical outcomes in group II compared to group I indicates that the increasing baseline plasma BNP concentration is associated with worsening clinical outcome.

This result was consistent with some other studies[13-19]. Kuklinska et al, in their study concluded that median plasma BNP value was higher in patients with adverse clinical outcomes (p<0.001). Patients with plasma BNP concentration >99.2pg/ml were significantly at higher risk of adverse clinical outcome. Logistic regression analysis showed that the plasma BNP concentration >99.2pg/ml was the strongest predictor of adverse outcome[17]. Foody (2006) found that after adjustment of multiple risk factors, patients with plasma BNP level >80pg/ml had significantly greater risk for death when measured at baseline[19]. In consistent with our findings He B et al, (2006) in their study demonstrated the prognostic value of plasma BNP and Creactive protein in patients with ACS undergoing percutaneous coronary intervention. They found that both plasma BNP and CRP were good predictors for early mortality and major adverse cardiac events but CRP had lost its predictive value after introduction of plasma BNP into the model, while BNP was still an independent predictor for mortality and major adverse cardiac events[20]. Through binary logistic regression analysis of plasma BNP concentration with respect to their good and bad clinical outcome keeping the group I in reference category, present study have shown the odds ratio 11.5 for group II (p-0.000) indicating 11.5 times higher chance of getting bad outcome in ACS subjects in group II having higher plasma BNP concentration than those in group I having low plasma BNP concentration. This result was consistent with several other studies[7,20,21]. In a study Morrow et al (2005) demonstrated that after adjustment of other clinical predictors like age, sex, renal function, hypertension, diabetes and prior heart failure; a baseline plasma BNP >80pg/ml was associated with a 2-fold higher long term risk of death (Adjusted hazard ratio 2.1)[7]. De Lemos et al, (2001) stated that the association of plasma BNP with clinical outcome remained significant in subgroups of patients who had STEMI, NSTEMI. In our study, this association was not significant among these subgroups of patients probably due to the small sample size[20]. In another study Morrow, de Lemos and Sabatine, (2003) showed that an elevated plasma BNP level >80pg/ml at presentation identifies patients with non ST elevation ACS who are at fivefold risk of developing new congestive heart failure or death (p<0.0001) independent of other clinical predictors[21]. It can be concluded from this study that higher baseline plasma BNP concentration is associated with more adverse clinical outcomes in ACS patients. Since the baseline plasma BNP concentration at the onset of event shows incremental prognostic value, so plasma BNP can be used clinically as a biomarker of prognosis in ACS patients.

References:

1. Ross R. Atherosclerosis: an inflammatory disease, N Eng J Med. 1999; 340:115-126.

2. Bhopal R. What the risk of coronary heart disease in south Asian? A review of UK research. Journal of Public Health Medicine. 2000; 22: 375-385.

3. Shah PK. New insights in the pathogenesis and prevention of acute coronary syndromes, Am J Cardiol. 1997; 79: 17-23.

4. Joshi P, Islam S, Pais P, Reddy S, Doraira P, Kazmi K, Pandey MR, Haque S, Mendis S, Rangarajan S, Yusuf S. Risk Factors for Early Myocardial Infarction in South Asians Compared With Individuals in Other Countries. JAMA. 2007; 297: 286-294.

5. Fletcher GF, Bufaino V, Costa F, Goldstein LB, Jones D, Smaha L, Smith SC Jr, Stone JN. Efficacy of drug therapy in the secondary prevention of cardiovascular disease and stroke. Am J Cardiol. 2007; 99(6) 1-35.

6. Vickery BG, Rector TS, Wickstrom SL, Guzy PM, Sloss EM, Gorelick PB, Garber S, McCaffrey DF, Dake MD, Levin RA. Occurrence of secondary ischemic events among persons with atherosclerotic vascular disease. Circulation. 2002;33(4): 901-906.

7. James SK, Lindahl B, Siegbahn A, Stridsberg M, Venge P, Armstrong P, Barnathan ES, Califf R, Topol EJ, Simoons ML, Wallentin L. N-terminal pro brain natriuretic peptide and other risk markers for the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease: a Global Utilization of Strategies To Open Occluded Arteries (GUSTO)-4 substudy, Circulation. 2003; 108(3): 275-281.

8. Yoshimura M, Yasue H, Okumura K, Ogawa H, Jougasaki M, Mukoyama M, Nakao K and Imura H. Different secretion patterns of atrial natriuretic peptide and brain natriuretic peptide in patients with congestive heart failure. Circulation. 1993; 87: 464-469.

9. Stein BC, Levin RI. Natriuretic peptide physiology, therapeutic potential, and risk stratification in ischemic heart disease. Am Heart J. 1998;135: 914-923.

10. Cheung BMY, Kumana CR. Natriuretic peptides: Relevance in cardiovascular diseases. JAMA. 1998; 280: 1983-1984.

11. Yasue H, Yoshimura M, Sumida H, Kikuta K, Kugiyama K, Jougasaki M, Okumura K, Mukayama M, Nakao K. Localization and mechanism of secretion of B- type natriuretic peptide in normal subjects and patients with heart failure. Circulation. 1994; 90: 195-203.

12. Morrow DA, de Lemos JA, Sabatine MS. Evaluation of B-type natriuretic peptide for risk assessment in unstable angina/non-ST- elevation myocardial infarction: B- type natriuretic peptide and prognosis in TACTICS-TIMI. J Am Coll Cardiol. 2003; 41: 1264-1272.

13. Maisel AS, Krisnaswamy P, Nowak RM, Abraham WT, Wu ABH, Mc Cord J et al. Rapid measurement of B- type natriuretic peptide in the emergency diagnosis of heart failure. N Eng J Med. 2002; 347: 161-167.

14. Motwani JG, McAlpine H, Kennedy N, Struhers AD. Plasma brain natriuretic peptide as an indicator for angiotensin converting enzyme inhibitor after myocardial infarction. Lancet. 1993; 341: 1109-1113.

15. Jernberg T, Stridsberg M, Venge P, Lindahl B. N-terminal pro brain natriuretic peptide on admission for risk stratification of patients with chest pain and no ST- segment elevation. J Am Coll Cardiol. 2002; 40: 437-445.

16. Omland T, Persson A, O'Brien R, Ng L, Karlsson T, Herltz J, Hartfor M, Caidahl K. N-terminal pro- B-type natriuretic peptide and long-term mortality in acute coronary syndromes. Circulation. 2002;106: 2913-2918.

17. Talwar S, Squire IB, Downie PF, Mccullough AM, Campton MC, Devies JE, Barnett DB and Ng LL. Profile of Plasma N-terminal pro BNP following acute myocardial infarction. Correlation with left ventricularsystolic dysfunction. Eur Heart J. 2000;21: 1514-1521.

18. De Lemos JA, Morrow DA. Brain natriuretic peptide measurement in acute coronary syndromes. Circulation. 2002;106: 2868-2870.

19. Foody JM. BNP has prognostic value after ACS, 2006, Retrieved December, 2009 from http://cardiology.jwatch.org/cgi/con nt/full/2006/126/4.

20. He B, Ding S, Pu J, Liu JP, Song W, Du YP, Shen JY, Jin SX, Sun Y, Shen L. Prognostic value of plasma brain natriuretic peptide and C-reactive protein in patients with acute coronary syndromes underwent percutaneous coronary intervention. Zhonghua Xin Xue Guan Bing Za Zhi. 2006;34(4): 349-352.

21. De Lemos JA, Morrow DA, Bentley JH, Omland T, Sabatine MS, McCabe CH, Hall C, Cannon CP, Braunwald E. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. N Eng J Med. 2001; 345(14): 1014-1024.

Original Article

DCIMCJ 2018 January; 5(1):89-96

Role of Amnitomy on Duration of Labour in Primigravidae

Khatun J[1], Siddiqua NM[2]

Abstract:

Objective: To see the effects of amniotomy and spontaneous rupture of membrane on duration of labour in primigravidae. Study design: Observational Cross-sectional study. Study setting and period: Department of Obstetrics and Gynaecology, Sylhet MAG Osmani Medical College Hospital, Sylhet, between December 2014 to May 2015. Study population: All term primigravidae in active labour admitted in the Dept of obstetrics and Gynecology. Methods: Women in active phase of labour and having cervical dilatation > 4 cm were enrolled for the study. Women in whose ARM done were included in amniotomy group and whose membrane were allowed to rupture spontaneously were included in non-amniotomy group. Progress of labour was monitored by partograph. Time taken from the enrollment to full dilatation of cervix was noted. Mode of delivery, post delivery complications, foetal outcome and APGAR score of the baby at 1 and 5 minutes were recorded and documented. Relevant data from history, physical examination and investigations were recorded in predesigned questionnaire. Result: There was a significant decreased in duration labour both 1st and 2nd stage in amniotomy group. The mean duration of 1st stage was 3.52± 1.27 hr in amniotomy group and 7.36±2.19 hr in non-amniotomy group. The mean duration of 2nd stage was 1.04± 0.51 hr in amniotomy group and 1.64± 0.55 hr in non-amniotomy group and the differences were statistically significant (p<0.05) between two groups. Most of the patients were delivered by normal vaginal delivery and LUCS was done in 18% patients of amniotomy group and 22 % in non-amniotomy group, the difference were not statistically significant (p>0.05) between two groups. Conclusion: Amniotomy significantly reduces the duration of labour when compared with the leaving the membranes intact until second stage without any effect on delivery outcome in the newborn or mother.

Keywords: Amniotomy, Labour

Introduction:

Labour has been termed the most dangerous journey a human ever under takes. The reason being that although it is a natural process but complications can arise at any time during its course[1]. Normal labour is a continuous process that has been divided into three stages[2]. First stage duration is 12 hours in primigravidae and 6hours in mutiparae, second stage duration is 2 hours in primigravidae and 30 minutes in multiparae, third stage duration is about 15 minutes in both primigravidae and in multiparae[3]. Amniotomy also called artificial rupture of membranes (ARM) is an intervention to induce or augment the labour[4]. Amniotomy was first introduced by Thomas Denman of Middlesex hospital in 1756[5]. It has long been in obstetric practice because of general belief that it reduces the duration of labourr[6-8]. When tension is by spontaneous or artificial rupture of membrane the presenting part directly press the cervix and force of distension of the cervix increased after rupture of membrane[9]. Amniotomy reduces length of labour. Amniotomy also detects meconium staining of amniotic fluid during foetal distress by direct examination of liqour where modern facilities of fetal monitoring is not easily available[10].

Amniotomy is a common obstetrical procedure with both benefits and risks. It has been associated with a 60-120 min reduction in labour duration mainly in nulliparae with no evidence of increased likelihood of fetal heart rate abnormalities or adverse neonatal outcomes[11]. Several studies in this regard revealed amniotomy to be effective in shortening delivery and decreasing variability of 5th minute Apgar score and that is why it is used extensively[12].

Materials and methods:

This study was a hospital based Observational cross sectional study, carried out in IPD (inpatient

1. Dr. Jamila Khatun, Associate Professor, Department of Obstetrics and Gynecology, Sylhet M.A.G Osmani Medical College, Sylhet.

2. Dr. Noor Mahal Siddiqua, Honorary Medical Officer, Department of Obstetrics and Gynecology, Sylhet M.A.G Osmani Medical College and Hospital, Sylhet.

Correspondence: Dr. Jamila Khatun
E-mail: mirshah1962@gmail.com.

Materials and methods:

This study was a hospital based Observational cross sectional study, carried out in IPD (inpatient department) of Obstetrics and Gynecology of Sylhet M.A.G Osmani Medical College and Hospital, Sylhet in between December 2014 to May 2015. Total 100 pregnant women in active labour (50 cases of amniotomy group and another 50 women were spontaneous rupture of membrane) were enrolled in this study. Data was collected by using a preformed questionnaire and check list. Cases were selected according to inclusion and exclusion criteria. Relevant infromations (according to questionnaire) were taken from patients. Women in whose ARM done were included in amniotomy group and whose membrane were allowed to rupture spontaneously were included in non-amniotomy group. Foetal heart rate was monitored by intermittent auscultation and progress of labour was monitored by partograph. Time taken from the enrollment to full dilatation of cervix was noted. Data was processed manually and analyzed with the help of SPSS (Statistical package for social sciences) Version 16.0.

Results:-

Total 100 primigravida in active labour were included in this study. There was a significant decrease in duration of labour (both 1st and 2nd stage) in amniotomy group. The mean duration of 1st stage was 3.52± 1.27 hour in amniotomy group and 7.36±2.19 hour in non-amniotomy group. The mean duration of 2nd stage was 1.04± 0.51 hr in amniotomy group and 1.64± 0.55 hr in non-amniotomy group. The differences were statistically significant ($p<0.05$) between two groups. Most of the patients were delivered by normal vaginal delivery. LUCS was done in only 18% patients of amniotomy group and 22% of non-amniotomy group, with no statistically significant difference between two groups($p>0.05$).

Table-I: Distribution of study patients according to age, height, weight, occupation and socio-economic condition:

Parameter	Amniotomy group (N= 50)		Non-amniotomy group (N= 50)		P-value
	n	%	n	%	
Age in year					
<20	9	18.0	7	14.0	0.59
20 – 25	36	72.0	39	78.0	0.49
>25	5	10	4	8.0	0.73
Mean ±SD	22.06±2.43		22.12±2.24		0.90
Height in cm					
< 150	13	26.0	15	30.0	0.66
150 – 155	29	58.0	28	56.0	0.84
>155	8	16.0	7	14.0	0.78
Mean ±SD	150.86±4.83		150.68±4.51		0.85

Parameter	Amniotomy group (N=50)		Non-amniotomy group (N= 50)		P-value
	n	(%)	n	(%)	
Weight in kg					
<55	9	18.0	11	22.0	0.62
55-65	35	70.0	34	68.0	0.83
>65	6	12.0	5	10.0	0.75
Mean ±SD	58.78±5.27		58.66±5.32		0.91
Occupation					
House wife	41	82.0	39	78.0	0.62
Teacher	4	8.0	5	10.0	0.73
Others	5	10.0	6	12.0	0.75
Socio-economic condition					
Lower class	23	46.0	26	52.0	0.55
Middle class	24	48.0	22	44.0	0.69
Upper class	3	6.0	2	4.0	0.65

Table-II: Distribution of study patients according to gestational age:

Gestational age(Wks)	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	n (%)	n (%)	
37- 38	8(16)	11(22)	0.44
39-40	37(74)	35(70)	0.66
41-42	5(10)	4(8)	0.73
Mean ±SD	39.16±1.71	39.24±1.13	0.78

The mean gestational age was 39.16±1.71 in amniotomy group and 39.24±1.13 in non-amniotomy group, but the difference was not statistically significant (p>0.05) between two groups.

Table-III: Duration of labour after enrollment:

Stage of labour	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	Mean±SD(Range)	Mean±SD(Range)	
Duration of 1st stage(hr)	3.52± 1.27(2, 6)	7.36±2.19(4, 11)	<0.00001
Duration of 2nd stage(hr)	1.04± 0.51 (0.5, 2)	1.64± 0.55 (0.7,2.5)	<0.00001

The mean duration of 1st stage was 3.52± 1.27 hr in amniotomy group and 7.36±2.19 hr in nonamniotomy group. The mean duration of 2nd stage was 1.04± 0.51 hr in amniotomy group and 1.64± 0.55 hr in non-amniotomy group and the difference was statistically significant ($p<0.05$) between two groups.

Table-IV: Distribution of study patients according to Mode of delivery:

Mode of delivery	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	n(%)	n(%)	
Normal vaginal delivery	38(76)	37(74)	0.82
Instrumental delivery	3(6)	2(4)	0.65
LUCS	9(18)	11(22)	0.62

76% had normal vaginal delivery, 6% had instrumental delivery and 18% had LUCS . In non-amniotomy group 74% had normal vaginal delivery, 4% had instrumental delivery and 22 % had LUCS, and the difference were not statistically significant ($p>0.05$) between two groups.

Table-V: Maternal complications during labour:

Complications	Amniotomy group (N= 11)	Non-amniotomy group (N= 16)	P-value
	n(%)	n(%)	
Cervical dystocia	2(4)	3(6)	0.65
Uterine inertia	1(2)	2(4)	0.56
Intrapartum eclampsia	1(2)	2(4)	0.56
Prolonged 2nd stage	4(8)	5(10)	0.73
Maternal distress	3(6)	4(8)	0.70

The difference of all maternal complications during labour were not statistically significant ($p>0.05$) between two groups.

Table-VI: Maternal complications after labour:

Complications	Amniotomy group (N= 11)	Non-amniotomy group (N= 16)	P-value
	n(%)	n(%)	
Perineal Tear	1(2)	1(2)	-
Post-partum haemorrhage	4(8)	5(10)	0.73
Cervical tear	2(4)	3(6)	0.65
Vaginal laceration	1(2)	1(2)	-
Uterine atony	1(2)	1(2)	-
Manual removal of placenta	1(2)	2(4)	0.56
Blood transfusion needed	1(2)	2(4)	0.56
Puerperial pyrexia	1(2)	1(2)	-

The difference of all maternal complications after labour were not statistically significant ($p>0.05$) between two groups.

Table-Vll: Distribution of study patients according to foetal out come:

Foetal out come	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	n(%)	n(%)	
Healthy baby	46(92)	44(88)	0.50
Asphyxiated	4(8)	5(10)	0.73
Still born	0(0)	1(2)	0.31
Admission to Neonatal ward	4(8)	5(10)	0.73

The difference was not statistically significant ($p>0.05$) between two groups.

Table-Vlll: Apgar score of the babies:

	Amniotomy group (N= 50)	Non-amniotomy group (N= 50)	P-value
	n(%)	n(%)	
Apgar score at 1 minute			
<3	3(6)	4(8)	0.70
4 – 6	7(14)	9(18)	0.59
>7	40(80)	38(76)	0.63
Mean±SD	8.08±2.12	7.42± 2.25	0.13
Apgar score at 5 minute			
<3	1(2)	2(4)	0.56
4 – 6	3(6)	3(6)	-
>7	46(92)	45(90)	0.73
Mean±SD	8.94±1.38	8.64±1.87	0.63

The difference of Apgar score at 1 minute and 5 minute were not statistically significant (p>0.05) between two groups.

Discussion:

In this study it was observed that majority of the patients (72% in amniotomy group and 78% in non-amniotomy group) belonged to age group 20 to 25 years and the mean age was 22.06±2.43 in amniotomy group and 22.12±2.24 in non-amniotomy group. Which is comparable with the study of Mikki et al.[11] Abdullah et al.[13] and Rasheed et al[14].

In this study it was observed that more than half of women the mean height was 150.86±4.83 in amniotomy group and 150.68±4.51 in nonamniotomy group. It is consistent with the study by Ghani et al[9]. The mean weight was 58.78±5.27 in amniotomy group and 58.66±5.32 in non-amniotomy group. In a study by Mikki et al. found mean weight 75.6+10.8 kg in the intervention group and 73.8+10.7 kg in the controlled group which is higher than the present study[11]. It may be due to geographical variation of weight of the women.

In this present study it was observed that majority of the patients (74% in amniotomy group and 70% in non-amniotomy group) belong to 39 to 40 weeks of gestation and the mean gestational age was 39.16±1.71 in amniotomy group and 39.24±1.13 in nonamniotomy group. Abdullah et al.[13] found mean gestational age 38.41±1.03 weeks.

Amniotomy is associated with a reduction in labour duration of between 60 and 120 minutes[7]. In this present study the mean duration of 1st stage was 3.52 ± 1.27 hr in amniotomy group and 7.36± 2.19 hr in non-amniotomy group/ the mean duration of 2nd stage was 1.04± 0.51 hr in amniotomy group and 1.64± 0.55 hr in non-amniotomy group and the difference was

statistically significant ($p<0.05$) between two groups. This indicates that amniotomy significantly reduced the duration of both 1st and 2nd stage of labour. In a study by Abdullah et a1.[13] mean duration of labour was 6.66±1.41 in amniotomy group and 7.60±1.75 in spontaneous rupture of membrane group. It was significantly low in amniotomy group than in spontaneous rupture of membrane group. Another study by Bellad et al. found mean duration of 1st stage of labour 4.76±1.64 hours in amniotomy group and 5.66±1.85 hours in non-amniotomy group[15]. The duration labour was significantly lower in amniotomy group. Similar findings regarding duration of labour were also observed by Mikki et al.[11] and Ghani et al.[9] which are consistent with the present study.

There was no significant difference in the mode of delivery beween two group. It was observed that in amniotomy group 76% had normal vaginal delivery, 6% had instrumental delivery and 18% had LUCS . In non-amniotomy group 74% had normal vaginal delivery, 4% had instrumental delivery and 22 % had LUCS, and the difference were not statistically significant ($p>0.05$) between two groups. Similar findings regarding mode of delivery were also observed by Ghani et al.[9] Bellal et al[15] and Naseer et al[16].

It was observed that the difference of all maternal complications during and after labour were not statistically significant ($p>0.05$) between two groups. It is similar to study by Ghani et al[9]

Majority of the newborn were healthy (92% in amniotomy group and 88% in non-amniotomy group). apgar score at 1 minute and 5 minute were not statistically significant ($p>0.05$) between two groups.

Conclusion:

It is concluded from the study that, amniotomy significantly reduces the duration of labour when compared with the leaving the membranes intact until second stage without any effect in cesarean section rates or rate of operative vaginal delivery. It does not increase the risk of any adverse outcome in the newborn or mother.

References:

1. Javed I, Bhutta S, Shoaib T. Role of partogram in preventing prolonged labour. J Pak Med Assoc 2007; 57(8) :408-411.

2. Archie CL. The Course and Conduct of Normal Labor and Delivery. In: DeCherney AH, Nathan L, Goodwin TM, Laufer N, editors. Current Diagnosis and Treatment Obstetrics and Gynecology.10th ed. New York: McGraw-Hill; 2007. p. 203 211.

3. Normal Labour. In: Koner H, editors. D.0 Dutta's Text Book of Obstetrics. 17th ed. Kolkata: New Central Book Agency(P)Ltd; 2011. p. 113-143.

4. Wolomly JJ, Tozin RR. Amniotomy for shortening Spontaneous labour: RHL Commentary [last revised:5 Jan 2009]. The WHO Reproductive Health Liabrary; Geneva:WHO.

5. Calder AA. Induction and augmentation of labour: In: Edmonds DK, editor Dewhurst's textbook of obstetrics and gynaecology for postgraduates 6th edition. London: Blackwell Science; 1999. 255.

6. Ajadi MA, Kuti 0, Oriji EO, Ogunnivi SO, Sule SS. The effect of amniotomy on the outcome of spontaneous labour in uncomplicated pregnancy. J of Obstet Gynaecol 2006;26(7):631. 631-634.

7. Fraser WD, Turkot L, Krauss I, Carrol G. Amniotomy for shortening spontaneous labour Conchrane data base systemic reviews 2006; issue Art No.: CD000015.

8. Incerti M, Locatelli A,Ghidini A, Civiello E, Malberti S, Consonni S, et al. Prediction of duration of active labour in nulliparous women at term. Am J Perinat 2008;25:859.

9. Ghani T , Rahim A, Begum F, Mahmuda B. Amniotomy shortens the induction delivery interval CBMJ 2013 July; 02(02):67- 70.

10. Majeed N, Tariq S. Comparison of Artificial Rupture of Membranes with Intact Membrane in Labouring Multigravidae. JRMC 2013;17(2):234-237.

11. Mikki N, Wick L, Asab NA, Rmeileh NMEA . A trial of amniotomy in a Palestinian hospital. Journal of Obstetrics and Gynaecology, May 2007; 27(4): 368 — 373.

12. Olfati F, laluha F. Effect of amniotomy in latent phase and active phase on rate of cesarean section. Academia Journal of Medicine November 2012; 1: 5- 8.

13. Abdullah A, Saboohi S, Hashami U. Effects of Amniotomy versus Spontaneous Rupture of Membrane on Progress of Labour and Foetal Outcome in Primigravidae. JLUMHS January-April 2010; 09 (1): 33-36.

14. Rasheed FA, Ahmed AA, Hussain SA. The Impact of Early Versus Late Amniotomy on Duration of Labor, Maternal and Neonatal Outcomes in Iraqi Primigravida with Spontaneous Labor. Medscience, 2014; 3:8132.

15. Bellad MB, Kamal P, Rajeshwar P. Does Artificial Rupture of Membranes (ARM) Reduce Duration of Labor in Primigravidae: A Randomized Controlled Trial. South Asian Federation of Obstetrics and Gynecology, January-April 2010;2(1):37-39.

16. Naseer N, Hag G, Soomro N. Active Versus Expectant Management of Labour Study of 100 Cases. Pakistan Journal of Surgery; 25(4): 274-278.

Review article

DCIMCJ 2018 January; 5(1):97-102

Emergence of Chikungunya in Bangladesh: A Systematic Review

Begum N[1], Hoque SM[2]

Abstract:

Chikungunya fever, caused by "Chikungunya virus," is an arthropod-borne viral disease transmitted by the bite of infected mosquitoes belonging to the genus Aedes. Chikungunya fever epidemics have been reported from several countries around the world. The disease that was silent for nearly 32 years re-emerged in the October 2005 outbreak in India that is still ongoing. The incubation period ranges from 3 to 12 days. The onset is usually abrupt and the acute stage is characterized by sudden onset of high-grade fever, severe arthralgias, myalgias, and skin rash. In the chronic stage, relapses that include sensation of fever, asthenia, exacerbation of arthralgias, inflammatory polyarthritis, and stiffness may be evident. Neurological, ocular, and mucocutaneous manifestations have also been described. Chronic arthritis may develop in about 15% of the patients. Viral culture is the gold standard for the diagnosis of Chikungunya fever. Reverse transcription polymerase chain reaction has also been found to be useful. Serodiagnostic methods for the detection of immunoglobulin M and immunoglobulin G antibodies against Chikungunya virus are more frequently used. There is no vaccine for this infection as well as no specific antiviral treatment for Chikungunya fever as it is poorly responsive to analgesia in its acute and chronic phase of the disease. To control the spread of the infection government, non-government officials should come forward and take necessary steps to aware and educate people about the infection so that people can avoid contact with mosquitoes. National surveillance can be run along with active community participation is required to eradicate the mosquitoes from the environment. In this review, we will characterize the epidemiology and global expansion of chikungunya virus, describe the clinical features and laboratory testing for the disease, and discuss measures needed for effective disease control and prevention.

Keywords: Chikungunya, emergence, Bangladesh

Background:

Chikungunya fever is one of the most rapidly spreading mosquito-borne viral illness of humans caused by the chikungunya virus (CHIKV) and recently in Bangladesh it has emerged as an important public health issue[1]. Aedes aegypti and Aedes albopictus mosquitoes are the main vectors of chikungunya in Asia and the Indian Ocean islands[2] (Figure 1). The name "Chikungunya" derived from local Tanzanian language means "that which bends up" or "stopped walk" due to contorted posture resulting from joint pain[3]. Although morbidity and mortality is not that high, patient suffers a lot from high fever and severe pain of the body, particularly the joints pain.

In fact, patients may suffer with the joint pain for weeks or months. During this period they cannot work properly and thus causing severe economic loss. Recently, complicated case of CHIKV infection has been reported where systemic involvement such as involvement of cardiovascular system was found[4].

Epidemiology:

Chikungunya fever is a global health problem. Outbreak of fever, rash and arthritis, similar to Chikungunya fever has been recorded as early as 1824 in India and elsewhere. However, the CHIKV was first isolated in 1953 from Tanzania and then in Asia[5].

1. Dr. Nurjahan Begum, Assistant Professor, Department of Microbiology, Dhaka Central International Medical College.

2. Dr. Syada Monira Hoque, Associate Professor, Department of Microbiology, Dhaka Central International Medical College.

Correspondence: Dr. Nurjahan Begum
E-mail: nurjahan.begum.akhi@gmail.com



Figure 1: Aedes aegypti mosquito

Later on several outbreaks of the disease occurred in Africa and Asia between 1960s to the 1980, but the global emergence of CHIKV actually started in 2004. In addition to Africa and South-East Asia (India, Bangladesh) where it is endemic, sporadic cases are regularly reported from other part of the world[6]. In fact, according to WHO, Chikungunya virus has been identified over 60 countries (Figure 2).

Bangladesh scenario:

In Bangladesh, the first case was reported in 2008 in northern Rajshahi and Chapainawabganj districts by an investigation team from the Institute of Epidemiology, Disease Control and Research (IEDCR) and ICDDR,B (International Centre for Diarrhoeal Disease Research, Bangladesh).[7]

In August 2011, suspected chikungunya fever outbreaks were detected in Dohar upazila of Dhaka district and Shibganj upazila of Chapainawabganj district. In Dohar upazila of Dhaka, the attack rate was 29% and almost one-third households had at least one suspected case and 89% of hatched mosquitoes were Aedes albopictus[8]. In 2014, Hassan et al. labeled chikungunya as an emerging disease in Bangladesh by analysing the chikungunya cases in a tertiary teaching hospital in Dhaka city[9]. Dhaka, the capital city of Bangladesh, recently swayed with a severe outbreak of chikungunya and there are so far 3,000 cases have been reported in different hospitals and clinics of Dhaka from May to July 2017[10].

The risky areas are: Uttara-4, Uttara-9, Middle Badda, Gulshan-1, Lalmatia, Pallabi, Maghbazar, Malibagh, Rampura, Tejgaon, Banani, Nayatola, Kuril, Pirerbagh, Rayer Bazar, Shyamoli, Monipuripara, Mohammadpur, Mohakhali, Mirpur-1 and Korail Slums[11]. A national guideline has been prepared for clinical management of Chikungunya fever in Bangladesh[12].

Structure of a Chikungunya virus:

Chikungunya virus is ssRNA positive sense enveloped virus with a genome of approximate 1.8 KB size that encode four non-structural (nsP1 to nsP4) and five structural (C, E3, E2, 6K, and E1) proteins. The virus is spherical in shape with a diameter of about 60–70 nm. These arthropod-borne viruses belong to the genus Alphavirus of the family Togaviridae. Like many other arboviruses, CHIKV are zoonoses[13].

Transmission:

The virus is transmitted from human to human by the bites of infected female mosquitoes. Most commonly, the mosquitoes involved are Aedes aegypti and Aedes albopictus, two species which can also transmit other mosquito-borne viruses, including dengue.

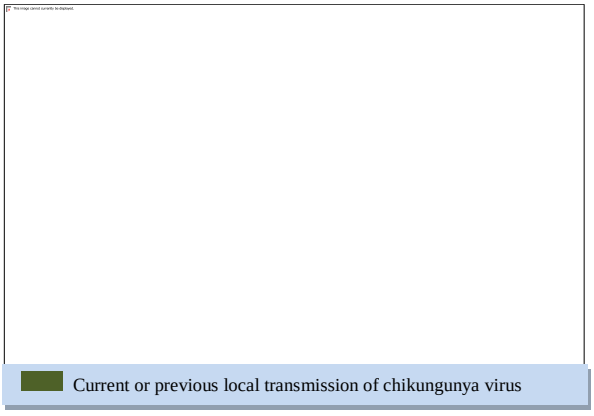


Figure 2: Countries and territories where Chikungunya cases have been reported (as of April 22, 2016). The map does not include countries or territories where only imported cases have been documented. (https://www.cdc.gov/chikungunya/geo)

The Aedes mosquito breeds in domestic settings such as flower vases, water-storage containers, air coolers, etc and peri-domestic areas such as construction sites, coconut shells, discarded household junk items (tyres, plastic and metal cans etc) and bites during day time. These mosquitoes can be found biting throughout daylight hours, though there may be peaks of activity in the early morning and late afternoon. Risk is highest in the rainy season when numbers of mosquitoes are at their greatest. Human beings serve as the chikungunya virus reservoir during epidemic periods. During interepidemic periods, a number of vertebrates have been implied as the reservoir. These include monkeys, rodents, birds and other vertebrates[14].



Figure 3: Maculopapular rash in Chikungunya fever

Signs and symptoms of Chikungunya fever:

Chikungunya fever affects all age groups and both genders are equally affected. The incubation period ranges from 2 to 12 days followed by bite of infected mosquito, with an average of 2 to 7 days. Prodromal symptoms are rare. In the acute stage, the onset is usually abrupt and sudden with high grade fever (usually 102-105ºF), severe arthralgias or arthritis affecting multiple joints, myalgia and skin rashes[15]. The acute bilateral and symmetrical rheumatism is typically extensive and progressive within a few days. Peripheral joints are frequently very painful and swollen, especially interphalangeal joints, wrists and ankles. Larger joints like knee, shoulder and spine are also involved. Pain tends to be worse in the morning, relieved by mild exercise and exacerbated by aggressive movements.

A transient petechial or maculopapular rash of the trunk and occasionally the limbs can also develop in half of the patients (Figure 3). Other non-specific symptoms include headache, nausea, vomiting, conjunctivitis, slight photophobia and anorexia[16,17]. Ocular inflammation from Chikungunya may present as iridocyclitis. Retinal lesions may also occur[18].

The fever may persist for 8 to 10 days. In some patients, a biphasic pattern of fever is also noticed. In a majority of the patients, the joint pains resolve in 1 to 3 weeks. However, the arthritis can persist in about 33% of patients for 4 months, 15% for 20 months, and in 12% for 3-5 years[19-22]. The chronic stage is characterized by unpredictable relapses that include sensation of fever, asthenia, and exacerbation of arthralgias and stiffness. Affected patients may manifest inflammatory polyarthritis, severe subacute tenosynovitis/bursitis (consequently nerve tunnel syndromes) in hands, wrists, and exacerbation of pain on movement in previously injured joints[23,24]. Some studies have documented occurrence of rheumatoid arthritis following Chikungunya fever, suggesting that the viral infection may have a role in the initiation or unmasking of rheumatoid arthritis[25].

Differential diagnosis:

It is hard to distinguish between chikungunya and dengue fever based on the clinical symptoms as both of them are transmitted by the same mosquito (Table 1). Chikungunya is more likely to cause high fever, associated with severe polyarthralgia, arthritis and lymphopenia whereas dengue fever causes neutropenia, thrombocytopenia, haemorrhage, shock and death[26].

Laboratory Diagnosis:

The diagnosis of CHIKV is based on ELISA and immunofluorescence test that detect anti-CHIKV IgM and IgG present in serum. Within 2-3 days after the onset of symptoms, the IgM antibodies are developed and may persist for several months[27]. On the other hand, the IgG antibodies developed in the convalescent phase, and are reported to be found after several months or even years following recovery[28].

Confirmatory diagnosis of CHIKV at molecular level is done based on detection of its genome by RT-PCR and real-time RT-PCR[29]. These are highly sensitive, specific and rapid test for CHIKV detection. For the isolation of the virus, insect and mammalian cell lines such as C636 and Vero cell lines are widely used[30,31].

Table 1: Clinical and laboratory features of Chikungunya virus infection compared with Dengue virus infection.

Traits	Chikungunya	Dengue
Fever (>39ºC)	+++	++
Arthralgia	+++	+/-
Arthritis	+	-
Hedache	++	++
Rash	++	+
Myalgia	+	++
Haemorrhage	+/-	++
Lymphopenia	+++	++
Neutropenia	+	+++
Thrombocytopenia	+	+++
Haemoconcentration	-	++

Treatment:

There is no specific antiviral drug treatment for Chikungunya. Chikungunya is a self limiting disease, treatment is symptomatic and supportive. Treatment is directed primarily at relieving the symptoms; including the joint pain using NSAIDs such as naproxen, paracetamol and ensuring adequate fluid intake[32].

Aspirin should be avoided due to its effect on platelets[33]. Some clinicians have used hydroxychloroquine/chloroquine for treating the viral arthropathy of chikungunya fever[34]. Published evidence does not support the use of corticosteroids, antibiotics or antiviral drugs in the management of chikungunya fever and indiscriminate use of these agents can contribute to thrombocytopenia, gastrointestinal bleeding, nausea, vomiting and gastritis. These may lead to dehydration, prerenal acute renal failure, electrolyte imbalance and sometimes hypoglycaemia[35].

Prevention and control:

There is no vaccine or specific medication available against Chikungunya infection[36]. Vector control is thus very important in controlling or preventing Chikungunya transmission. Elimination of breeding sites or source reduction is an effective method of control. Aedes aegypti is typically a container habitat species & breeds primarily in artificial container & receptacles. The best way is to encourage people to eliminate the mosquito habitats by emptying water containers once a week & keeping the permanent water containers covered with a tight fitting lid. Adoption of these methods can be encouraged through community based programmes. Legislation, strong public advocacy & community involvement can also help in vector control. Personal protection like long sleeve clothes, use of repellents, window nets play limited but useful role. Use of standard case management guidelines help in reducing the mortality due to Chikungunya. It is expected from the government specific strategic attitudes to form a critical awareness of citizens regarding public health so that society reaches a core of dignity of the individual.

References:

1. Weaver SC, Lecuit M. Chikungunya virus and the global spread of a mosquito-borne disease. N Engl J Med. 2015; 372:1231–1239.
2. Krishna MR, Reddy MK, Reddy SR. Chikungunya outbreaks in Andhra Pradesh, South India. Current Science 2006; 91: 570-571.
3. Bettadapura J, Herrero LJ, Taylor A, Mahalingam S. Approaches to the treatment of disease induced by chikungunya virus. Indian J Med Res. 2013; 138(5):762-765.
4. Alvarez MF, Bolívar-Mejía A, Rodriguez-Morales AJ, Ramirez-Vallejo E. Cardiovascular involvement and manifestations of systemic Chikungunya virus infection: A systematic review. F1000Research, 2017; 6: 390.

5. Robinson MC. An epidemic of virus disease in Southern Province, Tanganyika Territory, in 1952-53. I. Clinical features. Transactions of the Royal Society of Tropical Medicine and Hygiene 1955; 49(1):28-32.

6. Pialoux G, Gauzere BA, Jaureguiberry S, Strobel M. Chikungunya, an epidemic arbovirus. The Lancet Infectious Disease 2007; 7: 319-327.

7. ICDDR B. First identified outbreak of Chikungunya in Bangladesh, 2008. Health and Science Bulletin. 2009; 7(1):1-21.

8. Khatun S, Chakraborty A, Rahman M, Banu N, Rahman MM, Hasan SMM, et al. An Outbreak of Chikungunya in Rural Bangladesh, 2011. PLoS Neglected Tropical Disease. 2015; 9(7): e0003907

9. Hassan R, Rahman MM, Moniruzzaman M, Rahim A, Barua S, Biswas R, Biswas P, Mowla SG, Chowdhury MJ. Chikungunya –an emerging infection in Bangladesh: A case series. Journal of Medical Case Reports. 2014; 8(1):67.

10. Ul-Karim N. Bangladesh capital reeling from major outbreak of mosquito-borne disease chikungunya;2017. Available:http://news.xinhuanet.com/english/2017/07/12/c_136438598 [Accessed Aug. 2017]

11. The Daily Star. 21 areas in Dhaka city most risky for Chikungunya: Report; 2017. Available:http://www.thedailystar.net/health/21-areas-dhaka-city-most risky chikungunya-report1417462 [Accessed Aug. 2017]

12. Directorate General of Health Services (DGHS), Ministry of Health & Family Welfare. Government of People's Republic of Bangladesh. Bangladesh National Guideline on Clinical Management of Chikungunya Fever; 2017.

13. Powers AM, Logue CH. Changing patterns of chikunya virus: Re-emergence of a zoonotic arbovirus. Journal of General Virology 2007; 88(9):2363-2377.

14. WHO. SEA-CD-180 Guidelines on Clinical Management of Chikungunya Fever. http://www.wpro.who.int/mvp/topics/ntd/Clinical_Mgnt_Chikungunya_WHO_SEARO.pdf

15. Hoque MS, Ahmed ASMNU. Chikungunya fever and Bangladesh: Review and updates. DS (Child) HJ 2012; 28(2): 115-122.

16. Simon F, Parola P, Grandadam M, Fourcade S, Oliver M, Brouqui P, et al. Chikungunya infection: An emerging rheumatism among travelers returned from Indian Ocean islands. Report of 47 cases. Medicine 2007; 86:123-137.

17. Hochedez P, Hausfater P, Jaureguiberry S, Gay F, Datry A, Danis M, et al. Cases of Chikungunya fever imported from the islands of the South West Indian Ocean to Paris, France. Euro Surveill 2007; 12:42-43.

18. Mahendradas P, Ranganna SK, Shetty R, Balu R, Narayana KM, Babu RB, et al. Ocular manifestations associated with Chikungunya. Ophthalmology 2008; 115:287-291.

19. Pialoux G, Gaüzère BA, Jauréguiberry S, Strobel M. Chikungunya, an epidemic arbovirosis. Lancet Infect Dis. 2007; 7:319–327.

20. Fourie ED, Morrison JG. Rheumatoid arthritic syndrome after chikungunya fever. S Afr Med J. 1979; 56:130–132.

21. Kennedy AC, Fleming J, Solomon L. Chikungunya viral arthropathy: A clinical description. J Rheumatol. 1980; 7:231–236.

22. Brighton SW, Prozesky OW, de la Harpe AL. Chikungunya virus infection. A retrospective study of 107 cases. S Afr Med J. 1983; 63:313–315.

23. Simon F, Savini H, Parola P. Chikungunya: a paradigm of emergence and globalization of vector-borne diseases. Med Clin North Am. 2008; 92:1323–1343.

24. Simon F, Parola P, Grandadam M, Fourcade S, Oliver M, Brouqui P, et al. Chikungunya infection: an emerging rheumatism among travelers returned from Indian Ocean islands. Report of 47 cases. Medicine (Baltimore) 2007; 86:123–137.

25. Bouquillard E, Combe B. Rheumatoid arthritis after Chikungunya fever: A prospective follow-up study of 21 cases. Ann Rheum Dis. 2009; 68:1505–1506.

26. Sutiona DR, Gunawan JD. Dengue, Chikungunya and Zika: Differences in similarities. Indonesia International Institute for Life Sciences; Jakarta, Indonesia 2017; 44(3):176-178.

27. Malvy D, Ezzedine K, Mamani-Matsuda M, Autran B, Tolou H, Receveur M, et al. Destructive arthritis in a patient with chikungunya virus infection with persistent specific IgM antibodies. BMC Infectious Diseases, 2009; 9:200.

28. Cavrini F, Gaibani P, Pierro AM, Rossini G, Landini MP, Sambri V. Chikungunya: an emerging and spreading arthropod-borne viral disease. Journal of Infection in Developing Countries. 2009; 3:744-752.

29. Edwards CJ, Welch SR, Chamberlain J, Hewson R, Tolley H, Cane PA, Lloyd G. Molecular diagnosis and analysis of Chikungunya virus. Journal of Clinical Virology 2007; 39:271-275.

30. Mardekian SK, Roberts AL. Diagnostic Options and challenges for dengue and chikungunya viruses. BioMed Research International 2015; ID 34371. https://doi.org/10.1155/2015/834371

31. Deeba F, Islam A, Kazim SN, Naqvi IH, Broor S, and Ahmed A, et al. Chikungunya virus: recent advances in epidemiology, host pathogen interaction and vaccine strategies. Pathogens and Disease 2016; 74(3):ftv119.

32. Caglioti C, Lalle E, Castilletti C, Carletti F, Capobianchi MR, Bordi L. Chikungunya virus infection: An overview. The new microbiologica 2013; 36:211-227.

33. Jaffar-Bandjee MC, Das T, Hoarau JJ, Krejbich Trotot P, Denizot M, Ribera A, et al. Chikungunya virus takes centre stage in virally induced arthritis: Possible cellular and molecular mechanisms to pathogenesis. Microbes Infect 2009; 11:1206-1218.

34. Brighton SW. Chloroquine phosphate treatment of chronic Chikungunya arthritis. An open pilot study. S Afr Med J 1984; 66:217-218.

35. Mohan A. Chikungunya fever: clinical manifestations & management. Indian J Med Res. 2006; 124:471–474.

36. Suganthini Krishnan Natesan. Chikungunya Virus Treatment & Management. Available: http://emedicine.medscape.com/article/2225687-treatment [Accessed Aug. 2017]

Case Report

DCIMCJ 2018 January; 5(1):103-105

A Very Rare Case Report on a 4 Year Old Boy with Crigler-Najjar Syndrome Type-1 in Association with Sinus Venosus Type ASD

Salam W[1], Nahar K[2], Rahman MM[3], Adhikary AB[4], Hoque R[5], Islam N[6], Hossain A[7], Rahman CMM[8], Rahman KMA[9]

Abstract:

Crigler-Najjar syndrome (CNS) is a rare disorder and rares in association with congenital cardiac anomaly. A 4 year old boy was diagnosed as a case of sinus venosus type of Atrial Septal Defect (SVASD) in association with CNS. We surgically managed the SVASD without any complication.

Keywords: Crigler-Najjar Syndrome, sinus venosus ASD, surgical management

Introduction:

CNS is a rare autosomal recessive disorder of bilirubin metabolism. It is caused by mutation of bilirubin uridineglucoronosyltransferase gene (UGT1A 1) resulting in either complete deficiency of UGT enzyme (CNS type-I) or decreased activity of UGT. Incidence is less than 1 case per 1 million births, only a few hundred cases have been described[1].

1. Dr. Wahida Salam, Phase- B Resident, M.S. (Cardiovascular and Thoracic Surgery), BSMMU.
2. Dr. Kamrun Nahar, Phase- B resident, M.S. (Cardiovascular and Thoracic Surgery), BSMMU.
3. Dr. Md. Mostafizur Rahman, Professor, Department of Cardiac Surgery, BSMMU.
4. Dr. Asit Baran Adhikary, Chairman and Chief of Special Unit, Department of Cardiac Surgery, BSMMU.
5. Dr. Rezwanul Hoque, Professor, Department of Cardiac Surgery, BSMMU.
6. Dr. Nazmul Islam, Assistant Professor, Department of Thoracic Surgery, NIDCH.
7. Dr. Md. Aslam Hossain, Associate Professor, Department of Cardiac Surgery, BSMMU.
8. Dr. C.M. Mosabber Rahman, Phase- B Resident, M.S. (Cardiovascular and Thoracic Surgery), BSMMU.
9. Dr. Khan Md. Amanur Rahman, Medical Officer, Department of Cardiac Surgery, BSMMU.

Correspondence: Dr. Wahida Salam
E-mail:dr.wahida.salam@gmail.com

Crigler-Najjar (type 1) is the form of the disease that starts early in life where CNS (type 2)starts later in life.This rare variety of syndrome is rarely been associated with pregnancy[2]. But patient having CNS type-1 presented in association with cataract and another rare types of multiple cardiac anomalies (sinus venosus type of ASD with partial anomalous pulmonary venous connection and persistent left superior venacava) is very rare. The successful outcome after surgical correction of the cardiac defects in such a patient of rare association of this syndrome compelled us to report the case.

Case history:

A 4 year old boy got admitted here in our cardiac surgery department, BSMMU as a diagnosed case of Crigler-Najjar syndrome type-1 with an incidental finding of an Atrial Septal Defect imaged by 2D colour Doppler transthoracic echocardiography. Parents gave history that their child had yellow discolouration since first week of birth. For this they visited child special hospital and treated with phototherapy, but it was not improving satisfactorily. So they were referred to higher center of Paediatrichepatology department BSMMU for better management of their child. So they did and their child was diagnosed as a case of syndrome of unconjugated hyper bilirubinaemia was treated with phototherapy and Phenobarbitone. This time they noticed improvement and at this time bilirubin was

7.1 mg/dL from 22 mg/dL. So they were discharged and maintaining treatment schedule with regular follow up. Soon they noticed their baby with visual problem. They visited ophthalmologist and it was a bilateral cataract. The baby was thoroughly investigated. At that time, the child was found to have an ASD and was referred to cardiac surgery department of BSMMU. After admission we found hyper active precordium and systolic flow murmur over pulmonary region. Echocardiocardiography was repeated for every detail cardiac anomaly as well as to judge the operability. The echocardiography showed that the child had sinus venosus type of ASD (14mm), anomalous right upper pulmonary venous connection to right atrium near the opening orifice of SVC and also persistent left superior venacava. So our surgical team decided to do surgical correction of the anomaly.

Preoperative measures to avoid per and postoperative risks:

As the surgical correction was only option for treatment, we took all the measures to avoid certain life threatening per and postoperative complications like uncontrolled bleeding and anaesthetic drug hazards in context of high bilirubin. We also took consultation from Hepatology department and Anaesthesia department to avoid adverse outcome. We ensured a good number of whole blood, Fresh Frozen Plasma the day before surgical procedure. At the time of procedure the serum bilirubin level was 5.1 gm/dL.

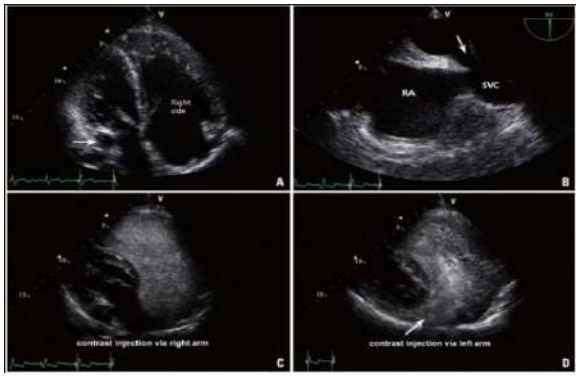


Fig: Echocardiographic images showing defects

RA= Right Atrium, SVC = Superior Vena Cava

Surgical management:

We started surgical procedure with standard median sternotomy and pericardiotomy. Aortic, SVC and IVC selective cannulation was done by 20 Fr, 14 Fr and 14 Fr cannula respectively. Aortic root cannulation done, Cardio Pulmonary Bypass (CPB) system was started and Cardioplegia was given through aortic root and cross clamp applied. PLSVC was identified, clamped and snared. RighAtriotomy was done for access to operative zone, an 8-10mm size sinus venosus type of ASD was indentified. The defect was closed appropriately by gluteraldehyde treated pericardial in such a way that right upper pulmonary venous blood was made to baffle into left atrium. Right atrium was closed by layers. Patient was weaned from CPB uneventfully and wound was closed in layers after keeping 1 epicardial pacing wire and two retrosternal drain tubes in situ. Total cross clamp time was 59 minutes and bypass time was 100 minutes.

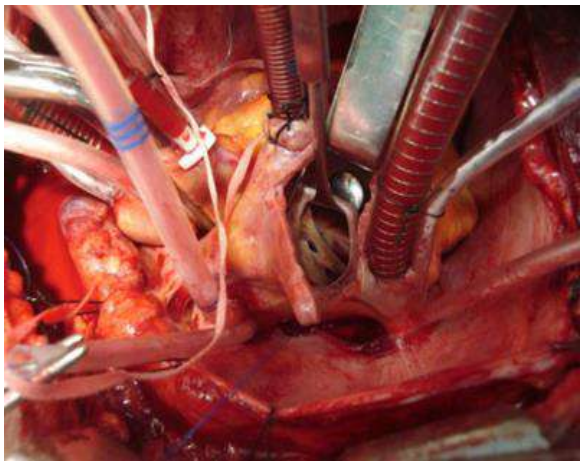


Fig: Sinus venosus ASD viewed peroperatively

Postoperative interval:

Patient was extubated 3 hours after completion of procedure and drain tube collection in immediate and early postoperative hours was in acceptable range. He was managed according to normal postoperative treatment protocol and required no special measures. Clinically there was no murmur and Doppler echocardiography showed the successful closure of defect.

The postoperative period was uneventful and the patient was discharged to home on 10 th postoperative day. After 1 month patient attended the out-patient department of cardiac surgery department, BSMMU and was found doing well.

Discussion:

Infants with CNS type-1 present with persistent jaundice at or soon after birth. Diagnosis is based on findings of total serum bilirubin between 20 and 45 mg/dL and presence of traces of bilirubin glucuronides in bile.[3] In our patient patient had serum bilirubin level of 22 mg/dL which consistent with the reference value. We could not confirm diagnosis by genomic DNA analysis or liver biopsy as they our beyond our scope of cardiac surgery faculty.

Sinus venosus type of atrial defect (SVASD) comprises only 12 per cent of ASD's All patients had a mid-systolic murmur and fixed splitting of the second sound.Echocardiography colour Doppler study can clearly demonstrate sinus venosus defects result from a deficiency in the wall that normally separates the right pulmonary veins from the superior venacava (SVC) and the right atrium (RA). This deficiency unroofs the right pulmonary veins, permitting them to drain into the SVC or into the RA[4]. In our case, we also confirmed our diagnosis by Doppler echocardiography.

The surgical outcome was smooth as there was very less amount of post operative bleeding. It correlates CNS type 1which is a nonhaemolytic variety of congenital hyper bilirubinemia.

Conclusion:

So, we can conclude that we can expect a good outcome after a complex surgical procedure if we take appropriate and timely measures as well as multidisciplinary collaboration for optimization of comorbidities. Also, this report gives an opportunity to evaluate the rare association of Crigler-Najjar syndrome, multiple congenital cardiac anomaly and cataract as a future field of interest.

References:

1. Chaudhary R, Maheshwari A, Deepmala, Tapparwal V. A rare case of Crigler-Najjar syndrome type II with pregnancy**,** International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2014;3(1): 261-262.

2. Paul JH, Sinaasappel W, Lotgering FK, Langendonk JG. Recommendations for Pregnancies in Patients with Crigler-Najjar Syndrome, JIMD Reports. 2012 [online]. Available at: DOI 10.1007/8904_2012_142 (Accessed: 22 April 2012).

3. Kumar P, Sasmal G, Gupta S, Saxena R, Kohli S. Crigler-Najjar syndrome type2 (CNS type2): an unwonted cause of jaundice in adult. 2017 [online]. Available at :http: //dx.doi.org/ 10.5455/2320 1770.ijrcog20140356 (Accessed: 2 February 2014)

4. Pragh S, Carrera ME, Sanders SP, Mayer JE, Pragh RV. Sinus venosus defects: unroofing of the right pulmonary veins—anatomic and echocardiographic findings and surgical treatment, American Heart Journal. 1994; 128(2): 365-379.

Case Report

DCIMCJ 2018 January; 5(1):106-110

Ectopic Parathyroid Adenoma: Surgical Correction and its Complication Management

Basnet N[1], Singh A[2], Pradhan R[3], Sunny SA[4], Adhikary AB[5], Islam N[6]

Abstract:

Ectopic parathyroid are most frequently found in the anterior mediastinum, in association with the thymus or the thyroid gland. Ectopic parathyroid glands are a major cause of persistent and recurrent Hyperparathyroidism. The treatment for an ectopic parathyroid adenoma is resection which can be performed via median sternotomy, transcervical approach or thoracoscopically.

Keywords: Ectopic parathyroid, hyperparathyroidism, hypercalcemia

Introduction:

Ectopic parathyroid are most frequently found in the anterior mediastinum, in association with the thymus or the thyroid gland[1]. The parathyroid glands arise in an ectopic site in 1-3% of the cases and may be found anywhere from the angle of the jaw to the pericardium as a consequence of a variability in the glandular tissue migration during the embryologic life. In more than 80% of the cases the ectopic mediastinal parathyroid glands are found within or in close contact with the thymus in the anterior mediastinum[2]. Ectopic parathyroid glands are a major cause of persistent and recurrent Hyperparathyroidism (HPT). Nonfunctional anatomic studies such as MRI may reveal a well-defined mass, but they are usually small (<3 cm). Technetium-99m-sestamibi scintigraphy is the most useful study to localize hyper functioning ectopic parathyroid adenomas in the mediastinum. This study can also be performed as a subtraction study with iodine-123. The treatment for an ectopic mediastinal parathyroid adenoma is resection. This is performed via a transcervical approach, via a median sternotomy, or, in experienced hands, thoracoscopically. Resection involves removal of the thymus and surrounding fat to include the adenoma. Intraoperative use of rapid parathormone levels confirms the successful localization and removal of the adenoma.

Ectopic parathyroid glands continue to be a diagnostic and operative challenge in patients with hyperparathyroidism[3]. Parathyroid crisis due to an ectopic parathyroid adenoma is even rarer, and thus, its diagnosis and treatment can usually be challenging.

Case report:

A 65-year-old female was referred from Surgical Endocrine Department to The department of Cardiac Surgery in Bangabandhu Sheikh Mujib Medical University as a parathyroid crisis due to an ectopic mediastinal parathyroid adenoma with her serum calcium and PTH markedly increased in short time.

1. Dr. Nishes Basnet, Phase-B Resident, MS (Cardiovascular and Thoracic Surgery), Bangabandhu Sheikh Mujib Medical University, Dhaka.
2. Dr. Alka Singh, Phase-B Resident, MS (Cardiovascular and Thoracic Surgery), Bangabandhu Sheikh Mujib Medical University, Dhaka
3. Dr. Rajat Pradhan, Phase-B Resident, MS (Cardiovascular and Thoracic Surgery), Bangabandhu Sheikh Mujib Medical University, Dhaka
4. Dr. Samir Azam Sunny Medical Officer (MS, CTVS), Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka.
5. Dr. Asit Baran Adhikary, Chairman and Chief of Special Unit, Department of Cardiac Surgery, BSMMU.
6. Dr. Nazmul Islam, Assistant Professor, Department of Thoracic Surgery, NIDCH.

Correspondence: Dr. Nishes Basnet
E-mail: nishesbasnet@gmail.com

The investigation results showed that serum calcium 12.1 mmol/L (N 2.08–2.60 mmol/L), phosphorus 1.90 mmol/L (N 0.81–1.62 mmol/L), creatinine 97 µmol/L (N 62–133 µmol/L), intact para thyroid hormone 2207.0 pg/mL (11-67 pg/mL), Hb 10.6 g/dl. Several intact serum parathyroid hormone (iPTH) tests were markedly elevated. The other laboratory tests were within the normal range. She was hypertensive for 2 years. She had H/O fracture right neck femur 14years back, H/O Leprosy 10 years back for which she took standardized regimen of oral drugs and was completely cured. H/O fracture upper end of right humerus 4 months back. She didn't complain of bone pain. No familial history of any such above mentioned conditions.She was then evaluated in our institution for the persistence of hypercalcemia and parathyroid crisis. Her heart, lungs revealed normal and abdominal USG revealed suggestive of cystitis. Liver and spleen were not palpable. There was no lymphadenopathy or palpable mass in the neck. Her complete blood cell count, thyroid hormones, cortisone and biomarkers for malignancy were normal. The ultrasonography of neck revealed features suggestive of multi nodular goiter and CT of the chest and lower neck showed an ovoid soft tissue density area measuring about 25x20x15 mm in the anterior mediastinum. On post contrast scan strong homogenous enhancement of the lesion suggestive of ectopic parathyroid at anterior mediastinum.

She underwent Technetium-99m-sestamibi (MIBI) scintigraphy scan. Early image was taken at 10mins showed both the lobes of thyroid gland normal in size with homogeneous radiotracer concentration. Focal areas of intense tracer activity were seen in superior mediastinum. Delayed images were acquired 2hours show significant washout of tracer from both the lobes of thyroid while the above mentioned area of focal intense tracer concentration in superior mediastinum became more intense and visible.Scan was positive for localization of parathyroid adenoma/hyperplasia in superior mediastinum.After fluid resuscitation, loop diuretic, and calcitonin treatment, the patient was then operated, standard median sternotomy was done. Parathyroid adenoma was identified which was 4cm x 4cm in size. Dissection of parathyroid adenoma was done.

Hemostasis was secured and sternotomy fixed with sternal wire chest closed in layers. Whole procedure was uneventful.But after 4 hours patient developed the color change of the left arm for which the patient was rushed to operation theatre suspecting it to be embolic occlusion.



Fig 1: Showing the color change of left hand



Fig 2: Color change with edema of left hand just before exploration

Transverse incision was made over the left cubital fossa, bracial artery was identified, proximal and distal control was taken. Fogerthy catheter was introduced, heparin and papaverin wash was given.

There was no embolic occlusion. Color change of ischemic site was observed. Radial and ulnar artery was felt for pulsation, initially there was decreased pulsation of the ulnar artery, then another longitudinal incision made to explore ulnar artery and compartment syndrome was released after which the ulnar pulsation reverted to normal. Heparin and papaverine wash was given blindly to the proximal and distal part of fingers. Color was changed to pale pink from black. Hemostasis was secured, wound over the cubital fossa closed in layers and other over the forearm was left open. The cause of thromboembolic manifestation could not be identified.

Discussion:

Parathyroid crisis is an uncommon life-threatening complication of primary hyperparathyroidism and its prognosis is poor; therefore, it requires aggressive medical therapy and early surgical treatment[1]. In the majority of cases, it is a complication of already diagnosed primary hyperparathyroidism. An ectopic parathyroid adenoma that causes primary hyperthyroidism is difficult to detect by various imaging modalities, because ectopic parathyroid adenomas are usually small between 1 and 2 cm[4]. Therefore, ectopic parathyroid adenomas are often detected either in the preoperative work up of patients who present with hypercalcemia or in postparathyroidectomy patient with persistent hypercalcemia[5]. The clinical and laboratory features of patients with primary hyperthyroidism due to ectopic adenomas have been reported to be more severe than those with ectopic adenomas, since the former may manifest with higher calcium levels and more frequent primary hyperthyroidism related bone disease[6]. The localization and treatment of an ectopic parathyroid adenoma that caused parathyroid crisis can usually be challenging[3].

Multiple diagnostic modalities for imaging the parathyroid glands include ultrasonography, CT, magnetic resonance imaging (MRI) and radionuclide scintigraphy[4]. Ultrasonography is commonly used to locate enlarged parathyroid glands due to its convenience and low cost. High-resolution ultrasound can accurately localize adenomas relative to the thyroid gland. However, its ability to detect abnormalities depends on the experience and skill of the operator, and therefore, its sensitivity in localization of enlarged parathyroid glands varies greatly (44%–87%)[7]. Just in our case, the ultrasonography didn't show the lesion.CT and MRI may further contribute to the identification of ectopic parathyroids and the differential diagnosis from other lesions[8]. However, the differential diagnosis of ectopic parathyroids from lymph nodes, thyroid, or thymus tissue depends on the location.

The other most widely used imaging technique, 99mTc-MIBI scintigraphy, has similar sensitivities as ultrasonography. However, when combined with ultrasonography, the overall sensitivity can be increased[9]. Dual-phase, dual-tracer 99mTc-MIBI scintigraphy has increased the sensitivity of detection of parathyroid adenomas (up to 90%)[10]. High-resolution ultrasound and parathyroid scintigraphy both have their own advantages. The former is good at localizing adenomas relative to the thyroid gland, whereas the latter is usually reserved for detecting adenomas in nodular thyroid disease and at ectopic sites, which incidence is up to 20% of patients[11]. There is numerous studies found that the typical retention of 99mTc-MIBI in the parathyroid adenoma was longer than that in the normal thyroid. However, in our case, 99mTc-MIBI showed early tracer uptake by both lobes of thyroid glands with fairly homogenous radio tracer concentration. Focal areas of intense tracer activity seen in superior mediastinum and in delayed phase taken at 2 hours showed significant washout of tracer from both lobes of thyroid while above mentioned area of focal intense tracer concentration in superior mediastinum became more intense and visible.

The combination of sestamibi scintigraphy and CT imaging accurately localized the tumor to the anterior mediastinum, thus highlighting the usefulness of combining multiple imaging techniques to locate ectopic active parathyroid gland. Hybrid imaging with SPECT/CT, which combines scintigraphic datasets (SPECT) and anatomical (CT) has become increasingly valuable over the last few years.

The combination of MIBI with ultrasonography raises the sensitivity to 78% to 96%[12] and with CT or MRI may raise the sensitivity and specificity to 100%[13]. These combinations are cost effective and are indicated as a means for routine preoperative localization of ectopic parathyroid adenomas, especially in cases with faint 99mTc-MIBI scans[14].

Surgery remains the only cure for patients with primary hyperparathyroidism. The literature review by Alesina *et al* has shown that video assisted thoracoscopic surgery (VATS) is a feasible and safe approach with overall low morbidity and mortality. Thepossibility of a minimally invasive single gland approach becoming the standard of care for such patients is a future we can look forward to[15].

Conclusions:

Parathyroid crisis is life threatening and its prognosis is poor, it requires aggressive medical therapy and early surgical treatment. The combination of imaging techniques has incremental value in localizing ectopic parathyroid adenomas over either technique alone.

References:

1. Ntaios G, Savopoulos C, Chatzinikolaou A, et al. Parathyroid crisis as first manifestation of primary hyperparathyroidism. Eur J Intern Med. 2007; 18:551–52.

2. Curley IR, Wheeler MH, Thompson NW, Grant CS. The challenge of the middle mediastinal parathyroid. World J Surg. 1988; 12(6):818-22.

3. Noussios G, Anagnostis P, Natsis K. Ectopic parathyroid glands and their anatomical, clinical and surgical implications. Exp Clin Endocrinol Diabetes. 2012; 120:604–10.

4. Ng P, Lenzo NP, McCarthy MC, et al. Ectopic parathyroid adenoma localized with sestamibi SPECT and image- fused computed tomography. Med J Aust. 2003; 179:485–87.

5. Vijayakumar V, Anderson ME. Detection of ectopic parathyroid adenoma by early Tc- 99m sestamibi imaging. Am Nucl Med. 2005; 19:157–59.

6. Mendoza V, Ramírez C, Espinoza AE, et al. Characteristics of ectopic parathyroid glands in 145 cases of primary hyperparathyroidism. Endocr Pract. 2010; 16:977–81.

7. Haber RS, Kim CK, Inabnet WB. Ultrasonography for preoperative localization of enlarged parathyroid glands in primary hyperparathyroidism: comparison with 99m technetium sestamibi scintigraphy. Clin Endocrinol. 2002; 57:241–49.

8. Beierwaltes WH. Endocrine imaging: parathyroid, adrenal cortex and medulla and other endocrine tumors. J Nucl Med. 1991; 32:1627–39.

9. Johnson NA, Tublin ME, Ogilvie JB. Parathyroid imaging: technique and role in the preoperative evaluation of primary hyperparathyroidism. AJR Am J Roentgenol. 2007; 188:1706–15.

10. Castellani M, Reschini E, Longari V, et al. Role of Tc-99m sestamibi scintigraphy in the diagnosis and surgical decision-making process in primary hyperparathyroid disease. Clin Nucl Med. 2001; 26:139–44.

11. Akerstrom G, Malmaeus J, Bergstrom R. Surgical anatomy of human parathyroid glands. Surgery. 1984; 95:14–21.

12. McHenry CR. What's new in general surgery: endocrine surgery. J Am Coll Surg. 2002; 195:364–71.

13. Zerizer I, Parsaï A, Win Z, et al. Anatomical and functional localization of ectopic parathyroid adenomas: 6-year institutional experience. Nucl Med Commun 2011; 32:496–502.

14. Elaraj DM, Sippel RS, Lindsay S, et al. Are additional localization studies and referral indicated for patients with primary hyperparathyroidism who have negative sestamibi scan results? Arch Surg 2010; 145:578–81.

15. Alesina PF, Moka D, Mahlstedt J, Walz MK. Thoracoscopic removal of mediastinal hyperfunctioning parathyroid glands: personal experience and review of the literature. World J Surg 2008; 32: 224–231.

Case Report

DCIMCJ 2018 January; 5(1):111-114

Food Bolus Impaction in a Case of Corkscrew Esophagus: A Rare Case report

Rahman MM[1], Adhikary AB[2], Rahman MM[3], Hoque MR[4], Ranjan R[5], Islam MN[6]

Abstract:

Corkscrew esophagus is the radiological sign of diffuse esophageal spasm which is a uncommon esophageal motility disorder. It may present with food bolus obstruction in old age. We are reporting such a case who had dysphagia since childhood and presented with food bolus obstruction in old age. Barium esophagogram revealed a twisted corkscrew like appearance of esophagus and endoscopy of upper GIT revealed presence of food bolus at distal esophagus which was removed by rigid esophagoscopy. Patient was discharged successfully with advice for follow up.

Keywords: Corkscrew esophagus, diffuse esophageal spasm, esophageal motility disorder

Introduction:

The spiral, twisted, corkscrew like appearance of esophagus due to intense tertiary esophageal contraction seen in contrast esophagogram is known as Corkscrew esophagus. It is the classical radiological feature of diffuse esophageal spasm which is a primary esophageal motility disorder[1]. It is five time less common than achalasia cardia[2]. Diffuse esophageal spasm usually occurs at middle age and afterwards but may occur at any age [3].

1. Dr. Md. Mushfiqur Rahman, Resident, Phase-B MS (Cardiovascular and Thoracic Surgery), Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka.
2. Professor Dr. Asit Baran Adhikary, Professor and Chairman, Department of Cardiac Surgery, BSMMU, Dhaka.
3. Professor Dr. Md. Mostafizur Rahman, Professor, Department of Cardiac Surgery, BSMMU, Dhaka.
4. Professor Dr. Md. Rezwanul Hoque, Professor, Department of Cardiac Surgery, BSMMU, Dhaka.
5. Dr. Redoy Ranjan, Medical Officer, Department of Cardiac Surgery, BSMMU, Dhaka.
6. Dr. Md. Nazmul Islam, Assistant Professor, Department of Thoracic Surgery, National Institute of Disease of Chest and Hospital (NIDCH), Dhaka.

Correspondence: Dr. Md. Mushfiqur Rahman
E-mail: mushfiq.ndc@gmail.com

Herein we reported a case of corkscrew esophagus presented with food bolus obstruction.

Case Report:

A 80 year old male patient, non-diabetic, normotensive, smoker for 35 years presented in the department of thoracic surgery of National Institute of Disease of Chest and Hospital (NIDCH) with complaints of painless, non-progessive dysphagia to solid and liquid food since childhood. . Whenever he used to take meal he sensed sticking of food bolus in his food passage for a variable time period after which it passes down quickly and spontaneously.



Fig-1: Barium swallow X-ray of esophagus: Corkscrew esophagus and the barium not passed to stomach suggestive of impacted food bolus at distal end of esophagus.

The more the food was solid, it took more time to pass down. The dysphagia used to precipitated by hot and cold liquid, rapid eating and stress. He also had occasional chest discomfort which was retrosternal, spasmodic, non-radiating and occurred only when the food bolus remained stuck in his food passage. Chest discomfort was associated with regurgitation of the undigested food. Therefore, he had to spend more time during taking a meal than others. He was accustomed with these problems since childhood and never visited any physicians. Two days before the admission in our hospital he experienced for the first time that, after taking a meal containing meat, the food bolus remained impacted in his food passage and was not passing down.



Figure-2: Endoscopy of upper gastrointestinal tract: Impacted food bolus in esophagus

Fig



Figure-3: Barium swallow X-ray of esophagus (A/P and lateral view) after removal of impacted food bolus: Corkscrew esophagus with passage of barium from esophagus to stomach

The food bolus impaction was associated with retrosternal chest discomfort. He had no history of weight loss, corrosive ingestion, chest radiotherapy or gastroesophageal reflux. His pulse was 82 b/min, regular, BP-100/70mmHg, no lymphadenopathy. Other parameters of general examinations were also normal. Systemic examinations including alimentary system examination revealed normal findings. The patient presented Barium swallow X-ray of esophagus during admission (fig-1) and it revealed corkscrew like twisted appearance of esophagus with presence of obstruction at distal end of esophagus probably due to impacted food bolus. During admission to thoracic surgery department, the patient also presented his recent endoscopy of upper gastrointestinal tract (fig-2) which confirmed the presence of food bolus in distal part of esophagus 35 cm from upper incisor teeth. Therefore, rigid esophagoscopy guided food bolus removal was done. Following the rigid esophagoscopy procedure, patient was able to ingest liquid initially and gradually semisolid food. So, patient was discharged 48 hours after the procedure with medications including.

Diltiazem oraly daily, advice regarding diet and follow-up visit with a repeat barium esophagogram. One week later the patient came for follow up with Barium swallow X-ray of esophagus (fig -3) which revealed corkscrew appearance of esophagus and the contrast passed distally to stomach indicative of successful removal of food bolus from distal esophagus. Patient also informed that after taking the calcium channel blocker (Diltiazem) regularly, his symptoms improved markedly and he feels even better than ever as he can take all kinds of foods now without sense of sticking and there has never been a episode of regurgitation since then. Therefore, patient was advised to continue the medication and to attend follow up visit on need basis.

Discussion:

Corkscrew esophagus which is the radiological appearance of diffuse esophageal spasm several segments of the esophagus contract simultaneously, preventing the propagation of the food bolus (aperistalsis) resulting dysphagia. Exact cause is unknown. Degenerative loss of inhibitory neurotransmitter (nitric oxide, VIP) secreting neurons in myenteric plexus in esophagus is known to be the possible pathology. There is associated muscular hypertrophy and degeneration of the branches of the vagus nerve in the esophagus. Diffuse esophageal spasm usually present with intense non cardiac chest pain, regurgitation of food and dysphagia that is non progressive involving both solid and liquids and precipitated by stress, rapid eating, hot and cold liquids, which is consistent with the symptoms of our patient since childhood[4]. Our patient presented to us with feature of food bolus impaction which is also observed in the study of others[5]. On contrast esophagogram diffuse esophageal spasm present as "rossary bead" or "corkscrew" like twisted appearance of esophagus which is observed in our patient and consistent with the study of others[6]. Our patient had his symptoms since childhood but he did not take any treatment or consultation for his illness as he was habituated with this life style.

But his symptoms worsen day by day and ultimately had food bolus obstruction at this age of 80 years probably due to age related degeneration which is also observed in the study of others[5]. The impacted food bolus of our patient was removed by rigid esophagoscopy. The esophageal musosa of our patient appeared normal and there was no obvious growth visible in rigid esophagoscopy. Thereby, besides removal of food bolus, the rigid esophagoscopy also aided to exclude the possibility of food bolus impaction due to the esophageal malignancy which is common at this old age. After removal of food bolus a barium esophagogram was done in our patient during follow up visit which was satisfactory as it revealed that, the barium has passed from esophagus to stomach excluding any obstruction at distal end of esophagus. Medical treatment is the mainstay of treatment of corkscrew esophagus that includes calcium channel blocker which was given in our patient and his symptoms of dysphagia improved markedly with disappearance of regurgitation of ingested food[4].

Conclusion:

No age is immune for esophageal motility disorder like corkscrew esophagus. Treatment aim is to relieve symptom and to improve quality of life as the pathology is irreversible here. Patients should be reassured and counseled about their disease, it's lifelong and benign nature, possible complications, therapeutic options and expected outcomes.

References:

1. Fonseca EKUN, Yamauchi FI, Tridente CF, Baroni RH. Corkscrew esophagus. Abdominal Radiology. 2017; 42: 985-86

2. Craddock DR, Logan A, Walabaum PR. Diffuse esophageal spasm. Thorax. 1996; 21:511.

3. Ismay G. Painful spasm of esophagus ("Corkscrew" Esophagus). BMJ. 1952;27:697.

4. Qadder MA, Vaezi MF. Esophageal motility disorders. In: Patterson GA, Cooper JD, Deslauriers J, Lerut AEMR, Luketich JD, Rice TW. Editors. Pearson's thoracic and espphageal surgery. Philadelphia. Churchill livingstone Elsevier. 2008:714-24

5. Ginsberg GG. Food bolus impaction. Gastroenterol Hepatolol. 2007; 3: 85-6.

6. Lipe DN, Borden N. Rare radiological pattern of diifuse esophageal spasm. West J Emerg Med. 2015; 16:426-2.