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From the Desk of Editor-in-Chief

We are delighted to inform that the Volume 5, Number 2 of the Dhaka Central International Medical College Journal (DCIMCJ) is going to be published very soon. In this issue we have added a new section, Medical Quiz: Images. 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

INFORMATION FOR AUTHORS

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Guidelines for the Authors:

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

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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.

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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.

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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.

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

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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 hoursreading 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.

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- Manuscripts are received with the explicit understanding that they are not under simultaneous consideration that are not under simultaneous by any other publication.
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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.
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.
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- Authors need to work closely with editors in developing or using such new publication formats and should submit supplementary electronic material for peer review.
- Double-spacing all portions of the manuscript- including the title page, abstract, text, acknowledgments, references, individual tables, and legends- and generous margins make it possible for editors and reviewers to edit the textline 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.

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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).

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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.
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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).
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- 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.

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- 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.

I. A. 6. b. Technical information:

- Identify the methods, apparatus (give the manufacturer's name and address in parentheses), and procedures insufficient detail to allow others to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and 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 for locatin, selection, extracting, and synthesizing data. These methods should also be summarized in the abstract.

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- Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals).

- Avoid relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size. References for the design of the study and statistical methods should be to standard works when possible (with pages stated).

- Define statistical terms, abbreviations, and most symbols.

- Specify the computer software used.

I. A. 7. 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.

I. A 9. References:

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

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- 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.

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- 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)

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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
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General outline for article presentation and format:

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- 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
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- Numerals at the beginning of the sentence spelt out

Tables and figures:

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  - Complete author information
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- **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
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- **Material and Methods:**
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  - 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
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  - Give your conclusion
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- **Acknowledgement:**
  - Acknowledge any person or institute who have helped for the study
- **Reference:**
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  - 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

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DCIMCJ

Editorial

DCIMCJ 2018 July; 5(2):14-21

Use of Rituximab in Renal Diseases

Nomany BMS[1], Chowdhury MAH[2], Alam MR[3], Gani MO[4], Alam MM[5]

Introduction:

Rituximab is a monoclonal chimeric anti-CD20 antibody. It is an effective B-Cell depleting agent and is usually used to treat certain types of cancer. Rituximab also offers an alternative to current immunosuppressive therapies for difficult-to-treat Nephrotic Syndrome. Recent data for its use support a wide range of conditions including renal diseases.

Historical perspective:

Rituximab is a murine/human chimeric anti-CD20 mAb that depletes B cells and was licensed in 1997 for the treatment of non-Hodgkin's lymphoma. A subsequent interest highlighted the roles in diseases with B cell dysregulation, inflammation, and autoantibody synthesis. T cell auto reactivity is B cell dependent through autoantigen presentation and co-stimulatory support from B cells. Therefore Rituximab may be effective in B and T cell mediated autoimmune diseases.

How Does Rituximab Work:

Rituximab reduces the number of harmful auto antibodies (e.g. ANCA, cry globulins, anti-phasphalipid antibodies etc.). Auto antibodies are produced by B-cells and attack healthy tissue and cells. The autoantibodies target neutrophils and cause neutrophils to stick and clump to the walls of small bood vessels in different tissues and organs of the body leading to inflammation. Rituximab decreases the number of B-cells by targeting specific marker on their cell surface called CD20 disrupting auto antibody production as well.

Lupus Nephritis (LN):

The standard treatment of lupus nephritis (LN) remains problematic because the current treatment regimen based on nonspecific immunosuppressants such as steroids, cyclophosphamide (CYP) and mycophenolate mofetil (MMF) has significant side effects and is often associated with refractory or relapsing disease. B-cell ablation with the monoclonal chimeric anti-CD20 antibody rituximab (RTX) has been considered as an alternative treatment option.

RTX is increasingly used in patients with lupus nephritis, but reported series were small and had a short follow-up. Catherine Melanderet el. analyzed clinical and histologic data of 20 patients who were treated with RTX for lupus nephritis and followed up for at least 12 months. RTX was administrated weekly for 4 wk at a dosage of 375 mg/m^2 of body surface area.

Results showed that 19 women and 1 man received rituximab as induction treatment for an active class IV (15 cases) or class V (5 cases) lupus nephritis. Rituximab was given for lupus nephritis refractory to standard treatment (12 cases), for relapsing disease (6 cases), or as first-line treatment (2 cases). Three patients received cyclophosphamide concomitantly with rituximab. Ten received new injections of rituximab as maintenance therapy. After a median

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3. Dr. Md. Rejaul Alam, Medical Officer, Department of Nephrology, BSMMU.
4. Dr. Mohammad Osman Gani, Associate Professor, Department of Medicine, Dhaka Central International Medical College.
5. Dr. Md. Monoarul Alam, Assistant Professor, Department of Medicine, Dhaka Central International Medical College.

follow-up of 22 months, complete or partial renal remission was obtained in 12 patients (60%). Lupus nephritis relapsed in one patient, who responded to a new course of rituximab. The achievement of B cell depletion 1 month after rituximab, was strongly associated with renal response. Rapidly progressive glomerulonephritis did not respond to rituximab. Therefore Rituximab is an interesting therapeutic option in relapsing or refractory lupus nephritis.[1]

The randomized controlled LUNAR trial failed to show any additive effect of RTX beyond a steroid–mycophenolate mofetil (MMF) combination for LN type III/IV/V in incident patients. Marc Weidenbuschet el. analysed existing evidence on this topic by performing a systematic analysis of reports that document outcomes of RTX treatment for refractory LN. Out of 233 reports, they selected 26 for analysis, which described 300 patients with a mean follow-up of 60 weeks. The complete or partial response criteria were met by 87% of patients with LN class III, 76% with class IV and 67% with class V, respectively. Mixed classes responded in 76% of patients. RTX induced complete responses in 60% (type III), 45% (type IV), 40% (type V) and 24% (mixed types), respectively. Their systematic review of existing evidence suggests that RTX effectively induces remission of LN in patients who have not achieved remission with standard therapies[2].

Steroid-Resistant Nephrotic Syndrome (SRNS):

The treatment of steroid-resistant nephrotic syndrome (SRNS) is challenging. Persistent proteinuria and hypoalbuminemia signifies in serious complications including progressive kidney disease. Intensive treatment regimens show varying results in inducing remission and are also associated with adverse effects. On the basis of knowledge that B lymphocytes are crucial in the pathogenesis of the nephrotic syndrome[3], Arvind Bagga et al examined the efficacy of treatment with rituximab in patients with SRNS that was resistant to high-dose corticosteroids, alkylating agents, and calcineurin inhibitors[4].

Five patients (three with initial resistance and two with late resistance to corticosteroids) between the ages of 2.8 and 16.0 years were included in the study. Renal-biopsy specimens showed minimal-change disease in two of the patients and focal segmental glomerulosclerosis in three.

They administered rituximab by intravenous infusion at a dose of 375 mg per square meter of body-surface area once weekly for 4 weeks; the patients continued to receive therapy with calcineurin inhibitors, alternate-day prednisolone, or both. During treatment with rituximab, the patients received cotrimoxazole prophylaxis for 6 months. Reduction in proteinuria was noted after the infusions. At a median interval of 4 weeks (range, 2 to 8) after the last rituximab dose, four patients had a complete remission (urinary albumin- trace/negative), and one patient had a partial remission (urinary albumin- 2+). Six months later, one patient had a relapse and was treated with prednisolone, which resulted in a partial response. Complete remission was maintained in three patients, despite the tapering of doses of corticosteroids and calcineurin inhibitors. The mean ratio of urinary protein to creatinine was 8.3 at baseline and 0.8 at follow-up ($P=0.02$, by analysis of variance), the mean serum albumin level rose from 1.4 to 3.4 g per deciliter ($P<0.01$), and the mean cholesterol level declined from 481 to 260 mg per deciliter ($P<0.05$); differences in leukocyte counts and levels of IgG were not significant, and none of the patients had serious infections.

Ashima Gulati et al reported the efficacy and safety of rituximab in patients with steroid-resistant nephrotic syndrome (SRNS) and steroid-dependent nephrotic syndrome (SDNS) refractory to standard therapy.[5] This was a cohort study in academic, tertiary care centers in India and the United States. Patients with SRNS or SDNS, not responding to medications or showing calcineurin inhibitor toxicity, treated with two to four doses of intravenous rituximab, and followed ≥12 months were included. Treatment was administered at a dose of 375 mg/m^2 once every weekfor fourdoses in

patients with SRNS and two doses for those with SDNS. Oral prednisone was given every other day at a dose of 1.5 mg/kg for 2 weeks, 1 mg/kg for 4 weeks, 0.75 mg/kg for another 4 weeks, and then 0.5 mg/kg. In patients receiving a calcineurin inhibitor, its dose was reduced to 50% at 3 months, with cessation, if possible, at 6 months. Therapy with other immunosuppressive agents was discontinued before treatment with rituximab, except in two adult patients with SRNS who received long-term therapy with MMF.

Results showed that 33 patients with SRNS and 24 with SDNS, with mean ages of 12.7 ± 9.1 and 11.7 ± 2.9 years, respectively, were included. Six months after rituximab therapy, 9 (27.2%) patients with SRNS showed complete remission, 7 (21.2%) had partial remission, and 17 (51.5%) had no response. At 21.5 ± 11.5 months, remission was sustained in 15 (complete: 7, partial: 8) patients. Of 24 patients with SDNS, remission was sustained in 20 (83.3%) at 12 months and in 17 (71%) at follow-up of 16.8 ± 5.9 months. The mean difference in relapses before and 12 months after treatment with rituximab was 3.9 episodes per patient per year. Therefore rituximab was safe and effective in inducing and maintaining remission in a significant proportion of patients with difficult SRNS and SDNS.

Membranous Nephropathy (MN):

The ideal treatment of patients with primary membranous nephropathy (MN) and persistent nephrotic syndrome (NS) is still a matter of debate. This is a major issue since these patients may progress to end-stage kidney disease (ESRD) in 5-10 years. Steroids, alkylating agents, and calcineurin inhibitors have been suggested to achieve NS remission and prevent ESRD in this population. Treatment benefits, however, are uncertain and are often offset by adverse events. Evidence that B cells play a crucial role in the pathogenesis of the disease, both as precursors of autoantibody-producing cells and as antigen-presenting cells, provided the background for explorative studies testing the role of B cell-depletion therapy with rituximab.

Marco Fiorentino et al. studied 38 patients with idiopathic MN treated with rituximab (in 13 patients as first-line therapy, in the remaining 25 after conventional immunosuppressive therapy)[6].

Following a baseline evaluation, they received intravenous infusions of rituximab at a dose of 375 mg/m^2 4 weekly (about 700 mg for standard BSA). Two patients received only two infusions of rituximab, because circulating B cells after the first infusions were $<5/mm^3$. The clinical and laboratory parameters for all patients at baseline and every month for the first 3 months and then every 3 months were evaluated, such as urinary protein excretion, serum creatinine, estimated glomerular filtration rate (eGFR) by the MDRD formula and white blood cell and lymphocyte subpopulation counts. Circulating B cell levels in peripheral blood were evaluated by the detection of CD19+cells. B cell depletion was described as a CD19+ cell count $<5/mm^3$ and <1% total lymphocytes count. When available, anti-phospholipase A2 receptor antibodies (anti-PLA2R Abs) were evaluated before and after the treatment.

The patients were analyzed for a 15-month median (interquartile range 7.7–30.2) follow-up, with serial monitoring of 24-h proteinuria, renal function and circulating CD19+ B cells.

The percentages of patients who achieved complete remission, partial remission and the composite endpoint (complete or partial remission) were 39.5% (15 patients), 36.8% (14 patients) and 76.3% (29 patients), respectively. The 24-h proteinuria was reduced significantly during the entire period of follow-up (from a baseline value of 6.1 g/day to 0.9 g/day in the last visit; $P < 0.01$), while albuminemia increased constantly (from a baseline value of 2.6 g/dL to 3.5 g/dL in the last observation; $P < 0.01$). Renal function was not significantly deteriorated during the observation period. Circulating CD19+ B cells were reduced significantly from the baseline value to the 24-month value ($P < 0.01$); data about anti-phospholipase A2 receptor antibodies were available in 14 patients, 10 of which experienced a

decreasing trend after treatment. No significant adverse events were described during and after infusions.

The present study confirmed that treatment with rituximab was remarkably safe and allowed for a large percentage of complete or partial remissions in patients with MN.

ANCA associated vasculitis (AAV):

Cyclophosphamide and glucocorticoids have been the cornerstone of remission-induction therapy for severe antineutrophil cytoplasmic antibody (ANCA)−associated vasculitis for the last 40 years. John H et al. conducted a multicenter, randomized, double-blind trial of rituximab **(375 mg/meter^2 /week for 4 weeks)** as compared with cyclophosphamide (2 mg/kg per day) for remission induction. Glucocorticoids were tapered off; the primary end point was remission of disease without the use of prednisone at 6 months[7].

The remission-induction period was 6 months. The rituximab group received intravenous rituximab **(375 mg/meter^2/ week for 4 weeks)** plus daily placebo−cyclophosphamide. The control group received placebo−rituximab infusions plus daily cyclophosphamide (2 mg/ kg, adjusted for renal insufficiency). Patients in the control group who had a remission between 3 and 6 months were eligible to switch from cyclophosphamide to azathioprine (2 mg/kg/day). Patients in the rituximab group with a remission during the same 3-to-6-month period were switched from placebo−cyclophosphamide to placebo−azathioprine.

The two treatment groups received the same glucocorticoid regimen: 3 pulses of methylprednisolone (1000 mg each), followed by prednisone at a dose of 1 mg/kg per day. The dose was tapered so that by 5 months, all patients who had a remission without disease flares had discontinued glucocorticoids.

Result showed that nine centers enrolled 197 ANCA-positive patients. Baseline disease activity, organ involvement, and the proportion of patients with relapsing disease were similar in the two treatment groups.

Sixty-three patients in the rituximab group (64%) reached the primary end point, as compared with 52 patients in the control group (53%), a result that met the criterion for noninferiority (P<0.001). The rituximab-based regimen was more efficacious than the cyclophosphamide-based regimen for inducing remission of relapsing disease; 34 of 51 patients in the rituximab group (67%) as compared with 21 of 50 patients in the control group (42%) reached the primary end point (P=0.01). Rituximab was also as effective as cyclophosphamide in the treatment of patients with major renal disease or alveolar hemorrhage. There were no significant differences between the treatment groups with respect to rates of adverse events[7]. Therefore it was concluded that rituximab therapy was not inferior to daily cyclophosphamide treatment for induction of remission in severe ANCA-associated vasculitis and may be superior in relapsing disease.

The RITUXVAS trial reported similar remission induction rates and safety between rituximab and cyclophosphamide based regimens for antineutrophil cytoplasm antibody (ANCA)-associated vasculitis at 12 months[8]. However, immunosuppression maintenance requirements and long term outcomes after rituximab in ANCA-associated renal vasculitis are unknown. In the rituximab group, B cell return was associated with relapse.

Renal Transplantation:

Rituximab is in widespread use in ABO blood group incompatible renal transplantation. It is an effective treatment for post-transplant lymphoproliferative disorder, HLA antibody incompatible renal transplantation and acute rejection. Recent evidence suggests rituximab may prevent the development of chronic antibody mediated rejection.[9] Rituximab may lead to an increase in infectious complications, although the evidence is not clear. Rarely, the drug can cause a cytokine release syndrome, thrombocytopenia and neutropenia. It has been

related to an increased risk of progressive multifocal leucoencephalopathy and, recently, deaths from cardiovascular causes. Trials examining the effects of rituximab in induction therapy for compatible renal transplantation and the treatment of chronic antibody mediated rejection are ongoing.

Throughout the past years Nils Lachmann et al. stepwise modified their immunosuppressive treatment regimen for patients with antibody-mediated rejection (ABMR).[10] Here, they describe three consecutive groups treated with different regimens. From 2005 until 2008, we treated all patients with biopsy-proven ABMR with rituximab (500 mg), low-dose (30 g) intravenous immunoglobulins (IVIG), and plasmapheresis (PPH, 6x) (group RLP,n=12). Between 2009 and June 2010, patients received bortezomib (1.3 mg/m^2, 4x) together with low-dose IVIG and PPH (group BLP,n=11). In July 2010, we increased the IVIG dose and treated all subsequent patients with bortezomib, high-dose IVIG (1.5 g/kg), and PPH (group BHP,n=11). Graft survival at three years after treatment was 73% in group BHP as compared to 45% in group BLP and 25% in group RLP. At six months after treatment median serum creatinine was 2.1 mg/dL, 2.9 mg/dL, and 4.2 mg/dL in groups BHP, BLP, and RLP, respectively (=0.002). Following treatment, a significant decrease of donor-specific HLA antibody (DSA) mean fluorescence intensity from 8467+/-6876 to 5221+/-4711 (p=0.001) was observed in group BHP, but not in the other groups. Their results indicate that graft survival, graft function, and DSA levels could be improved along with stepwise modifications to their treatment regimen from RLP to BHP.[10]

Mixed cryoglobulinemia:

Mixed cryoglobulinemia syndrome (MCS) is a systemic vasculitis characterized by multiple organ involvement due to the vascular deposition of cryoglobulins. B-lymphocyte expansion represents the underlying pathological alteration frequently triggered by hepatitis C virus (HCV) infection. The treatment of MCS syndrome is generally based on antiviral drugs and/or immunosuppressors, among which rituximab has been usefully employed for both cutaneous and visceral MCs organ involvement.

De Vita S et al conducted a long-term, prospective, randomized controlled trial evaluating rituximab (RTX) therapy for severe mixed cryoglobulinemia or cryoglobulinemic vasculitis (CV)[11].

Fifty-nine patients with CV and related skin ulcers, active glomerulonephritis, or refractory peripheral neuropathy were enrolled. In CV patients who also had hepatitis C virus (HCV) infection, treatment of the HCV infection with antiviral agents had previously failed or was not indicated. Patients were randomized to the non-RTX group (to receive conventional treatment, consisting of 1 of the following 3: glucocorticoids; azathioprine or cyclophosphamide; or plasmapheresis) or the RTX group (to receive 2 infusions of 1 gm each, with a lowering of the glucocorticoid dosage when possible, and with a second course of RTX at relapse).Patients in the non-RTX group who did not respond to treatment could be switched to the RTX group. Study duration was 24 months.

Survival of treatment at 12 months (i.e., the proportion of patients who continued taking their initial therapy), the primary end point, was statistically higher in the RTX group (64.3% versus 3.5% [P < 0.0001]), as well as at 3 months (92.9% versus 13.8% [P < 0.0001]), 6 months (71.4% versus 3.5% [P < 0.0001]), and 24 months (60.7% versus 3.5% [P < 0.0001]). The Birmingham Vasculitis Activity Score decreased only after treatment with RTX (from a mean ± SD of 11.9 ± 5.4 at baseline to 7.1 ± 5.7 at month 2; P < 0.001) up to month 24 (4.4 ± 4.6; P < 0.0001). RTX appeared to be superior therapy for all 3 target organ manifestations, and it was as effective as conventional therapy. The median duration of response to RTX was 18 months. Overall, RTX treatment was well tolerated.

RTX monotherapy represents a very good option for severe CV and can be maintained over the long term in most patients.

How is Rituximab Administered?

Rituximab is a clear liquid given intravenously in a hospital. Patients are often pre-medicated with antihistamine and steroid injections to prevent allergic reactions and is given slowly over a period of several hours. While receiving Rituximab a patient is closely monitored for adverse side effects and can expect to have blood pressure as well as other vitals monitored very closely.

Side effects of Rituximab:

Infusion reactions to rituximab occur in 20 to 40% and are mostly mild, although severe reactions including meningism, anaphylaxis, and serum sickness have been reported.[12-14] In 2006, the Food and Drug Administration reported the occurrence of progressive multifocal leukoencephalopathy in two patients with lupus after rituximab.[15] Late-onset neutropenia is also a transient phenomenon after rituximab that may be more common in those previously exposed to cytotoxic drugs.[16] IgG levels are unchanged after rituximab, the CD20 antigen is not present on plasma cells, but multiple courses lead to modest falls in IgG concentration.[17] Occasional patients develop hypogammaglobulinemia and recurrent infection requiring IgG replacement. Thus, IgG levels should be monitored, and falling levels should influence decisions to repeat treatment with rituximab. As an antibody, rituximab's half-life is reduced in nephrotic states, but it is not known how this influences responses and the need for re-treatment. Tissue resident B cells, especially in lymphoid organs and at sites of inflammation, are more resistant to depletion than circulating cells, and elevated B cell stimulating factor (BLyS), found in active lupus and vasculitis, impair rituximab-induced B cell lysis and associate with shorter clinical responses.[18,19] These factors may explain cases of rituximab failure and the observation that repeated rituximab after minor or partial responses leads to a larger treatment effect.

Rituximab can cause some reactions during the time the drug is being given or shortly after. These are called infusion reactions. They will usually occur with the first dose and are less common with later doses. To help prevent this type of reaction, Acetaminophen and Diphenhydramine are given before Rituximab. However, the patients may experience a reaction during the infusion and 24 hours afterwards: headache, fever, chills, gastritis, nausea, diarrhea, heartburn, flushing, night sweats, weakness, muscle or joint pain, back pain, or dizziness.

Rituximab in pregnancy:

Despite counseling to avoid pregnancy, women may inadvertently become pregnant during or after rituximab treatment. Using the rituximab global drug safety database, Eliza F. Chakravarty et al. identified 231 pregnancies associated with maternal rituximab exposure. [20] Maternal indications included lymphoma, autoimmune cytopenias, and other autoimmune diseases. Most cases were confounded by concomitant use of potentially teratogenic medications. Of 153 pregnancies with known outcomes, 90 resulted in live births. 22 infants were born prematurely; with one neonatal death at 6 weeks. 11 neonates had hematologic abnormalities, 4 neonatal infections were reported (fever, bronchiolitis, cytomegalovirus hepatitis, and chorioamnionitis). 2 congenital malformations were identified: clubfoot and cardiac malformation. So, women should be counseled to avoid pregnancy for 12 months after rituximab exposure. US FDA pregnancy category: C. Therefore women of childbearing potential should use effective contraception while taking this drug and for 12 months following treatment. Postmarketing data indicate that B cell lymphocytopenia generally lasting less than 6 months can occur in infants exposed to this drug in utero.

Rituximab in breastfeeding mother:

Rituximab is IgG. Maternal IgG is excreted in human milk and this drug is detectable in milk from animal studies. But it is a large protein molecule, the amount in milk is low and absorption is unlikely because it is probably destroyed in the infant GI tract. Therefore some experts say that if this drug is required by the mother, it is not a reason to discontinue breastfeeding.

Conclusion:

The use of rituximab in the treatment of the adult primary glomerular diseases has emerged recently, although not yet established as first-line therapy in international guidelines. In patients with steroid-dependent minimal change disease or frequently relapsing disease, and in patients with idiopathic membranous nephropathy (IMN), several retrospective and prospective studies support the use of rituximab to induce remission, whereas in idiopathic focal and segmental glomerulosclerosis (FSGS), the use of rituximab has resulted in variable results. Evidenceis still lacking for the use of rituximab in patients with immunoglobulin A nephropathy (IgAN) and idiopathic membranoproliferative glomerulonephritis (MPGN). Rituximab is also considered an alternative therapy for refractory lupus, lupus nephritis, and vasculitis. But their use is not without hazard, and important concerns over risk for infection remain. Investment in glomerulonephritis by the biologics industry is necessary to extend the current observations and offer our patients the potential for improved outcomes in the future.

Acknowledgement:

1. Melander C, Sallée M, Trolliet P, Candon S, Belenfant X, Daugas E, et al. Rituximab in Severe Lupus Nephritis: Early B-Cell Depletion Affects Long-Term Renal Outcome. Clin J Am SocNephrol. 2009;4(3):579–587.

2. Weidenbusch M, Römmele C, Schröttle A, Anders HJ. Beyond the LUNAR trial. Efficacy of rituximab in refractory lupus nephritis.Nephrology Dialysis Transplantation. 2013; 28(1):106–111.

3. Grimbert P, Audard V, Remy P, Lang P, Sahali D. Recent approaches to the pathogenesis of minimal-change nephrotic syndrome. Nephrol Dial Transplant 2003;18:245-248.

4. ArvindBagga,AditiSinha,AshaMoudgil.Rituximab in Patients with the Steroid-Resistant Nephrotic Syndrome. N Engl J Med. 2007; 356:2751-2752.

5. Gulati A, Sinha A, Jordan SC, Hari P, Dinda AK, Sharma S, et al. Efficacy and Safety of Treatment with Rituximab for Difficult Steroid-Resistant and -Dependent Nephrotic Syndrome: Multicentric Report. Clin J Am Soc Nephrol. 2010;5(12): 2207–2212.

6. Fiorentino M, Tondolo F, Bruno F, Infante B, Grandaliano G, Gesualdo L et al. Treatment with rituximab in idiopathic membranous nephropathy. Clin Kidney J. 2016;9(6): 788–793.

7. Stone JH, Merkel PA, Spiera R, Seo P, Langford CA, Hoffman GS, et al. Rituximab versus Cyclophosphamide for ANCA-Associated Vasculitis. N Engl J Med. 2010; 363(3):221-232.

8. Jones RB, Furuta S, Tervaert JW, Hauser T, Luqmani R, Morgan MD, et al. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis: 2-year results of a randomised trial. Ann Rheum Dis. 2015 Jun;74(6):1178-82.

9. Barnett AN, Hadjianastassiou VG, Mamode N. Rituximab in renal transplantation. Transpl Int. 2013;26(6):563-75.

10. Lachmann N, Duerr M, Schönemann C, Pruß A, Budde K, Waiser J. Treatment of Antibody-Mediated Renal Allograft Rejection: Improving Step by Step. Journal of Immunology Research. 2017;(1-4):1-9.

11. De Vita S, Quartuccio L, Isola M, Mazzaro C, Scaini P, Lenzi M, et al. A randomized controlled trial of rituximab for the treatment of severe cryoglobulinemicvasculitis. Arthritis Rheum. 2012;64(3):843-53.

12. Lindholm C, Borjesson-Asp K, Zendjanchi K, SundqvistAC, Tarkowski A, Bokarewa M. Longterm clinical and immunological effects of anti-CD 20 treatment in patients with refractory systemic lupus erythematosus. J Rheumatol. 2008; 35(5): 826–833.

13. Smith KG, Jones RB, Burns SM, Jayne DR. Long-term comparison of rituximab treatment for refractory systemic lupus erythematosus and vasculitis: Remission, relapse, and re-treatment. Arthritis Rheum.2006; 54: 2970–2982.

14. Fleischmann RM. Safety of biologic therapy in rheumatoid arthritis and other autoimmune diseases: Focus on rituximab. Semin Arthritis Rheum. 2008;38(4):265-80.

15. FDA: Information for Healthcare Professionsls: Rituximab, 2006. Available at: http:/www.fda.gov/CDER/Drug/InfoSheets/HCP/rituximab.pdf. Accessed July 7, 2008.

16. Nitta E, Izutsu K, Sato T, Ota Y, takeuchi K, Kamijo A, et al. A high incidence of late-onset neutropenia following rituximab-containing chemotherapy as a primary treatment of CD20-positive B-cell lymphoma: A single-institution study. Ann Oncol. 2007;18(2): 364–369.

17. Keystone E, Fleischmann R, Emery P, Furst DE, van Vollenhoven R, Bathon J, et al. Safety and efficacy of additional courses of rituximab in patients with active rheumatoid arthritis: An open-label extension analysis. Arthritis Rheum. 2007; 56: 3896–3908.

18. Gong Q, Ou Q, Ye S, Lee WP, Cornelius J, Diehl L, Lin WY et al. Importance of cellular microenvironment and circulatory dynamics in B cell immunotherapy. J Immunol. 2005; 174: 817–826.

19. Pers JO, Devauchelle V, Daridon C, Bendaoud C, Berre R, Bordron A, et al.BAFF-modulated repopulation of B lymphocytes in the blood and salivary glands of rituximab-treated patients with Sjogren's syndrome. Arthritis Rheum. 2007; 56: 1464–1477.

20. Chakravarty EF, MurrayER, Kelman A, Pamela Farmer P. Pregnancy outcomes after maternal exposure to rituximab. Blood. 2011;117(5):1499-1506.

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Original Article

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Prevalence of Hypertension in Obese Adult Population in a Tertiary Care Hospital of Bangladesh

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Abstract:

Background: Hypertension and obesity is a growing burden in developing countries. Hypertension is the leading cause of death in the world and it is the most easily controllable risk factor for stroke, myocardial infarction, heart failure, peripheral vascular disease, aortic dissection, end stage renal failure. Obesity is the most common nutritional disorder in world wide as well as in our country. The prevalence of hypertension in obese patient is increasing rapidly, but there is no current study on prevalence of hypertension in obese adult population of Bangladesh. Objectives: To assess the prevalence of hypertension in obese adult population in a tertiary care hospital of Bangladesh.Material and methods: A cross-sectional observation survey was performed among 200 obese adult patients of either sex who were admitted to the Dhaka Medical College Hospital during March, 2013 to September, 2013. Results: The overall prevalence of hypertension in obese adult population was (n=200) 36 %. This was more in males (n=100, 48%) compared to females (n=100, 24%) and this difference was statistically significant (p <0.05).The mean age was higher in hypertensive participants than that of non hypertensive. It was seen that prevalence of hypertension in obese patient increased with age. As the age increased, the prevalence of hypertension also increased. At the age group of 31 – 40 years it was 23% and this increased sharply to 45.1% at the age of 60 years and above. Older age, male sexes were significantly higher among hypertensive compared to normotensive. Factors like sedentary physical activity, tobacco use and family history of hypertension were associated with hypertension.Conclusion: The prevalence of hypertension in obese population was found to be high in this study, since obesity and hypertension occur together and cause serious complications, it is strongly suggested that measures are adopted to decrease prevalence of obesity and its underlying complications. Awareness programs are required at the level of the general public for successful implication of preventive programs. Hence there is need for primordial prevention efforts on large scale.

Keywords: Hypertension, noncompliance, obesity

Introduction:

The relevance of both hypertension and obesity , as important public health challenges, is increasing worldwide. Compared with the year 2000, the number of adult with hypertension is predicted to increase of high blood pressure is stronglycorrelated with body mass index (BMI)[2]. Hypertension is a disease of 60% to a total of 1.56 billion by the year 2025[1].

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Hypertension, a condition developed as a result complex etiology, affecting 972 million people Worldwide. It is estimated that the worldwide prevalence of hypertension could increase from 26.4% in 2000 to 29.2% in 2025[1]. Representative data on the prevalence of hypertension in a Bangladeshi population are lacking. A few studies with small sample sizes have been done which cannot provide sufficient information due to their non-representative ness of Bangladesh at large[3].

Obesity is defined as excessive accumulation of fat in body resulting in increase weight beyond that considered desirable with regard to age, height and bone structure and is a state of excess body weight, which is regarded as a pre-morbid addiction disorder,

defined as 20% above a person's standard weight[4]. The prevalence of obesity is increasing, and obesity is estimated to be a major leading cause of mortality and morbidity, causing an estimated 2.6 million deaths worldwide and 2.3% of the global burden of disease[5] .obesity is associated with two- to six-fold increase in the risk of developing hypertension[6].

Obesity is an important risk factor for obstructive sleep apnea but obstructive sleep apnea may be more closely associated with the enlarged abdomen than overall body obesity . Obstructive sleep apnea has been linked to hypertension in both clinical and epidemiological studies. As such, obstructive sleep apnea may be an important mechanism linking obesity and hypertension in some individuals[7]. It has been attributed that about 7.1 million Deaths are due to high blood pressure globally[8].

Elevated blood pressure due to obesity can cause long-term damage to the body's vital organs and functions. Research reports emphasize that obesity increase the risks of high BP , coronary heart disease, ischemic stroke, type II diabetes mellitus and certain cancers. Worldwide about 58% of diabetes mellitus and 21% of ischemic heart disease are attributable to BMI more than 21 kg/m² [9]. Body mass index (BMI) is positively and independently associated with morbidity and mortality from hypertension, cardiovascular disease, type II diabetes mellitus and other chronic diseases[10].

Developing countries are increasingly faced with a double burden of hypertension and other cardiovascular diseases, along with infection and malnutrition[11,12].

Major coronary risk factors are smoking, hypertension, dyslipidemia, diabetes and obesity. Other risk factors that are considered to be important are fat distribution, family history of premature CHD and life style risk factors[13]. The world health organization recommended that development of national programs for the prevention and control of CHD through simultaneous adoption of several strategies.

Hypertension places an excessive financial burden on populations and health systems, consuming scarce resources[14].Population- based preventive approaches are, thus, central for the management of elevated blood pressure in developing countries, where clinic-based care for complication is not a feasible option[15, 16].

Rationale of the study:

Aim of this study to asses' prevalence of hypertension in obese adult population in a tertiary care hospital of Bangladesh. Globally, High Blood pressure is estimated to cause of 7.1 million deaths about 13% of total death. Data related to prevalence of hypertension in Bangladesh are often insufficient, suffer from statistical flaws, and are not readily available. In Bangladesh non communicable disease (NCD) survey 2010 shows that prevalence of hypertension is 17.9% in general, 18.5% in men and 17.3% in women[17].This data confirm that hypertension is a major public health problem in Bangladesh. Several studies have showed in Bangladesh that changes in dietary patterns, physical activity levels, life style associated with affluence and migration to urban area are related to increasing frequencies of obesity and the risk of hypertension. From these studies I could detect the obese patient in different age population, and observe the prevalence of hypertension in obese population. This study will hopefully stimulated future research and act as valuable source of information. So it is very important to do such study.

Materials and Methods:

A cross-sectional observation survey was performed among 200 obese adult patients of either sex who were admitted to the Dhaka Medical College Hospital during March, 2013 to September, 2013. Purposive sampling method was used. Data was collected using a semi-structured questionnaire from the study subjects after taking informed written consent. No extra cost was imposed on the patient. Ethical clearance was taken from the Institutional Review Board, Dhaka Medical College Hospital.

Inclusion criteria:

1. Adult Patient in the age group of 20-80 years.
2. Obese male and Female individual.
3. Non pregnant women.

Exclusion criteria:

1. Age below 20 and above 80 years
2. Non obese male and female.
3. Pregnancy in women.

Results:

Table-1: Prevalence of hypertension in all study subjects.

Total study subjects	Group	No. of patients	Percentage
Hypertension 72		36%	
N=200			
Non-Hypertension	128	64%	

Table 1- shows the prevalence of hypertension in all study subjects. Out of total 200 study subjects, 72 were hypertensive and 128 were not. The prevalence rate of hypertension was 36%.

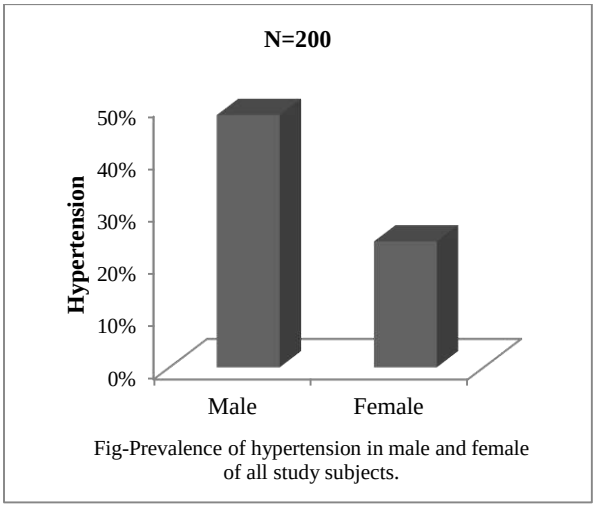

Fig-Prevalence of hypertension in male and female of all study subjects.

Figure-1: Showed among the 200 study subjects, 100 were male and 100 were female. Out of 100 male, 48 were hypertensive, and Out of 100 female, 24 were hypertensive. The prevalence rate of hypertension in male and female was 48% and 24% respectively.

Table-2: comparison of sex in hypertension and non hypertension in the study subjects.

Group	Sex of the study population		Chi- square	P-value
	Male	Female		
Hypertension	48	24		
Non-Hypertension	52	76	6.25	<0.05
Total	100	100		

Table-2:shows the comparison of hypertension between male and female. There was statistically significant difference between the two groups in both male and female ($P < 0.05$).

Table-3:Comparison of B M I (kg/m²) inhypertension and non hypertensionin the study subjects.

Group (B M I in kg/m²)	Mean± SD	t-value	p-value
Hypertension	29.76±1.88		
		- 0.91	>0.01
Non-Hypertension	29.49±2.05		

Table-3: shows the comparison of B M I in hypertension and non hypertension in the study subjects. Among the study subjects the hypertension patient's mean ± SD of B M I were 29.76±1.88 and non hypertension participant's mean ± SD of B M I were 29.49±2.02. This was statistically not significant between the two groups ($p>0.01$).

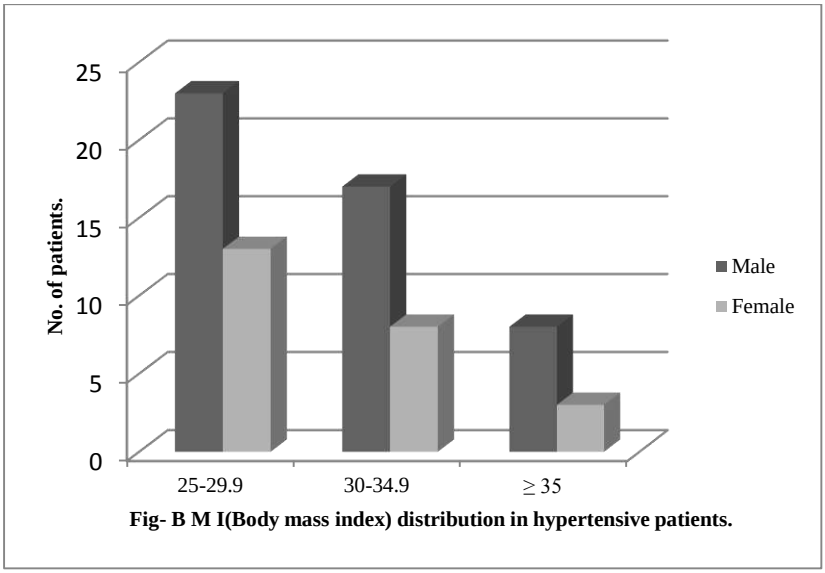

Fig- B M I(Body mass index) distribution in hypertensive patients.

Figure-2: shows distribution of B M I (Body mass index) in hypertensive patients. Among the participant's more patients present at the group of B M I (body mass index) 25-25.9 kg/m², and less patient present at B M I ≥35 kg/m² .

Table-4: Prevalence of hypertension in different age group of all study subjects.

Age group (%)	Hypertension (%)	Non-Hypertension	Male (%)	Female (%)
20-30	2(16.66%)	10(83.34%)	2(16.66%)	0
31-40	6(23.07%)	20(77%)	4(15.38%)	2(7.69%)
41-50	24(36.92%)	41(63.08%)	16(24.61%)	8(12.30%)
51-60	22(37.93%)	36(62.07%)	16(25.30%)	6(12.63%)
61-70	14(45.16%)	17(54.84%)	8(26.80%)	6(18.35%)
71-80	4(50.0%)	4(50.0%)	2(25.0%)	2(25.0%)
Total	72 (36%)	128(64%)	48(48%)	24(24%)

Table-4: shows the prevalence of hypertension in different age group of all study population .Among the study subject prevalence of hypertension increased with age. At the age group of 20-30 it was (16.66%) and increased sharply to (45.16%) at the age group 61-70 years.

Table-5: Correlation of hypertension with family history, smoking, physical activity, sex & age of all study subjects.

Correlation of Hypertension with	r- value	p - value
Family history	- . 228	<0.01
Smoking	- .126	<0.01
Sedentary Physical activity	- .141	<0.01
Sex	- .023	<0.05
Age	-.286	<0.01

Table-5: shows the correlation of hypertension with age, sex, family history, sedentary physically activity and smoking of all study subjects. There was statistically significant association of hypertension with family history (p<0.01), sedentary physically activity (p<0.01), smoking (p<0.01), sex (p<0.05) and age (p<0.01).

Discussion:

Aim of this study was to explore the prevalence of hypertension in obese adult patients who admitted in Dhaka medical college hospital. The response was satisfactory. Blood pressure was measured in all study subjects. In this study, out of 200 obese patients, 72 were hypertensive and 128 were non hypertensive. The overall prevalence of hypertension was 36%. Observed that the prevalence of hypertension in obese population was higher than the prevalence of hypertension in general Bangladeshi population[3,17]. This finding was consistent with other south Asian studies [2,16], khan S B et al showed that the prevalence of hypertension in obese (60%) was more then non-obese patients (40%)[16], similar finding were reported by a Saudi study there the prevalence of hypertension was higher in the obese group (8.4%) compared to the non-obese group (3.5%)[18], and Tesfaye F et al reported the prevalence of hypertension in obese population was more compared to non-obese in three population in Africa and Asia[8]. All these studies in different population groups have confirmed that the prevalence of hypertension increased significantly in the obese. These results may be closely related to diet and physical activity, especially at different age group. The dietary factor was mainly attributed to the involvement in social activities such as wedding parties, where the diet is mostly rich in calories and high in fat. Other factors include lack of physical activities and low energy expenditure. Weight loss clearly is one of the most potent non-pharmacological means of lowering blood pressure and ought to be the first line of treatment for hypertension.

In this study showed that the prevalence of hypertension in males was 48% and females was 24%. This difference was statistically significant ($p < 0.05$), Prevalence of hypertension was significantly higher in males than females. Similar finding was observed by Ali A T and Crowther N J studies[19], they reported the prevalence of hypertension in obese adults 38.4% for men and 32.2% for women, compared with 18.2% for men and 16.5% for women with a body mass index (BMI) less than 25 kg/m² [19].This studies finding was consistent with in this studies. But Mohsen A et al showed that the prevalence of hypertension in Saudi was more in obese female (8.7%) then male (7.8%)[18] and the Framingham heart study, estimated that obesity, accounted for approximately 26 percent of cases of hypertension in men and 28 percent in women.

In the present study also showed that the mean age in hypertensive patients was 49.67±10.45 compared to non hypertensive patients 40.88±12.75 and this difference was statistically significant (p<0.001). The mean age was higher in hypertensive participants than that of non hypertensive. Similar finding was observed by Ahmed N study in Pakistan; where the mean age in hypertensive participants was 53.7±12.9 [20].Countries with an ageing population in developed countries will be expected to have a higher prevalence of hypertension than developing countries with a younger population's such as Bangladesh, but there ware studies, which have documented a high prevalence rate of hypertension in developing countries.

Gender wise prevalence of hypertension among different age group was increased. As the age

increased, the prevalence of hypertension also increased in both the sexes. In this study, at the age group of 31 – 40 years it was 23% among them 15.3% in males and 7.6% in females and this increased sharply to 45.1% among them 26.8% in males and 18.3% in females at the age group of 61-70 years and above. This study showed that the prevalence of hypertension in obese patients progressively increasing with age, and that were similar findings with a south Asian study[7],Humayun A and Shah S A showed that the prevalence of hypertension in obese in Peshawar at the age ≥60 years was 27%[7], and Mufanda J et al reported the prevalence of hypertension in obese participants, 18.5% in males and 21% in females at the age group of 60 years and above in Eritrea[21].All the studies agree with the fact that prevalence of hypertension in obese was increased with age. Age probably represents an accumulation of environmental influences and the effect of genetically programmed senescence in body systems.

Among the study subjects maximum obese patients was present at the age group of 41-50 years, but more female obese patients was present at the age group of 51-60 years and male patients present at the age group of 41-50 years. Observed that obesity increased with age and that were similar findings with Eritrea study[21]. Obesity increased with age probably from reduced physical activity associated with ageing thereby leading to less energy expenditure.

In these study maximum patients was present in 29-29.9 kg/m² B M I group and more hypertensive patients was 29-29.9 kg/m² and 28-28.9kg/m² B M I group, among them more male hypertensive patients was present 28-28.9 kg/m² B M I group, and more female hypertensive patients was present 30-30.9 kg/m² B M I group. Mean B M I of hypertensive patients was 29.76±1.8and non hypertensive patients was 29.49±2.05, which was statistically not significant (p>0.01).Similar finding was observed by Khan S B et al study in Pakistan[16], where mean B M I of obese hypertensive patient was 29.22 ±3.22. Finding consistent with this study.

In this study also showed that positive family history, smoking and sedentary physical activity was significantly associated with hypertension in the study population.

Conclusion:

Prevalence of hypertension in obese population is high in the present study which supports the increasing trend in the communities of Bangladesh which are under the epidemiological transition. Obesity is an independent risk factor for hypertension; therefore efforts should be geared towards promoting healthy eating habits and maintenance of healthy weight through health education. Although this study does not provide more data representative of Bangladesh, it gives some information. Large-scale study using classical definition for hypertension that would be representative of Bangladesh at large remains to be done. More studies are suggestive to evaluate the prevalence of hypertension in obese population of Bangladesh.

References:

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. The Lancet. 2005; 365:217- 223.

2. Humayun A, Shah AS, Sultana R. Relation of Hypertension with body mass index and Age in Male and Female population of Peswere, PAKISTAN. J Ayub Med Coll Abbotabad. 2009;21(3):63-65.

3. Zaman MM, Rouf MA.Prevalence of hypertension in a Bangladeshi adult population. Journal of Human Hypertension 1999; 13:547–549.

4. Obesity: Mosby's Dental Dictionary, 2nd edition, 2008, elsever Inc.

5. Ezzati M, Martin H, Skjod S, Hoorn SV. Trends in National and State-Level Obesity in the USA after correction or self-report bias: Analysis of Health Surveys. J R Soci Med 2006; 99:250–7.

6. Deshmukh PP, Gupta SS, Dongne AR, Bharmbe MS, Maliya C, Kaur S, Garg BS. Relationship of anthropometic indication with blood pressure level in rural wardha. Indian. J.Med. 2006;123:657-664.

7. Naik JL, dudekula AB, Reddy KSN. Association between body mass index and hypertension: A cross sectional study in adult male population. Asian J Exp Biol Sci 2012; 3920:368-377.

8. Tesfaye F, Nawi NGV, Minh H, Byass P, BerhanelY, Bonita R, Wall S. Association between body mass index and blood pressure across three populations in Africa and Asia. J Hum Hypert. 2007; 21: 28–37.

9. World Health Organization. Reducing risks, Promoting Healthy Life World Health Report: Geneva.2002.

10. Pi-Sunyer FX. Medical hazards of obesity. Ann Intern Med. 1993; 119: 655–660.

11. Murray CJL, Lopez AD. Global Burden of Disease and Injury Series. Global Health Statistics: Harvard School of Public Health: Boston, MA.1996.

12. World Health Organization. Diet, Nutrition and the Prevention of Chronic Diseases, Report of a Joint WHO/FAO Expert Consultation. WHO Technical Report Series No.2003; 916: Geneva.

13. Wilson PWF, D Agostino RB, Levy D, Nelanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk Factor categories. Circulation 1998; 97:1837-1847.

14. Collins R, Peto R, McMahon S, Herbert P, Fiebach NH, Eberlein KA. Blood pressure, stroke, and coronary heart disease. Part II. Effects of short-term reduction in blood pressure: overview of randomized drug trials in an epidemiological context. Lancet 1990; 335: 827–883.

15. MacMahon S, Neal B, Rodgers A. Hypertension – time to move on. Lancet 2005; 365: 1108–1109.

16. Khan SB, Noor L, Rehman HU, Hameedullah , Hafeezullah M, Awan ZA, Din SU, Shah SS. Prevalence of hypertension among obese and non obese patient with coronary artery disease. J Ayub Med Coll Abbottabad 2010;22(2):130-133.

17. World Health Organization. Bangladesh NCD risk factor survey 2010, WHO, http:/ /www. Whoban. org/Link Files/Publication NCD_ FACT_ SHEET.

18. Mohsen A, El-Hazmi, Arjumand S. Warsy. Prevalence of hypertension in obese and non obese Saudi. Saudi Medical Journal 2001; 22 (1): 44-48.

19. Ali A T, Crowther N J. Health risks associated with obesity. JEMDSA . 2005;10(2):56-61.

20. Ahmed N, Anwar W, Waqas H. Obesity, hyperlipidemia and hyperuracemia in young and old hypertensive patients. J Ayub Med Coll Abbottabad. 2009; 21(4):53-56.

21. Mufunda J, Mebrahtu G, Usman A, Nyarango P, Kosia A, Ghebrat Y, Ogbamariam A, Masjuan M, GebremichaelA.The prevalence of hypertension and its relationship with obesity: results from a national blood pressure survey in Eritrea. Journal of Human Hypertension. 2006; 20:59–65.

Original Article

DCIMCJ

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Local Application of Steroid on the Wound after Mastectomy Promote Early Removal of Drain and Reduce Seroma Formation

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Abstract:

Background: Seroma formation is the most common postoperative sequelae after breast cancer surgery.Different methods have been used to reduce this seroma but none have been solely effective.It is believed that this seroma is an inflammatory response during wound healing. Therefore this study was aimed to evaluate whether applying methylprednisolone to the wound immediately after mastectomy and axillary dissection had any effect on the time of drain removal and postmastectomyseroma formation. Method: The study included female patients with primary operable breast cancer who were randomly allocated in two groups each group included 20 patients. In group 1 all patients underwent mastectomy with axillary dissection (level II) and the wound was closed keeping a drain in situ. In group 2 patients underwent the same surgery and Injection methylprednisolone acetate (Depomedrol 80 mg) was applied locally to the wound prior to closure. Drain was kept in situ.Primary endpoint was the total drain volume, drain removal time, and whether there was any seroma formation that required aspiration after drain removal. Secondary endpoint included frequency of side effects and complications. Results: Total 40 patients were included in the study. The mean age of the study population was 59 years (SD 6.57) ranging from 46 years to 70 years. The mean amount of the drain was 40.61 ml (SD 12.50), maximum amount was 64 ml and minimum 23 ml. From the ANOVA test, we found that mean amount of drain was 30.92ml patient who received steroid and 50.30 ml who did not receive it. However, one cannot comment without statistical significance. For this, we used the F value which was 60.80 and *P*=.000 which indicated it was statistically significant. Aspiration was not required.Conclusion Seroma formation observed to be a post traumatic inflammatory response after mastectomy can be reduced by local application of methylprednisolone on the wound.

Keywords: Mastectomy, seroma formation, methylprednisolone, inflammatory response, wound healing

Introduction:

Breast cancer remains the most common cancer among woman in Bangladesh. It accounts for 69% cancer death in women in Bangladesh[1]. Incidence was 22.5 per 100000 females[2]. Surgery among the other modalities of treatment plays a leading role. Seroma is extremely common after mastectomy with an incidence of 10-85 %[3]. It is the serous fluid which collects under the skin flaps and axilla after dissection. This seroma impairs healing process which is why a drain is commonly left in situ[4]. There are other several techniques that have been adopted to reduce seroma formation such as, use of tranexamic acid, fibrin glue, quilting, use of ultrasonic dissection instead of electrocautery, but no single method has been reliably effective. Oertili et al[5] concluded from their study that tranexamic acid given perioperatively and postoperatively at a dose of 1g three times daily can produce a significant reduction in mean postoperative volume drainage. The efficacy of shoulder immobilization after mastectomy was investigated by Knight et al[6]. Estes and Glover showed that suction drain left

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in situ for a prolong period maintains physical contact between contagious surfaces and facilitates adhesion[7]. O'Dwyer et al[8] demonstrated that seroma formation was significantly less when dead space was obliterated by suturing the skin flaps to muscle. Lindsey et al[9] applied topical fibrin glue in operative site in Sprague-Dawley rat model and similarly decreased seroma formation following mastectomy. The mechanism underlying seroma formation was initially considered as collection of lymphatic fluid due to disruption of lymphatic drainage after dissection[10, 11]. Now it has been proved through various studies identifying cell types and proteins in seroma fluid that seroma formation after mastectomy is an inflammatory response to surgical trauma[12-14].In our study we preferred to use closed suction drainage after mastectomy in all our patients and observe the effect of local application of single dose of methylprednisolone after mastectomy on drain output ,drain removal time, and complications.

Methods:

This study included female patients with primary breast carcinoma.

Place of study- BIRDEM General Hospital

Study period- January 2016 –January 2018

Type of study- Case-control

Patient number- Group 1 -20 patients , Group 2 – 20 patients

Inclusion criteria:

1) All patients with primary breast carcinoma.
2) Both diabetic and non diabetic patients were included.

Exclusion criteria:

1. Patient treated with neoadjuvant therapy and distant metastasis.
2. Patients on glucocorticoids for any other disease within last three months.
3) Patients with psychiatric disorders.(on drugs altering sympathetic and hormone response)
4) Patients who did not give consent to participate in the study.

Written informed consent was taken from all patients.

Treatment Given:

Mastectomy with axillary dissection (level I, level II) was performed in all patients using the same technique, mastectomy flap dissection by diathermy and sharp axillary dissection. In Group I patientshaemostasis was ensured and the wound was closed in layers leaving a closed suction drain in situ inserted through medial end of lower flap near sternum. In the second group the same technique was applied and Injecton methylprednisolone acetate 80mg (DEPOMEDROL 80mg) dissolved in normal saline was sprayed on the wound and then closure started. The closed suction drain was kept locked for 30 minutes then released to ensure that the drug remains in contact with the wound. All patients were given prophylactic antibiotics.

Assessment:

The drain volume was daily recorded and drain removed when collection was less than 20ml. The wound was inspected for necrosis, dehiscence, or infection. Blood sugar level was monitored in all diabetic patients postoperatively (F, ABF, AI, AD) . Patients were discharged after drain removal and followed up for following four weeks to observe wound healing and check for seroma formation which may require aspiration.

Statistical Analysis:

Statistical analysis was carried out using statistical package for social sciences (SPSS) version 23.

Results:

Total 40 patients were included in the study. The mean age of the study population was 59 years (SD 6.57) ranging from 46 years to 70 years. The mean amount of the drain was 40.61 ml (SD 12.50), maximum amount was 64 ml and minimum 23 ml (Table 1). Among the study patients 26 (65%) had

history of diabetes and 14 (35%) did not have diabetes.

Table-1: Descriptive analysis of age and drain amount

	Minimum	Maximum	Mean	Standard deviation
Age	46	70	59.05	6.57
Drain amount (ml)	23	64	40.61	12.50

We performed scatter plot among age and drain amount to see the gross correlation. There was no correlation (Figure 1).

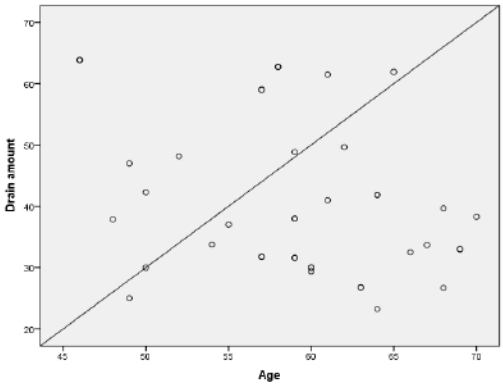

Figure 1: Scatter plot of age and drain amount

We also performed pair scatter plot about the drain amount and duration of the keeping drain in situ. We found linear correlation between these two variables (Figure 2). It means that for more drain amount the duration of the keeping drain was long.

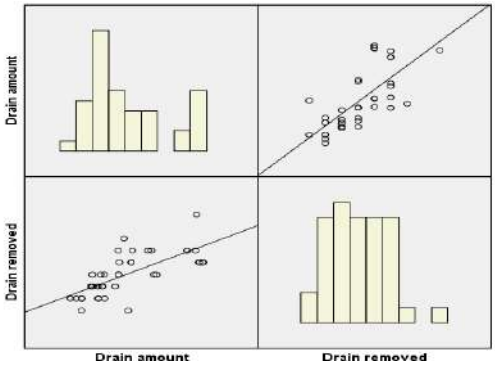

Figure 2: Pair scatter plot between drain amount and duration of drain

We also examined the gross relationship between the steroid treatments and drain amount. The box plot illustrates that the average amount of drain was lower among the patients who received steroid compared to the patients who did not receive(Figure 3).

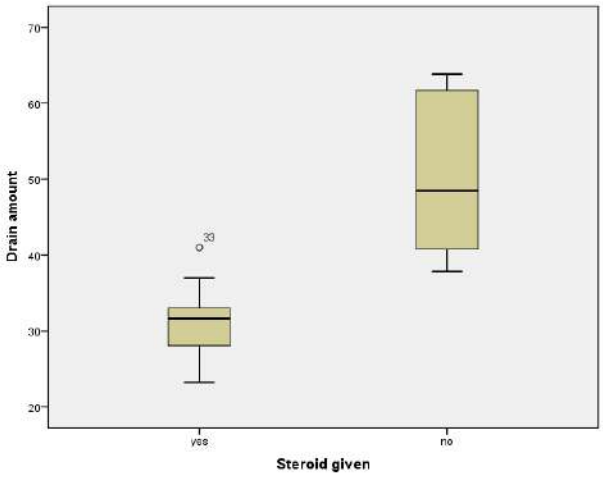

Figure 3: Box plot of drain amount and steroid treatment

The study hypothesis was

H_0: There is no relationship between steroid treatment and drain amount

H_A: There is relationship between steroid treatment and drain amount

As, we have two groups of patients. To examine the variance between two groups, we performed Anova test. From the Anova test, we found that mean amount of drain was 30.92ml in patients who received steroid and 50.30 ml who did not. We used the F value which was 60.80 and *P*=.000 which indicated it was statistically significant (Table 2 & 3).

Table-2: Anova Result

	Mean	Standard deviation	CI 95%
Steroid given	30.92	4.009	(29-32.84)
Steroid not given	50.30	10.33	(45.46-55.13)

Table-3: Anova Result: Level of sigficance

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	3754.590	1	3754.590	60.803	.000
Within Groups	2346.494	38	61.750		
Total	6101.084	39			

As *P value <.05*, we can reject the null hypothesis and accept the alternative hypothesis. So, we can say that there was a strong relationship between steroid treatment and drain amount.

During follow up patients of Group I had no incidence of wound infection or flap necrosis and aspiration was not required .Patients of Group II in whom steroid was applied had similar results.

Discussion:

Seroma can occur after many surgical procedures but is the most prevalent postoperative sequelae after breast surgery. The previous concept of seroma formation is debatable indicating that seroma is more likely an inflammatory than lymphatic leakage. Watt-Boolsen et al investigated seroma fluid and found significant higher concentration of granulocytes than lymphocytes in the fluid[12], whereas lymph fluid is characterized by 95% dominance of lymphocytes as seen in thoracic duct[15, 16]. Endoscopic exploration of seroma cavity has revealed a nearly serous lined cavity consisting of CD3 and CD20 lymphocytes and CD68 macrophages observed by immunohistochemistry[17]. Therefore, lymph seems to be an unlikely source for the seroma formation however, some spillage can occur after surgery. On the otherhandSzesci et al showed that seroma formation after mastectomy has a proinflammatory component as induced by high levels of interleukin-6 and interleukin-8[18]. The authors also reported high concentration of growth factors especially transforming growth factor beta (TGF-beta). Loo et al alsoreported elevated interleukin-6 during first 5 days after mastectomy[19]. Considering inflammatory response as the source of seroma formation, steroid being an anti inflammatory drug should be an ideal candidate to use in preventing seroma formation. Steroids act by inhibition of leucocyte infiltration at inflammation site, interference in function of inflammatory response and suppression of humoral immune response.

Some of the net effects include reduction in oedema and scar tissue formation. The numerous adverse effects related to corticosteroids are mainly dose related[20]. Glucocorticoids are used as an anti-inflammatory drug in many diseases and are administered as a local intramuscular or intraarticular injection of methyl prednisolone acetate. The use of steroid has been explored in other type of surgeriesincluding colonic resection[21], head neck surgery[22], plastic surgery[23], cardiac surgery[24]. Taghizadeh et al[25] reported that injecting 80 mg of Triamcinolone into the cavity after seroma aspiration following autologusLatissimusdorsi breast reconstruction decreased the total number of aspirations. Talha et al[26] in their study concluded that post mastectomy seroma is a pro inflammatory process and can be reduced by administering intravenous hydrocortisone on induction of anaesthesia and 2 hours later. In the study by Qvamme et al[27] methyl prednisolone was administered into the wound cavity in 2 groups. One group underwent mastectomy with sentinile lymph node biopsy (M+SLNB) and the other mastectomy with level I and level II axillary clearance (M+ALND).They showed that steroid exerted a highly significant preventive effect against seroma in M+SLNB but not in M+ALND and suggested further studies to clarify results. Maryam . A.Khan[28] in her study gave injection Depomedrol 120mg intravenously 1 hour before surgery and found significant decrease in seroma formation.

However, the study by Okholm et al[29] suggested no effect of steroids on seroma formation after mastectomy. In our study the same surgical technique was applied to all patients to ensure standardization of technique and in addition injection Depomedrol was given locally to the second group of patients. We found that seroma formation in this group was less and statistically significant, drain removal was earlier. There was no wound infection or delay in wound healing. However, antibiotics were used in all patients. Both diabetic and nondiabetic patients were taken in as participants of the study as the study place is a leading diabetic hospital of Asia and most patients are diabetic. The preoperative and postoperative blood sugar was monitored by departmental protocol (Fasting, after breakfast, after lunch, after dinner) and managed accordingly. There was no marked rise in blood sugar. The single dose of steroid did not cause a difference in wound healing. All the patients were followed up weekly for 4 weeks but none of the patients from both groups required aspiration. Postoperative administration of steroid may exert an additional beneficial effect if tumour cells remain in surgical field. Long term observations are needed to answer these questions. There were a few short comings in this study as sample size other co founders like body weight, breast size were not taken into consideration .Antibiotics were given so chances of infection was not properly evaluated.

Conclusion:

The present study demonstrated a lower total drainage volume during postoperative period in the methylprednisolone group compared with control group and drain removal was also earlier. Postoperative aspiration of seroma was not required in any patient of both groups.

References:

1. International Agency for research on cancer 2008.GLOBACON 2008: Cancer Incidence and Mortality worldwide.
2. Uddin AF, Khan ZJ, Islam J& Mahmud A. Cancer care scenario in Bangladesh.South Asian Journal of cancer 2013;2(2),102-4.
3. Kuroi K, Shimozuma K, Taguchi T, Imai H, yamashiro H, Ohsumi S et al. Pathophysiology of seroma in breast cancer. Breast Cancer 2005;12;288-93.
4. Vitug AF, Newman LA Complications in breast surgery. Surg Clin North Am 2007; 87:431-451.
5. Oertli D, Laffer U, Haberthuer F, Kreuter U, Harder F Perioperative and postoperative tranexamic acid reduces the local wound complication rate after surgery for breast cancer. Br J Surg 1994; 81:956-959.
6. Knight CD Jr, Griffen FD, Knight CD Sr Prevention of seromas in mastectomy wounds: the effect of shoulder immobilization. Arch Surg 1995; 130:99-101.
7. Estes NC, Glover JL. Use of vacutainer suction as a convenient method of resolving postmastectomyseromas. Surg Gynecol Obstet 1982;155:561-562.
8. O'Dwyer PJ, O Higgins NJ, James AG. Effect of closing dead space on incidence of seroma after mastectomy. SurgGynecolObstet 1991; 172:55-56.
9. Lindsey WH, Masterton TM, Spotnitz WD, Wilhelm MC, Morgan RF. Seroma prevention using fibrin glue in a rat mastectomy model. Arch Surg 1990; 125:105-107.
10. Shamley DR, Barker K, Simonite V, Beardshaw A. Delayed versus immediate exercises following surgery for breast cancer: a systematic review. Breast Cancer Res Treat 2005; 90: 263-71.

11. Kuroi K, Shimozuma K, Taguchi T, Imai H, Yamashiro H, Ohsumi S, et al. Evidence-based risk factors for seroma formation in breast surgery. Jpn J ClinOncol. 2006; 36(4): 197-206.

12. Watt-Boolsen S, Nielsen VB, Jensen J, Bak S. Postmastectomyseroma. A study of the nature and origin of seroma after mastectomy. Dan Med Bull 1989; 36: 487–489.

13. McCaul JA, Aslaam A, Spooner RJ, Louden I, Cavanagh T, Purushotham AD. Aetiology of seroma formation in patients undergoing surgery for breast cancer. Breast 2000; 9: 144–148.

14. Montalto E, Mangraviti S, Costa G, Carrega P, Morandi B, Pezzino G, et al. Seroma fluid subsequent to axillary lymph node dissection for breast cancer derives from an accumulation of afferent lymph. Immunol Lett. 2010; 131: 67-72.

15. Bierman HR, Byron RL, Kelly KH, Gilfillan RS, White LP, Freeman NE, et al. The characteristics of thoracic duct lymph in man. J Clin Invest 1953; 32(7): 637-49.

16. Merrigan BA, Winter DC, O'Sullivan GC. Chylothorax. Br J Surg 1997; 84: 15-20.

17. Al-Gaithy ZK, Ayuob NN. Vascular and cellular events in post mastectomy seroma: an immunohistochemical study. Cell Immunol 2012; 272: 130-6.

18. Szecsi PB, Larsen J, Hørby J, Axelsson CK. Seroma production after breast cancer surgery has a pro-inflammatory component. Open Breast Cancer J 2012; 4: 11–17.

19. Loo WT, Sasano H, Chow LW. Pro-inflammatory cytokine, matrix metalloproteinases and TIMP-1 are involved in wound healing after mastectomy in invasive breast cancer patients. Biomed Pharmacother 2007; 61: 548-52.

20. Jules-Elysee KM, Lipnitsky JY, Patel N, Anastasian G, Wilfred SE, Urban MK, et al. Use of low dose steroids in decreasing cytokine release during bilateral total knee replacement. RegAnesth Pain Med 2011; 36(1):36-40.

21. Schulze S, Andersen J, Overgaard H, Nørgard P, Nielsen HJ, Aasen A, et al. Effect of prednisolone on the systemic response and wound healing after colonic surgery. Arch Surg. 1997; 132(2): 129–135.

22. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. J Am CollSurg 2002; 195: 694–712.

23. Berberich T, Haecker FM, Kehrer B, Erb TO, Günthard J, Hammer J et al. Postpericardiotomy syndrome after minimally invasive repair of pectusexcavatum. J PediatrSurg 2004; 39: e1–e3.

24. Park GM, Lee JY, Kim YG, Boo SJ, Song JM, Kang DH et al. Recurrent postoperative effusive–constrictive pericarditis associated with steroid discontinuation. J Cardiovasc Ultrasound 2009; 17: 102–105.

25. Taghizadeh R, Shoaib T, Hart AM, Weiler-Mithoff EM. Triamcinolone reduces seroma re-accumulation in the extended latissimusdorsi donor site. J PlastReconstrAesthetSurg 2008; 61: 636–642.

26. Talha A, Ramadan R, Abdelhamid S, Hamdi S. Postmastectomyseroma: how much is it affected by serum levels of IL-6 andCRP and how much is it reduced by intravenous hydrocortisone injection? Egyptian J Surgery 2015; 34:17-21.

27. Qvamme G, Axelsson CK, Lanng C, Morteson M, et al. Randomized clinical trial of prevention ofseroma after mastectomy by local

methylprednisolone injection. Br J Surg 2015; 102(10):1195-203

28. Khan MA.Effect of preoperative intravenous steroids on seroma formation after modified radical mastectomy.JAyub Med CollAbottabad 2017;29(2)207-10.

29. Okholm M, Axelsson CK. No effect of steroids on seroma formation after mastectomy. Dan Med Bull 2011; 58: A4241.

Original Article

DCIMCJ

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Utilization of Antenatal Care among Women of Selected Slums of Dhaka City

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Abstract:

Maternal health services have a potentially critical role in the improvement of reproductive health. The use of health services is related to the availability, quality and cost of the services, as well as to social structure, health beliefs and the personal characteristics of the users. Antenatal care (ANC) is an important determinant of high maternal mortality rate and one of the basic components of maternal care on which the life of mothers and babies depend. A Cross-sectional survey was carried out urban settlements in Mohammadpur area of Dhaka City. 100 married women in the age range 15-49 years were interviewed. Socio-demographic characteristics of women who received and who did not receive antenatal care in their previous pregnancy. Education and ANC is significantly related suggesting that the higher the level of education the higher is the likelihood of receiving ANC during pregnancy because educated women are aware about the importance of ANC during pregnancy. There is a strong association between the income of the respondents and ANC received by the respondents. This study indicates that overall knowledge about antenatal care was found to be better among women who had utilized antenatal care as compared to women who did not receive antenatal care. There is also a need to evaluate the services provided by government health facilities and to find out why women are not utilizing the government health services though these services are available at subsidized rate.

Keywords: Antenatal care, mortality, maternal health, urban slum

Introduction:

Millions of women in developing countries experience life threatening and other serious health problems related to pregnancy or childbirth. Complications of pregnancy and childbirth cause more deaths and disability than any other reproductive healthproblems[1]. This situation is worse in developing countries like Bangladesh due to inadequate access to modern health services and poor utilization. Despite the government serious commitment to deliver health facilities to the doorsteps of urban people through innovative approaches, such as Essential Service Package (ESP), the utilization of health service is still far below any acceptable standard[2].

Over the past decades, impressive studies have been made in reducing levels of infant and childhood mortality and increasing levels of contraceptive use in developing countries. In contrast, progress in reducing levels of maternal mortality and in making pregnancy and child bearing safer for women, despite being a central element of the millennium development goals, has been much slower[3].

Although exact figures remain elusive an estimated 525,000 women, almost all from developingcountries, continue die each year from maternal causes[4].

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In Bangladesh, antenatal care (ANC) usually refers to pregnancy related care provided by a health provider either in a medical facility or at home[5].

The necessities of ANC services by explaining the numerous advantages of them which may include monitoring health of the mother and baby during pregnancy, anticipating difficulties at pregnancy and labor with early treatment to reduce the risks for mother and child, facilitating the better use of emergency obstetric care services, disseminating health education and information, and so on[6].

These facilities imply that antenatal visits may confer benefits to both mother and baby, not only because women with serious conditions such as hypertensive diseases in pregnancy can be diagnosed and kept under observation, but also because a dialogue can be initiated which may facilitate the use of skilled care when the need arises[7].

Pregnancy and maternal health issue are culturally sensitive in Bangladesh. Like most of maternal health issues, proper care during pregnancy and childbirth is important to the health of both of the mother and child. Antenatal care is recognized as a major component of comprehensive maternal health care. It is the care that pregnant women should have during her pregnancy for protection of her and safe delivery. ANC is reachable through health service interventions. Antenatal care is essential for detection and treatment of problems during pregnancy and can improve the timely and appropriate use of delivery care services. A pregnant woman needs to visit health facilities/providers at certain intervals for antenatal care check up. Evidence suggests that adequate antenatal care use has association with improved pregnancy outcome[8].

Due to rapid urbanization and industrialization so many women are coming from rural to urban areas for better opportunity and startliving in slums andlow economic conditions. The prevalence of reproductive health problemsamong women of reproductive ages in urban slums of Dhaka city is very high. Because of the poverty, low level of education and lack of accessibility health service utilization is very low. Women, especially poor women are often trapped in a cycle of ill health exacerbated by child bearing and hard physical labor. Many women in urban areas receive little nutrition during pregnancy. Timely antenatal check up has an impact in the reduction of maternal morbidity and maternal deaths. In the absence of not having proper antenatal check up may cause problem in pregnancy and various complications. To achieve MDG-5, reduction of maternal death will be an important strategy for Bangladesh. The present study would help in understanding the antenatal care utilization of urban slum poor women of Dhaka and would also identify the important factors related with antenatal care utilization[9].

Methodology:

The study design was cross-sectional. The study populations were married women of reproductive ages of urban slums of Dhaka city. The survey was designed to obtain a broad health profile of the urban population in Bangladesh. This particular study only focused on the urban slum population of Dhaka city. In-depth interview through individual questionnaire for women were used for collection of information. All interview questionnaires were checked for their internal consistency to exclude missing or inconsistent data. Data entered in to the data file using statistical software called SPSS (Statistical Package for Social Science). Data checked, cleaned and edited properly before analysis. Data was analyzed in the SPSS and frequency distribution, Chi-Square and appropriate statistical test done for important variables. Each of the respondents were informed about the study and requested to provide verbal consent before starting the interview. To identify the factors that can influence the health seeking behavior of urban poor women related to ANC services, sexually transmitted diseases and morbidity of the children. It is expected that the

findings would help policy makers, population scientists and planners to the understanding of health care utilization of urban slum poor women and can consider strategies for improving the health care utilization of the poor urban slum women.

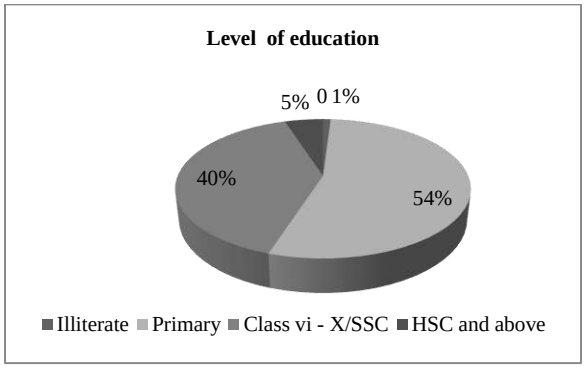
Results and findings:

Socio-economic and demographic characteristics:

According to the sample characteristic, the mean age of the respondents was 30 years and about 16 % women's age was below 20, 25 %women's age was between 20-24 suggesting about 40 %respondents were above 25 years.

Among those who attended school 54% had primary education followed by secondary and SSC passed 40%. Only 5% passed higher secondary and above shown in Figure 1.

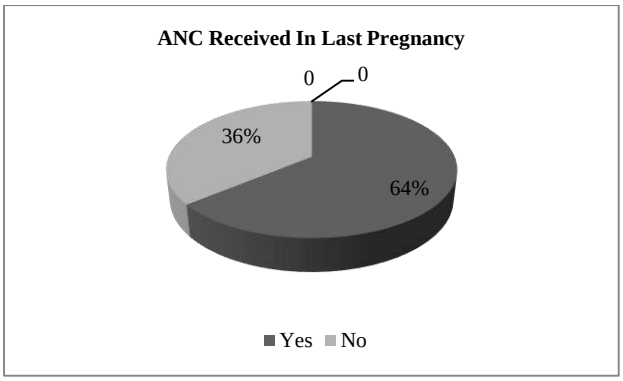
Figure 1: level of education



The median incomes of the respondents were Taka 1644 and Taka 1400 respectively.

More than one third of the respondents (36%) reported their family income was less than 5000 Taka and 44% of the respondents mentioned that family income was between 5000-10000 and (21%) reported that their family more than or equal to 10000 Taka. The study results also shows that access to basic needs of the slum dwellers. Information on access to electricity, source of drinking water and access to toilet facility was also collected in the survey. As evident from the table, 95.4% of the households had access to electricity. Piped water (outside) is the predominant source ofdrinking water, which is40.4%.Only 12.2% household use tube well (inside) water and 33.5% household use piped water (inside). Only 15% slum households had sanitary toilets (septic tank or modern toilet facility) at the time of survey; 40.7% households used open toilet indicating health hazards of the slum dwellers. The respondents who were pregnant were asked whether they received ANC during the last pregnancy and the information gathered in this respect is shown in Figure 2 among the respondents 64% women received ANC during last pregnancy.

Figure 2: ANC Received in Last Pregnancy



Access to mass media an important determinant of health care services during the pregnancy. Information collected in this regard. Information on the access to mass media of the respondents was collected and is presented in Table 1. As information suggests over 81% of the respondents mentioned that they have access to mass media.

Table 1: Access to Mass Media

Variables		Total	
Mass media access		Frequency	Percentage (%)
	Yes	81	81%
	No	19	19%
Total		100	100%

Association between ANC and socio-economic and demographic characteristics

Association between age and ANC were investigated through Chi-square analysis. The value of Chi-square (2.55) is significant at 5% level of significance indicating that age of the respondents was an important determinant whether or not to receive ANC.

Table 2: Association between ANC and age

Age in years	Antenatal care received		
	Frequency	Frequency	Frequency
	No	Yes	Yes
< 25 years	28	32	60
≥ 25 years	19	21	40

Association between income and ANC was also investigated through Chi-square analysis. The value of Chi-square (7.1; p>.01) shows that there was a strong association between the income of the respondents and ANC received by the respondents.

Table 3: Association between Income and ANC

Monthly Income (Taka)	Antenatal Care Received		
	No	Yes	Total
	Frequency	Frequency	Frequency
<5000	12	24	36
5000-10,000	10	34	44
≥ 10,000	2	19	21

The chi-square between education and ANC is significantly related suggesting that the higher the level of education was the likelihood of receiving ANC during pregnancy because educated women were aware about the importance of ANC during pregnancy.

Table 4: Association between Education level and ANC

Education level	Antenatal Care Received		
	No	Yes	Total
	Frequency	Frequency	Frequency
No education	1	0	1
Primary	20	34	54
Secondary	9	31	40
Higher Secondary +	1	4	5

Table 5 shows that the in recent years' access to mass media like TV play significant role with ANC. Access to TV helps the respondents to aware about the importance of TV in disseminating information on ANC during the pregnancy. Besides information maternal and child health care its importance in the reduction of maternal and child mortality are highlighted in mass media which significantly helps the TV watchers to know what to during the pregnancy period. The Chi-square analysis shows that there was a strong association between TV watchers and ANC.

Table 5: Association between Mass Media and ANC

Mass Media Access	Antenatal Care Received		
	No	Yes	Total
	Frequency	Frequency	Frequency
Yes	35	46	81
No	11	8	19

Conclusion:

This study indicates that overall knowledge about antenatal care was found to be better among women who had utilized antenatal care as compared to women who did not receive antenatal care. Women of reproductive age (15-49) need to recognize the importance of antenatal care and to receive such care in the community. Underlying this need, there is also a need to uplift the socio-economic status and literacy level through community based education.

In particular, there is need to increase reproductive health education, highlighting the importance of seeking antenatal care, and recognition of sign and symptoms and danger signs in pregnancy. Women are very much reluctant to select place of delivery and skilled personnel at delivery until they faced serious complications. Health seeking behavior is highly distinctive among the poor and the rich women.

Findings of this study may have some policy implications, merit additional comment and recommendations that would help to Government to achieve improvement in maternal health.

1. As in increase in both male and female education and literacy and consequently a probable raise in the social status can be expected result in improved maternal health in Bangladesh. Education may provide awareness for the use of ANC service.

2. Absence of major socio-cultural barriers must be capitalized by targeting all husbands and mother in laws to infuse the idea of delivery planning and make further improvement in the existing knowledge of women on early ANC, timing of first and all subsequent ANC visit.

3. Desired numbers of ANC by pregnant mothers from medically trained provider can be ensured. The availability of quality service providers and ANC provider in the service centers and can be ensured.

Refferences:

1. Wagstaff A, Claeson M. The Millennium Development Goals for Health Rising to the Challenges, Washington DC: World Bank 2004.

2. Chakraborty N, Islam MA, Chowdhury RI, Bari W, Akhter HH. Determinants of the use of maternal health services in rural Bangladesh. Health Promotion International. 2003;18(4): 327-337.

3. World Health Organization (WHO), Maternal Mortality in 2000: Estimates Developed by WHO, UNICEF and UNFPA Geneva WHO 2004.

4. Ministry of Health and Family Planning Welfare (MOHFW), Bangladesh National Strategy for Maternal Health, Dhaka, Bangladesh: MOHFW, 2001.

5. Matthews Z, Mahendra S, Kilaru A, Ganapathy S. Antenatal care, care seeking and morbidity in rural Karnataka, India: results of a prospective study. Asia-Pacific Population Journal. 2001;16(2): 11-28.

6. WHO/UNICEF, Antenatal care in developing countries: promises, achievements and missed opportunities: an analysis of trends, levels and differentials, 1999-2001, World Health Organization, 2003, Geneva.

7. Vanneste AM, Ronsmans C, Chakraborty J, Francisco AA. Prenatal screening in rural Bangladesh: from prediction to care. Health Policy and Planning.2000; 15(1): 1-10.

8. Gortmaker SL. The effects of Prenatal Care upon the Health of the Newborn, American Journal of Public Health. 1979;69 (7): 653-660.

9. Kabir R, Khan HTA. Utilization of Antenatal care among pregnant women of Urban Slums of Dhaka City, Bangladesh. Journal of Nursing and Health Science. 2013;2(2):15-19.

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Doctors of Bangladesh Are in High Risk of Metabolic Syndrome

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Abstract:

Introduction: Metabolic syndrome (MS) or Syndrome X or Insulin Resistance Syndrome, a global epidemic, is a cluster of risk factors for CHD, DM2, stroke and other various medical problems, which affects specially those who lead sedentary and stressful life. Among them doctors are a most important group because of their professional and social responsibilities. They of both developed and developing countries are increasingly vulnerable.Objectives: The aim was to see the prevalence of MS among the doctors of Bangladesh. Material and methods: In this cross sectional study, by convenient and purposive sampling technique, 25-55 years aged 500 Bangladeshi doctors (male 334, female 166) were enrolled. The study was carried out in the Department of Biochemistry, BSMMU, Shahbag, Dhaka, Bangladesh. Study subjects were categorized on the basis of sex and age groups (25-40yrs. & 40-55yrs.). MS was diagnosed by modified NCEP ATP III criteria. Prevalence of MS was measured at 95% CI. Statistical significance was set at p<0.05.Results: Prevalence of MS was found 38.8% (24.6% male, 14.2% female); 36.8% within male doctors and 42.8% among female doctors. That in age group 25-40 years were 34.5% (male 17.9%, female 16.6%); 29.3% among male & 42.6% among female and in age group 40-55 years were 46.0% (male 35.8%, female 10.2%); 46.9% among male & 43.2% among female. It was found significantly higher in female in younger age group, but in total subject and male doctors it was higher in older age group. Conclusion: It can be concluded, the prevalence of MS is very high among the doctors of Bangladesh and younger female doctors are becoming more vulnerable.

Keywords: Metabolic syndrome, prevalence, NCEP ATP III.

Introduction:

Metabolic syndrome (MS) is a cluster of widely prevalent multi-factorial medical disorders that presents in a distinct, albeit heterogeneous phenotype and increases the risk of developing cardiovascular disease and diabetes[1]. Metabolic syndrome (MS) is also termed as Syndrome X or Insulin Resistance Syndrome[2-4.] There are different sets of criteria fordiagnosis of MS.The first formal definition of the MS was put forward in 1998 by the World Health Organization (WHO). This report was finalized in 1999 for individual having insulin resistance with any two of hypertension, dyslipidemia, central obesity and high urinary albumin excretion rate or high urinary albumin: creatinine ratio[5]. The European Group for the Study of Insulin Resistance (EGIR) and International Diabetes Federation (IDF) published a separate set of criteria thereafter[6,7].

In 2001, the National Cholesterol Education Program Adult Treatment Panel III (NCEP: ATP III, 2001)4 published a new set of criteria based on common clinical measurements: Waist circumference (WC), blood lipids, blood pressure, and fasting glucose[8]. Metabolic syndrome (MS) is recognized worldwide as an important public health concern and the prevalence of MS varies considerably worldwide. Some studies estimate that about 47 million adults in United States (almost 25%) have MS, and the numbers continue to grow[9]. In line with the risingprevalence of obesity, the metabolic syndrome is also increasing in developing countries.

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The recent data shows that one fourth to one third of urban population of India has the metabolic syndrome[10]. In another study it was showed that Bangladeshis among the entire South Asian immigrants in UK had highest risk of morbidity and mortality from hypertension, DM2 and coronary artery disease (CAD) and these are emerging as major health problems in Bangladesh[11,12]. Beyond cardio-vascular disease (CVD) and DM2, individuals with MS are susceptible to other life threatening medical problems like polycystic ovarian syndrome, fatty liver, cholesterol gallstones, asthma, sleep disturbances and some forms of cancer[5]. Many components of MS are associated with the sedentary lifestyle including increased adipose tissue (predominantly central), reduced HDL-C and a trend toward increased triacylglycerol, blood pressure and fasting serum glucose in genetically susceptible. Practicing physicians involved in clinical care are important segment of public health care delivery system. They have good access to information on disease frequency and determinants. Therefore, knowledge and awareness regarding the health consequences of lifestyle changes are generally expected to be high among clinicians. There is paucity of data on the lifestyle-associated disorders among physicians, though there is some data from Australia[8,13,14]. New Zealand[15], United Kingdom[16] and United States of America[17,18]. Young Indian physicians found to have high rates of cardio-metabolic risk factors in comparison to the general population (29.0% vs. 24.8%) and the proportion was higher in male doctors (30.2% vs. 25.3%) while in the general population, it was more among females (36.2% vs. 22.9%). They concluded that doctors need to have motivation to follow good health care practices which they advocate to their clients[11]. Most studies from developed countries also show that doctors, generally do not take good care of their health[8,15,19]. But study and data regarding MS among doctors are very rare. As MS can be prevent easily, it is imperative to identify individuals with metabolic syndrome early so that lifestyle interventions and treatment can be started to prevent the developmentof diabetes and/or cardiovascular diseases.

Doctors need to be motivated to practice good healthcare habits that they advocate to their clients. So, our study was designed to find out the magnitude of MS among doctors of Bangladesh.

Materials and Method:

500 doctors of Bangladesh of both sexes having minimum MBBS degree was enrolled in this cross sectional study by purposive and convenient sampling technique strictly maintaining inclusion and exclusion criteria. A data collection sheet was prepared for this purpose which included all the variables of interest. Metabolic Syndrome (MS) was defined according to modified NCEP-ATP III, 2001as presence of ≥3 of Central obesity:Waist circumference >90cm(male), >80cm(female), Dyslipidaemia: S. TAG ≥150mg/dl, S. HDL-C <40mg/dl (male), <50mg/dl (female), Blood pressue(BP): ≥130/85 mmHg, Fasting plasma glucose: ≥6.1mmol/L. Ethical clearance for the study was taken from proper authority. All the study subjects were thoroughly appraised about the nature, purpose, implications, procedure, benefits and risk of the studyand were assured about privacy and confidentiality; and about adequate free treatment of any risk developed during this study, and about their freedom to withdraw themselves from the study any time. Interest of the subjects was not compromised to safeguard their rights and health. Finally informed written consent of all study subjects were taken free of duress without exploiting any weakness of the subjects.

After taking verbal and informed written consent from all the study subjects, anthropometric measurements including height, weight, waist circumference and hip circumference were taken in all study subjects and WHR, WHtR& BMI were calculated. Systolic and diastolic blood pressure was recorded in sitting position. Then with full aseptic precaution, 5ml venous blood from each study subject was collected after an overnight fast (12 hours) in a disposable plastic syringe and was delivered immediately into a clean dry test tube, which was kept in standing position till clot formation.

Then serum was separated after centrifuging at 3000 rpm for 5 minutes and was collected in eppendorf tube, labeled properly and stored in ultra freezer at –35ºC until analytical measurement of serum glucose, serum triacylglycerol and serum HDL-C were done using the following Laboratory method: (1) Estimation of serum glucose concentration: Glucose oxidase (GOD-PAP) method[20], (2) Estimation of serum triglyceride concentration: Enzymatic GPO-PAP method[21], (3) Estimation of serum HDL cholesterol concentration: Enzymatic end-point CHOD-PAP method[22].

All data were recorded in a preformed data collection sheet and was analyzed by using SPSS version 14.0 for windows. Prevalence of metabolic syndrome in total study subjects as well as in male and female were determined at 95% confidence interval (CI) based on the modified NCEP-ATP III criteria. Age, anthropometric & biochemical indices and blood pressure were reported as the mean ± SD; and prevalence of MS was expressed in percentages. Statistical significance was set at $p<0.05$. Proportion test was done to compare the prevalence of metabolic syndrome between male & female and different age groups.

Results and Observation:

Among 500 Bangladeshi doctors 334(66.8%) were male and 166(33.2%) were female.

Age range of the study subjects was 25 to 55years with mean age (m±SD) 38.7±8.4yrs in total study subjects, 39.7±8.9yrs in male doctors and 36.7±7.1 yrs in female doctors. Distribution of male and female doctors is shown in Fig: 1.

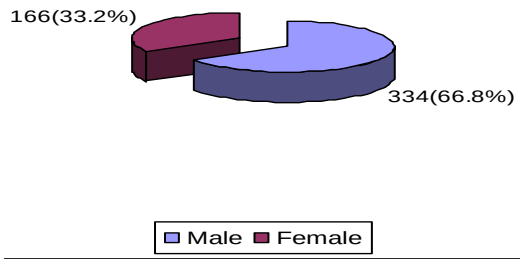

Figure-1: Distribution of study subjects

Table-1: Anthropometric indices (mean±SD) of study subjects

Parameters	Total study subjects (n=500)	Male (n=334)	Female (n=166)
Height (cm)	164.2±3.0	164.5±2.8	163.7±3.1
Weight (kg)	67.8±5.2	67.9±5.1	67.7±5.2
WC (cm)	91.0±5.3	91.1±4.3	91.0±6.8
HC (cm)	92.7±5.3	92.6±5.3	92.8±5.3
WHR	1.0±0.1	1.0±0.1	1.0±0.1
WHtR	0.6±0.0	0.6±0.0	0.6±0.0
BMI	25.4±2.2	25.3±2.2	25.5±2.3

WC: Waist circumference, **HC**: Hip circumference, **WHR**: Waist to hip ratio, **WHtR**: Waist to height ratio, **BMI**: Body mass index.

m±SD of anthropometric, biochemical and other indices are shown in Table 1 & 2.

Table-2: Biochemical and other indices (mean±SD) of study subjects

Parameters	Total study subjects (n=500)	Male (n=334)	Female (n=166)
SBP (mmHg)	129.0±9.4	130.1±8.9	126.9±10.2
DBP (mmHg)	75.6±5.4	76.2±5.1	74.4±5.9
FSG (mmol/L)	5.8±1.0	5.9±1.1	5.7±0.9
TAG (mg/dl)	190.4±95.6	195.7±91.9	179.8±102.3
HDL-C (mg/dl)	41.9±9.3	40.4±7.9	44.7±11.0

SBP: Systolic blood pressure, **DBP**: Diastolic blood pressure, **FSG**: Fasting serum glucose, **TAG**: Triacylglycerol, **HDL-C**: High density lipoprotein cholesterol.

Table-3: Distribution of the components of MS among the study subjects

Parameters		Total (n=500)	Male (n=334)	Female (n=166)
WC (M >90cm, F >80cm)		315	178	137
BP	SBP (>130mmHg)	222	156	66
	DBP (>85mmHg)	41	34	7
FSG (>6.1mmol/L)		141	108	33
TAG (>150mg/dl)		192	102	90
HDL-C (M<40mg/dl,F<50mg/dl)		281	152	129

WC: Waist circumference, **BP**: Blood pressure, **SBP:** Systolic blood pressure, **DBP**: Diastolic blood pressure**, FSG**: Fasting serum glucose, **TAG**: Triacylglycerol, **HDL-C**: High density lipoprotein cholesterol.

Out of 334 male, 178 had waist circumference >90cm and 137 female out of 166 had waist circumference >80cm. 156 and 34 male had SBP >130mmHg and DBP >85mmHg whereas 66 and 07 female had SBP >130mmHg and DBP >85mmHg respectively. FSG >6.1mmol/L found in 108 male and 33 female, TAG >150mg/dl found in 102 male and 90 female doctors. HDL-C <40mg/dl was found in152 male and HDL <50mg/dl was found in 129 female doctors respectively (Table 3).

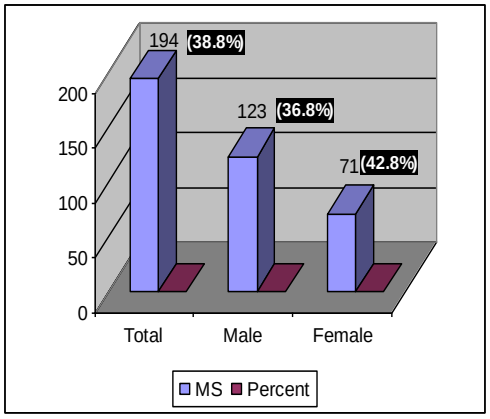

Figure-2: Frequency and prevalence of metabolic syndrome (MS) among the study subjects

Out of the total population (n=500), 194 had metabolic syndrome, of which 123 were male and 71 were female. The prevalence of MS (95% CI) among the total population was found to be 38.8% (male 24.6% & female 14.2%) and that within male doctors and female doctors were 36.8% and 42.8% respectively (Fig-2).

According to the age, total study subjects were classified into two groups, 25-40years and 40-55years.

Table-4: Frequency and Prevalence of Metabolic Syndrome in different age groups of study subjects

Age group (years)		Number	Frequency of MS	Prevalence
25-40	Both sex	313	108	34.5%
	Male	191	56	29.3%
	Female	122	52	42.6%
40-55	Both sex	187	86	46.0%
	Male	143	67	46.9%
	Female	44	19	43.2%

In the age group 25-40years, total doctors were 313, of which 191 were male and 122 were female. In the age group 40-55years, total doctors were 187, of which 143were male and 44 were female. In age group 25-40 yrs. 108 (male 56 and female52) doctors and in age group 40-55 yrs. 86 (male 67 and female 19) doctors found to have MS. Prevalence of MS in age group 25-40 yrs. and 40-55 yrs were 34.5%, and 46.0% respectively and that of male and female in age group 25-40 yrs and 40-55 yrs was 29.3% vs. 42.6% and 46.9% vs. 43.2% respectively (Table-4).

Comparisons of Metabolic syndrome in different age groups were done. MS was found significantly higher in female in age group 25-40yrs, whereas in age group 40-55 yrs. It was insignificant in male and female. MS in both sex of both age groups were compared and found significantly higher in older age group.

Discussion:

In this cross sectional study, our aim was to measure the prevalence of metabolic syndrome (MS) among the Bangladeshi doctors. The doctors are members of affluent society. They usually live sedentary life. But they have experience different types of physical and mental stress due to their professional activities.

The prevalence of metabolic syndrome was high among doctors in our study. In total participants the prevalence was 38.8% (male 36.8%, female 42.8%). As our participants were doctors they could be comparable with persons of same profession and other sedentary workers. Our finding was supported byRamachadran et al. They concluded that in India, doctors had high prevalence of metabolic syndrome[19].

This finding was also supported by the statement of many other investigators[9,10,23]. In our study 123 (36.8%) male doctors & 71 (42.8%) female doctors were suffering from metabolic syndrome.

In most of the studies in different countries around the world, prevalence of MS was found higher in female than male[24].

But in some other studies done in different developing countries around the world including South Asian region prevalence of MS found higher in male which is contrary to our findings[25]. In a study among young physicians, Ramachandran also showed that the prevalence of MS was higher among male doctor (30.2%) than female (25.3%) which is contrary to our findings[19].

We have found the prevalence of MS in 25-40yrs age group was 34.5% (male 29.3%, female 42.6%) and in 40-55yrs age group was 46.0% (male 46.9%, female 43.2%).

A study in rural Japan carried out in 2008 showed a low prevalence of MS and it was 4.6% in males and 4.25 in females[26]. Another study carried out in 2006 on rural Bangladeshi women also revealed low prevalence of MS (<3%)[27].

It is contrary to our study. Morimoto et al. (2008) explained that lower prevalence of MS may be due to consumption of traditional Japanese food and the higher levels of regular physical activities of the farmers[26].

Zaman et al. (2006) explained that physical activity level in this agricultural population is high because of their traditional lifestyle. Regular physical activity reduces obesity, increases HDL cholesterol, and decreases triglycerides[27].

On the contrary our samples were living with less physical activity, habit of taking rich food and stressful life. So it is likely that the prevalence of metabolic syndrome will be more in our study.

However epidemiologic studies have demonstrated differences in prevalence by age, gender, and ethnicity. Most, but not all, studies reported a higher prevalence of the metabolic syndrome among women compared with men[28].

At age group 25-40yrs, the prevalence of MS found significantly higher in female than male in our study. Among total study subjects & male doctors, it was also found significantly higher in 40-55yrs age group.

Conclusion:

It can be apparently concluded that, the prevalence of metabolic syndrome is alarmingly high among the doctors of Bangladesh. Prevalence of MS increases with age in both sexes. Female doctors of relatively younger age group are becoming more vulnerable.

Recommandation:

Awareness regarding health care should be built up among the doctors. This study should be carried out in a large scale as well as in different sectors of population.

References:

1 Gogia A, Agarwal PK.Metabolic Syndrome. Indian J Med Sci.2006; 60: 72-81.

2 Haller H. Epidemiology and associated risk factors of hyperlipoproteinemia. Z Gesamte Inn Med. 1977; 32(8): 124-8.

3 Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes. 1988(37): 1595-607.

4 NCEP ATP III: Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001; 285: 2486–2497.

5 Grundy SM, Brewer HB Jr, Cleeman JI. Defnition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/ American Heart Association conference on scientific issues related to definition, Circulation. 2004; 109 (3): 433-8.

6 Balkau B, Charles MA. Comment on the provisional report from the WHO consultation: European Group for the Study of Insulin Resistance (EGIR). Diabet Med.1999;16: 442–443.

7 Anthony Fauci S. Harrison's principles of internal medicine, McGraw-Hill Medical. ISBN 0-07-147692-X.

8 Kay MP, Mitchell GK, DelMar CB. Doctors do not adequately look after their own physical health.Med J. 2004; 181: 368–70.

9 Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults:findings from the third National Health and Nutrition Examination Survey. JAMA.2002; 287(3): 356-9.

10 Misra A, Khurana L. The Metabolic Syndrome in South Asians: Epidemiology, Determinants, and Prevention, MetabSyndrRelatDisord, 2009;Nov 9. [Epub ahead of print]

11 McKeigue PM, Marmot MG, Syndercombe CYD, Cottier DE, Rahman S, Riemersma RA. Diabetes hyperinsulinemia and coronary risk factors in Bangladeshis in East London. Br Heart J.1988;60: 390-396.

12 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(5):1047-53.

13 Wachtel TJ, Wilcox VL, Moulton AW. Physicians' utilization of health care. J Gen Intern Med. 1995; 10: 261-5.

14 Nyman K. The health of general practitioners: A pilot survey. Aust Fam Phy. 1991; 20:637-41,644-45.

15 Richards JG. The health and health practices of doctors and their families. N Z Med J.1999; 26: 96–9.

16 Baldwin PJ, Dodd M, Wrate RM. Young doctors' health – II. Health and health behavior. Soc Sci Med. 1997; 45: 41-4.

17 Frank E, Breyan J, Elon L. Physician disclosure of healthy personal behaviors improves credibility and ability to motivate.Arch Fam Med. 2000; 9: 287-90.

18 Frank E. Physician Health and Patient Care. JAMA.2004; 291-637.

19 Ramachandran A, Snehalatha C, Yamuna A, Murugesan N. High Prevalence of Cardiometabolic Risk Factors among Young Physicians in India. JAPI. 2008; 56: 17-20.

20 Barham D, Trinder P. An improved colour reagent for the determination of blood glucose by oxidase system. Analyst. 1972; 97: 142-145.

21 Allian CA, Poon LS, Chan CGS, Richmond W, Fu PC. Enzymatic determination of total cholesterol. Clinical chemistry.1974; 20: 470.

22 Bucolo G, David M. Estimation of serum triglyceride. Clinical chemistry. 1973; 19: 476-482.

23 Youden WJ. Index for rating diagnostic tests. Cancer. 1950;3:32-35.

24 Florez H, Silva E, Fernandez V, Ryder E, Sulbaran T, Campos G, et al. Prevalence and risk factors associated with the metabolic syndrome and dyslipidemia in White, Black, Amerindian and Mixed Hispanics in Zulia State, Venezuela.Diabetes Res ClinPract. 2005;69: 63–77.

25 Marquezine GF, Oliveira CM, Pereira AC, Krieger JE, Mill JG. Metabolic syndrome determinants in an urban population from Brazil: social class and gender-specific interaction.Int CardiolJ.2008; 129: 259–265.

26 Morimoto A, Rimei N, Suzuki N, Matsudaira T, Taki K, Tsujino D, et al. Low prevalence of metabolic syndrome and its components in rural Japan. Tohoku J. Exp. Med. 2008; 216: 69-75.

27 Zaman MM, Ahmed J, Choudhury SR, Numan SM, Islam MS, Parvin K. Prevalence of Metabolic Syndrome in Rural Bangladeshi Women. Diabetes Care. 2006;29(6): 1456-1457.

28 Razzouk L, Muntner P.Ethnic, gender, and age-related differences in patients with the metabolic syndrome. CurrHypertens Rep.2009; 11(2): 127-32.

DCIMCJ

Original Article

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Factors Influencing Discontinuation of Antihypertensive Drugs in an Urban Population

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Abstract:

Background and aims: Hypertension is a chronic non-communicable disease causing considerable morbidity and mortality. This study aims to find out different factors associated with discontinuation of antihypertensive drugs in an urban population. Methods: This was an observational cross sectional study carried out in medicine out-patient department of Dhaka Medical College Hospital from January to July 2017. Fifty adult patients diagnosed as hypertensive within last 1 year, took antihypertensive medications for at least 3 months and discontinued drugs completely for last 3 months were included in the study using purposive sampling method. Results: Mean age of the respondents was 51 years. Thirty patients were diagnosed as hypertensive by graduate physician, 10 patients by specialist physician and 10 diagnosed by other non medical personnel. ACEI or ARBs were most commonly prescribed antihypertensive drugs (32%). Of the 30 patients diagnosed by graduate physicians, 19 (63%) were counseled about hypertension and its complication. Eight patients out of 10 were counseled by specialist physicians. Those who diagnosed by non medical personnel were not counseled at all. Only 20 patients were counseled about side effect of anti hypertensive drugs. Of the 30 patients diagnosed by graduate physicians only 13 (43.3%) patients were counseled about side effect of drugs. On the other hand 10 patients were diagnosed by specialist physicians, of them 7 patients were counseled. Fifteen (50%) out of 30 patients were investigated before prescribing antihypertensive drugs by graduate physicians. Ten out of 10 patients (100%) were investigated before prescribing antihypertensive drugs by specialist physicians. Only 15 (30%) patients went for follow up. Thirteen patients (26%) stopped drug as they were feeling better, 11 patients (22%) stopped due to normalization of blood pressure, 9 patients (18%) stopped drug because of advice from non health professionals, 6 patients due to side effect of drugs and 6 patients due to financial constraints. Conclusion: Most of the factors responsible for discontinuation of drugs are subject to modification by appropriate patient education and counseling.

Keywords: Antihypertensive drugs, noncompliance

Introduction:

Hypertension is one of the commonest chronic medical problems[1]. It is associated with enormous economic and personal burden through increased risk of heart disease, stroke and kidney disease[2–4]. The prevalence of hypertension is variable in different countries- 20% in the USA, and 25–50% in different regions in Europe[5]. In Bangladesh, a population surveywas carried out by Bangladesh Society of Medicine in collaboration with Directorate General of Health Services and World Health Organization from November 2009 to April 2010 which found that prevalence of hypertension is 17.9% in general, 18.5% in men and 17.3% in women[6]. In another study among senior citizens, 44.8% were found to be hypertensive[7].

Although many effective therapies are available, hypertension still remains poorly controlled in most

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parts of the world. In the third National Health and Nutrition Examination Survey, nearly half of the hypertensive patients were not taking any prescription drugs, and only one-fourth of those who were taking drugs were having adequate control of blood pressure[8]. Non-compliance of patients to the prescribed treatment is a central reason for failure to control blood pressure in those receiving therapy. Approximately half of the hypertensive patients do not comply with treatment, and half of those with resistant hypertension are actually non-compliant[9,10]. Such high levels of non-compliance are of concern, taking into account the serious consequences of hypertension on cardiac, renal and cerebrovascular morbidity and mortality[11].

To improve compliance it is imperative to find out the factors leading to non-compliance to medications. Numerous studies have identified different factors such as age, race, gender, socio-economic factors etc. that are associated with non-compliance[12,13]. Unfortunately, there is scarce data in our country about the factors which lead to discontinuation of antihypertensive drugs. Therefore, this study aims to find out different factors associated with discontinuation of antihypertensive drugs in an urban population.

Materials and Methods:

This was an observational cross sectional study carried out in medicine out-patient department of Dhaka Medical College Hospital from January to July 2017. Adult patients who have been diagnosed as hypertensive within last 1 year, took antihypertensive medications for at least 3 months and discontinued drugs completely for last 3 months were included in the study. Those patients who took drugs for less than 3 months before discontinuation and patients taking drugs irregularly without complete discontinuation were excluded. Assuming a prevalence of 17.9% (WHO 2010[6]) and using the formula $n= z^2pq/d^2$, the estimated sample size was 56.4. However, 50 patients were included. Purposive sampling method was used. Data was collected using a semi-structured questionnaire from the study subjects after taking informed written consent. No extra cost was imposed on the patient. Ethical clearance was taken from the Institutional Review Board, Dhaka Medical College Hospital.

Results:

Total 50 patients were included in this study. of them, 25 were male and 25 female. Mean age of the respondents was 51 years. Sixteen (32%) patients were illiterate.

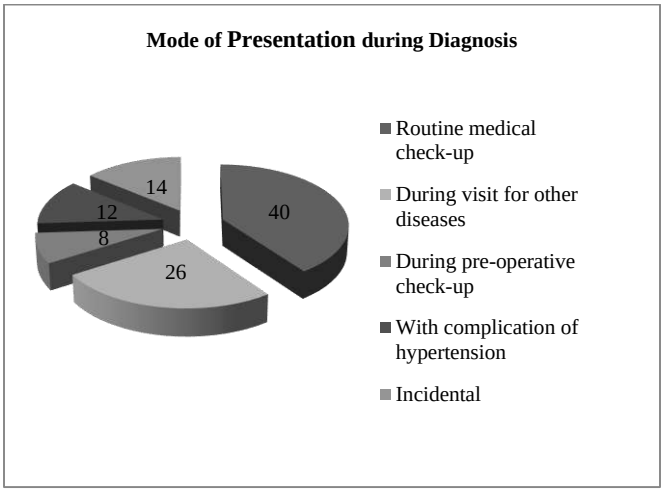

Figure-1: Mode of presentation during diagnosis of hypertension (N=50)

Regarding the mode of diagnosis, 20 (40%) patients were diagnosed during routine medical checkup, 13 (26%) during visit for other diseases, 7 (14%) patients diagnosed incidentally, 6 (12%) during complication of hypertension (e.g: stoke, MI, LVF), and 4 patients were diagnosed during pre operativecheck up (Figure-1).

Table-1: Personnel who diagnosed hypertension (N=50)

Personnel	n	%
Graduate physician	30	60
Specialist physician	10	20
Health worker	1	2
Paramedic	5	10
Quack	3	6
Others	1	2
Total	**50**	**100**

Of the 50 study subjects, 30 were diagnosed as hypertensive bygraduate physician, 10 patients diagnosed by specialist physician and 10 diagnosed by other non medical personnel (Table-1).

Table-2: Antihypertensive drug(s) prescribed to the patients at diagnosis (N=50)

Drug(s)	n	%
ACEI or ARB	16	32
β-blocker	7	14
Calcium channel blocker (CCB)	5	10
CCB plus β-blocker	4	8
CCB plus ARB	2	4
ARB plus diuretics	4	8
β-blocker plus diuretics	3	6
Could not remember	9	18
Total	**50**	**100**

In this table it is evident that ACEI or ARBs were most commonly prescribed antihypertensive drugs (32%).

Table-3: Counseling regarding hypertension and its complications (N=50)

Personnel involved	Counseled n(%)	Not counseled n(%)	Can not remember n(%)	Total n(%)
Graduate physician	19 (63.3%)	8 (26.7%)	3 (10.0%)	30 (100.0%)
Specialist physician	8 (80.0%)	2 (20.0%)	0 (0.0%)	10 (100.0%)
Health worker	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Paramedic	0 (0.0%)	4 (80.0%)	1 (20.0%)	5 (100.0%)
Quack	0 (0.0%)	3 (100.0%)	0 (0.0%)	3 (100.0%)
Others	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Total	**27 (54.0%)**	**19 (38.0%)**	**4 (8.0%)**	**50 (100.0%)**

Of the 30 patients diagnosed by graduate physicians, 19 (63%) were counseled about hypertension and its complication. Eight patients out of 10 were counseled by specialist physicians. Those who diagnosed by non medical personnel were not counseled at all (Table-3).

Table-4: Counseling regarding adverse effect of antihypertensive drugs (N=50)

Personnel involved	Counseled n(%)	Not counseled n(%)	Cannot Remember n(%)	Total n(%)
Graduate physician	13 (43.3%)	13 (43.3%)	4 (13.4%)	30 (100.0%)
Specialist physician	7 (70.0%)	3 (30.0%)	0 (0.0%)	10 (100.0%)
Health worker	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Paramedic	0 (0.0%)	5 (100.0%)	0 (0.0%)	5 (100.0%)
Quack	0 (0.0%)	3 (100.0%)	0 (0.0%)	3 (100.0%)
Others	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
Total	**20 (40.0%)**	**26 (52.0%)**	**4 (8.0%)**	**50 (100.0%)**

Only 20 patients were counseled about side effect of anti hypertensive drugs. Of the 30 patients diagnosed by graduate physicians only 13 (43.3%) patients were counseled about side effect of drugs. On the other hand 10 patients were diagnosed by specialist physicians, of them 7 patients were counseled. Those who were diagnosed by others were not counseled about side effect of anti hypertensive drugs (Table-4).

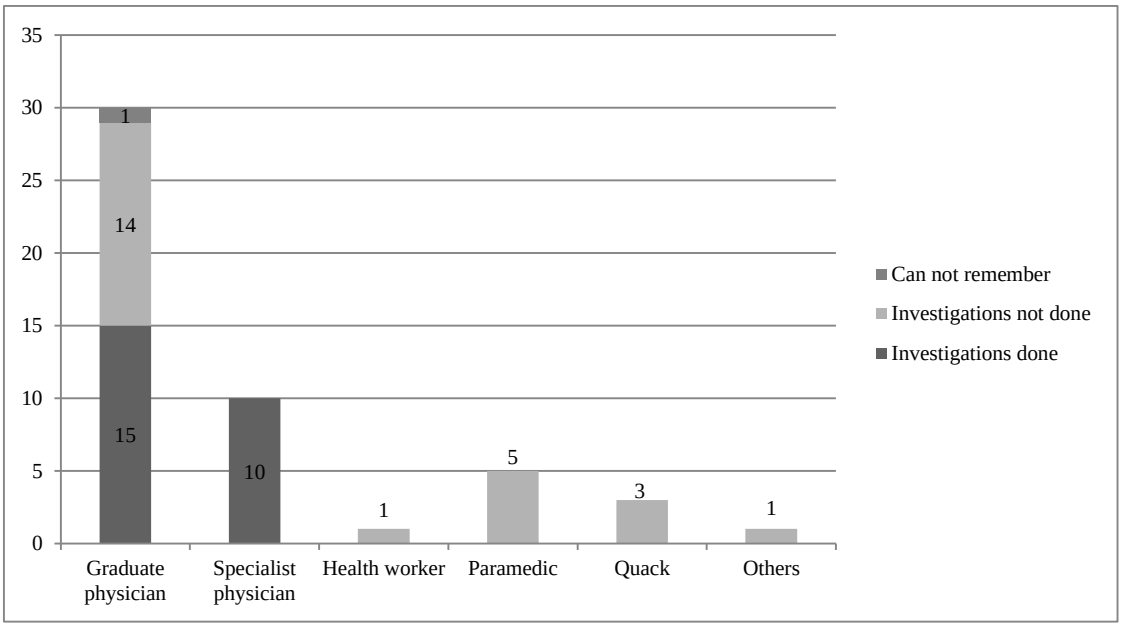

Figure-2: Whether investigations were done before prescribing antihypertensives (N=50)

Fifteen (50%) out of 30 patients were investigated before prescribing antihypertensive drugs by graduate physicians. Ten out of 10 patients (100%) were investigated before prescribing antihypertensive drugs by specialist physicians. Those who were diagnosed by others were not investigated at all (Figure-2).

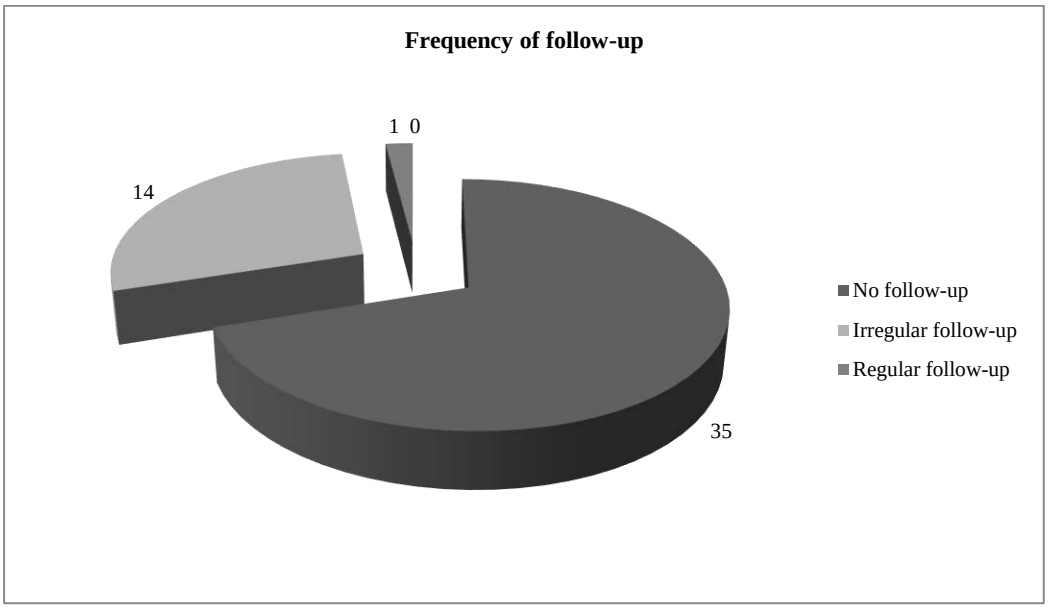

Figure-3: Frequency of follow-up visit (N=50)

Figure-3 shows that out of 50 patients, only 15 (30%) patients went for follow up .Of them only 1 patient went for follow-up regularly.

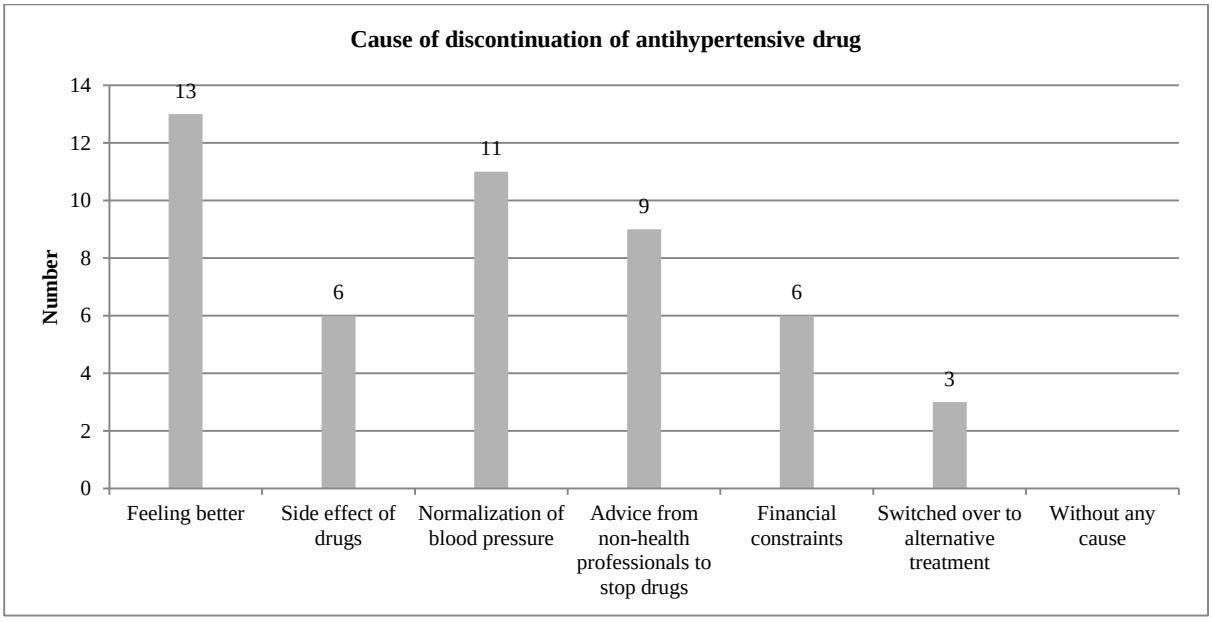

Figure-4: cause of discontinuation of antihypertensive drug (N=50)

Of the study subjects, 13 patients (26%) stopped drug as they were feeling better, 11 patients (22%) stopped due to normalization of blood pressure, 9 patients (18%) stopped drug because of advice from non health professionals, 6 patients due to side effect of drugs and 6 patients due to financial constraints (Figure-4).

Discussion:

We conducted our study on 50 hypertensive patients who have discontinued antihypertensive drugs on their own for at least 3 months. Of them 25 were male and 25 female. Mean age of the respondents was 51 years. Sixteen (32%) patients were illiterate. In a study by Hossain et al (2015) in Dhaka Medical College Hospital, 103 patients were male and 43 female. In another study carried out in 4 hospitals in Dhaka city, 26 were males (52 %) and 24 (48 %) were females out of 50 hypertensive patients[14]. The study done by Hasan (2016) found that of 100 hypertensive patients, 63% were male and 37% were female. The mean age was 37 ±11.3 years in his study[15]. Regarding level of education, Hasan (2016) found that 30% patients had completed their primary education, 27% completed their graduation, 23% taking higher secondary school certificate and 20% were illiterate[15].

In our study, 20 patients(40%) were diagnosed as hypertensive during routine medical check-up, 13 patients (26%) diagnosed during visit for other diseases, 7 patients (14%) diagnosed incidentally, 6 (12%) diagnosed when presented with complication of hypertension and 4 (8%) during preoperative check up.

Most of the patients diagnosed as hypertension by doctors – 40 patients (80%). Only 10 patients (20%) diagnosed by other healthcare personnel. Of the 30 patients diagnosed by graduate physicians, 19 (63%) were counseled about hypertension and its complication. Eight patients out of 10 were counseled by specialist physicians. Those who diagnosed by non medical personnel were not counseled at all. Only 20 patients were counseled about side effect of anti hypertensive drugs. Of the 30 patients diagnosed by graduate physicians only 13 (43.3%) patients were counseled about side effect of drugs. On the other hand 10 patients were diagnosed by specialist physicians, of them 7 patients were counseled. Those who were diagnosed by others were not counseled about side effect of anti hypertensive drugs. So, it revealed that patients diagnosed by qualified doctors were better counseled about hypertension, its complications and side effect of drugs. Hossain et al (2015) found in their study that 132 patients out of 146 were counselled by doctor regarding life style modifications. One-hundred and five of them had knowledge of hypertension, and 95 were aware of daily taking of anti-hypertensive medications[14].

ACEI or ARB were most commonly used drugs in hypertensive patients in this study-16 patients (32%) started with ACEI or ARB, 7 patients (14%) started with beta blocker,5 patients(10%) started with calcium channel blocker and 4 patients (8%) started with beta blocker and calcium channel blocker combination. Hasan (2016) found in his study that among 100 study population 61.6% patients received monotherapy and 38.4% patients were prescribed combined therapy for the management of hypertension. Among the mono-therapy mostly used drugs were ARBs (37.3%), CCB (32.8%), and ACEI (17.9%), Beta Blocker (BB) (6%), Alpha Blocker (AB) (3%) and Thiazide and non-thiazide diuretics 1.5% each. Among combination drug therapy ARB+CCB were used 28.1% and CCB+BB were also 28.1% and use of ARB + Diuretics were 25%, ACEI +CCB 3.1%, ACEI + Diuretics 3.1%, Thiazide and Non Thiazide Diuretics was 3.1% and other drugs was used for 9.5%[15]. Liu et al (2008) found in their study in Taiwan that the most frequently prescribed antihypertensive regimens, ranked in order of prescribing frequency, were: CCBs (17.7%), beta-blockers (14.5%), ACEIs (8.2%), CCBs + beta-blockers (7.7%), others (5.3%), diuretics (4.4%), CCBs + ACEIs (4.0%), ARBs (3.0%), CCBs + ARBs (2.6%), beta-blockers+ diuretics (2.4%)[16]. Another study by Khaja et al (2001) found that the frequency of different drugs used as monotherapy was: beta blockers 58.8%, ACEIs 14.2%, CCBs 11.1%, diuretics 8.1% and alpha-methyl dopa 7%[17].

Most of the study subjects did not undergo follow up at all. Only 15 patients (30%) underwent routine follow up; of them only 1 patient was regularly on follow up. Alam et al (2014) performed a study on 287 hypertensive patients in Dhaka and Chandpur,

and found that 83.3% patients visited a healthcare provider at least onceafter enrolment in the study. Over three quarters of the patients with hypertension in Dhaka and a third in Matlab visited professionally qualified doctors (76.7% vs 36.6%, p<0.000), including MBBS/MDs or more highly qualified practitioners. The rest visited drug sellers, including pharmacists, village doctors or owners of small drug outlets with or without diplomas or certificates for medical practice[18].

Causes of discontinuation of antihypertensive drugs were variable; 13 patients (26%) stopped drugs as they felt better, 11 patients (22%) stopped due to normalization of blood pressure, 9 patients stopped due to influence of non health professionals, 6 due to side effect of drugs and 6 patients stopped due to financial constraints. Three patients switched to conventional treatment. Gosmanova et al (2014) found that important causes of discontinuation of antihypertensive drugs were visual, hearing or cognitive impairment, immobility of patients, poor knowledge about disease, cultural beliefs, poor understanding of why drugs are needed, fear of taking drugs and possible adverse effects, substance dependence, complexity of drug regimen, duration of drug regimen (lifelong), lack of immediate benefits of therapy, actual of perceived side effects, frequent changes in regimen, cost of treatment, health illiteracy, lack or limited access to pharmacy, lack of positive reinforcement from provider, lack of provider's knowledge about adherence etc[19].

Conclusion:

Hypertension is a chronic non-communicable disease associated with life threatening complications. To prevent these complications, strict control of blood pressure is needed, which depends mostly on patients understanding of the disease and compliance with the medications. The responsibility of patient education, in turn, is mostly dependent on the treating physician. Our study found out that many hypertensive patients are having medications without proper counseling and advice, and consequently discontinuing drugs and/or being lost from follow-up.

Therefore, physicians as well as policy makers should be aware of these factors which lead a patient to become non-compliant, and try to recognize and alleviatethem during the management of a hypertensive patient.

References:

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation 2014; 129: e28–e292.

2. Cherry DK, Hing E, Woodwell DA, Rechtsteiner EA. National Ambulatory Medical Care Survey: 2006 summary. Natl Health Stat Report 2008: 1–39.

3. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014; 311: 507–520.

4. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics— 2012 update: a report from the American Heart Association. Circulation 2012; 125: e2–e220.

5. TNS opinion and social health in European Union. Special Eurobarometer 272e/Wave 66. 2nd September, 2007.

6. World Health Organization. Bangladesh NCD risk factor survey 2010, WHO, http://www.whoban.org/LinkFiles/Publication_NCD_FACT_SHEET.pdf.pdf.

7. Moni MA, Rahman MA, Haque MA, Islam MS, Ahmed K. Blood pressure in relation to selected anthropometric measurements in senior citizens. Mymensingh Med J 2010; 19:254–8.

8. Burt V, Whelton P, Roccels E, Brown C, Cutler JA, Higgins M, Horan MJ, Labarthe D. Prevalence of hypertension in the US adult population: results from the Third National Health and Nutrition Examination Survey, 1988-1991. Hypertension 1995; 25: 305-313.

9. Sharkness CM, Snow DA. The patient's view of hypertension and compliance. Am J Prev Med 1992; 8: 141-146.

10. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. Compliance with antihypertensive therapy among elderly Medicaid enrollees: the roles of age, gender, and race. Am J Public Health 1996; 86: 1805-1808.

11. Clark T. Improving compliance and increasing control of hypertension: needs of special hypertensive populations. Am Heart J 1991; 121: 664-669.

12. The sixth report of the Joint National Committee on Prevention, detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997; 157: 2413-2444.

13. Wang PS, Bohn RL, Knight E, Glynn RJ, Mogun H, Avorn J. Noncompliance with Antihypertensive Medications: The Impact of Depressive symptoms and Psychosocial Factors. J Gen Intern Med 2002; 17: 504-511.

14. Hossain SZ, Islam MR, Biswas S, Hossain MZ, Biswas PK, Islam N, Hossain MA, Rahaman MH. Pattern of Compliance to Antihypertensive Medications in Hypertensive Patients in a Tertiary Care Hospital in Bangladesh. J Dhaka Med Coll. 2015; 24(1): 62-66.

15. Hasan MJ. Pattern of drugs prescribed for treatment of hypertensive patients: Bangladesh. Afr J Pharm Pharmacol 2016; 10 (25): 521-525.

16. Liu PH, Wang JD. Antihypertensive medication prescription patterns and time trends for newly-diagnosed uncomplicated hypertension patients in Taiwan. BMC Health Services Research 2008; 8:133.

17. Khaja KAJA, Sequeira RP, Wahab AWMA, Mathur VS. Antihypertensive drug prescription trends at the primary health care centers in Bahrain. Pharmacoepidemiology and Drug Safety 2010; 10: 219-227.

18. Alam DS, Chowdhury MAH, Siddiquee AT, Ahmed S, Niessen LW. Awareness and control of hypertension in Bangladesh: follow-up of a hypertensive cohort. BMJ Open 2014;4: e004983.

19. Gosmanova EO, Kovesdy CP. Adherence to antihypertensive medications: is prescribing the right pill enough? Nephrol Dial Transplant 2015; 30: 1649–1656.

DCIMCJ

Original Article

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Total Laparoscopic Hysterectomy- Study of 50 Cases in a Tertiary Care Hospital

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Abstract:

Objective (1) To analyze the case variety and (2) To assess the outcome and complications of patients who underwent total laparoscopic hysterectomy in tertiary care hospital Methods: It was a retrospective cross-sectional study done on total laparoscopic hysterectomy (TLH) patients in ShaheedSuhrawardy Medical College Hospital. Study period was from January 2016 to December 2017. Total 50 cases were included in the study. Indications of total laparoscopic hysterctomy, method of operation, intra operative and post operative complications, duration of the operation, length of hospital stay and blood loss in patients who underwent total laparoscopic hysterectomy were retrospectively evaluated.Results:Total 50 patients underwent total laparoscopic hysterectomy were included in this study. The mean age was 43.74. The most common indication for hysterectomy was fibroid uterus. The mean operation time was 2.2hrs. Average blood loss was 200ml. Average hospital stay was4.3 days. Main complication was hemorrhage which was about 8%, conversion from laparoscopy to laparotomy done in 6% patients.Conclusion:Total laparoscopic hysterectomy is a preferred method to abdominal hysterectomy because it is associated with a more favourable surgical outcome. The laparoscopic approach is an acceptable treatment modality in the current gynecological practice. Total laparoscopic hysterectomy is more beneficial to patients because of low estimated blood loss, less analgesic use, low intraoperative and post operative complications rates, less post-operative pain, more rapid recovery and short hospital stays. The percentage of total laparoscopic hysterectomy is still very low. The longer operative time in total laparoscopic hysterectomy is an unfavourable learning curve. Extensive training of surgeons and whole surgical team are often cited as reasons.

Keywords: Total laparoscopic hysterectomy, laparotomy, treatment modality

Introduction:

Hysterectomy is one of the most commonly performed surgeries, with nearly 500,000 women undergoing the procedure in inpatient settings annually in the united states alone[1]. Abdominal, vaginal and laparoscopic techniques are the surgical techniques used for hysterectomy. Hysterectomy was first performed vaginally by Recamier in 1829[2]. Abdominal hysterectomy was first performed by Charles Clay in 1843[3] Harry Reichperformed the First laparoscopic hysterectomy (LH) in 1989[4]. Currently,it is recommended that minimally invasive surgical techniques should be used if hysterectomy is planned for non malignant disease[5]. Abdominal hysterectomy causes more pain and discomfort than vaginal or laparoscopic methods[6]. Vaginal hysterectomy performed mainly for uterine prolapse and other indications depends on uterine size, coexistent adnexal disease and the previous abdominal surgical operations. Laparoscopic hysterectomy (LH) is more preferable because it offer a more rapid recovery period, less blood loss, low risk of incision infection and earlier discharge from hospital[7]. In this study, the data of 50 patients who underwent TLH in our hospital were analysed retrospectively.

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Methods:

The data of 50 patients who underwent total laparoscopic hysterectomy (TLH) operation at Shaheed Suhrawardy Hospital, Department of

obstetrics and Gynecology between January 2016 to December 2017 were analysed.

The files of the patients were evaluated retrospectively during discharge with respect to age, parity, history of previous surgery, indications of hysterectomy, duration of operation, intra operative and post operative complications, estimated blood loss and length of hospitalization. Multiparous patientsof reproductive age group &post menopausal patients with various benign uterine pathology were included in this study. Patients with previous two or more caesarian section, H/O extensive abdominal surgery, H/O Severe endometriosis, patients with severe cardiac disease or compromised lung function, uterine size > 20 wks, known case of uterine malignancy, $2^{nd}/3^{rd}$ degree prolapse with cystocoele&rectocoele were excluded from the study.

Before operation, general, abdominal and pelvic examinations were performed. Mechanical bowel preparation was done on the day before operation. Prophylactic antibiotic was administered. All operations performed under general anesthesia and in dorsal lithotomy position by senior gynecologist. Foley catheter was inserted. A manipulator was applied in the uterine cavity. Approximately 1.5 cm transverses incision was made on supra-umbilical crease. Duration of operation was calculated by measuring time between first incision and last suture on skin. Abdomen was entered with a 10 mm trocer, pneumo peritoneum created & 10 mm zero degree telescope introduced. Later on three 5mm port were made including one ipsilateral port on surgeon's left side. The patients were placed in Trendelenburg position as far as possible. Harmonic scalpel and monopolar electro-coagulation was used in operation. As uterine manipulator Cohen's canula was used initially. Later on laparoscopic myoma screw used.Colpotomizer was used in vagina during separation of cervix from vagina. After monitoring the intra-abdominal area and thecourse of the ureter, the round ligament, the ovarian ligament and the infundibulo pelvic ligament of both sides were cut after being coagulated.

The anterior and posterior leaves of the broad ligament were dissected, the bladder was separated from the cervix by blunt and sharp dissection. Uterine arteries were coagulated and cut on both sides. After parametrialtissuse around the cervix coagulated with harmonic, then cutted and bleeding areas were coagulated. The entire vaginal wall was circularly separated from cervix using monopolar L-tipped cautery with the help of uterine manipulator in vaginal route. The surgical material was removed through the vaginal route. The vaginal cuff was closed by late absorbable suture materials, Because retrospective design of the study, ethical committee approval and patients consent were not obtained.

Results:

Total abdominal hysterectomy (TAH) patients were 369 during study period, among these 50 patients underwent hysterectomy laparoscopically. So incidence of TLH among TAH was 13.92%.

Maximum age group of patient was between 41-45yrs (52%) (Table-1) Fibroid uterus indication in 46% cases, Adenomyosis in 30% cases (Table-II). The mean age of the patients was 43.74 & the mean parity was 1.6 mean duration of operation was 2.2hrs. Average blood loss was 200ml. Average hospital stay was 4.3 days (Table-III). Intra operative hemorrhage occured in 8% cases. The procedure was switched from laparoscopy to laparotomy in 3 patients because of uncontrollable bleeding & later on difficult manipulation.

Table-I: Age distribution of patients

Age group of patient undergoing TLH (yrs)	No. of patient (N-50)	Percentage
<35	01	2%
36-40	10	20%
41-45	26	52%
46-50	09	18%
51-55	02	4%
56-60	02	4%

Table-II: Indication for TLH

Indication of TLH	No. of patient(N-50)	Percentage
Elongated cervix	02	4%
Fibroid uterus	23	46%
DUB	05	10%
Adenomyosis	15	30%
Chronic PID	05	10%

Table-III: Summary of Patient Underwent TLH

Mean Age	43.74 (35-60 yrs)
Parity	1.6 (0-5)
Mean duration of procedure	2.2 hr (75 min - 4hr)
Uterine size	4-14 wks
Average blood loss	200 ml (50-800ml)
Average hospital stay	4.3 day (48hrs- 7 days)

Table-IV: Complication of TLH vs open surgery

Complication	No. of patient(n-50)	Percentage
Hemorrhage	04	8%
Switching from laparoscopic approach to open surgery	03	6%

Discussion:

Hysterectomy is the second most common gynaecologic surgery after cesarean sections performed by gynaecologist. It has a wide range of indications including dysfunctional uterine bleeding, myoma uteri, gynaecologic cancer, uterovaginal prolapse, endometriosis, adenomyosis, pelvic inflammatory disease & obstetric complications[8]. In our study, mean age of patient was 43.74yrs & mean parity was 1.6. Mean duration of procedure was 2.2hrs & average hospital stay was 4.3 days.

In another study[9,] mean age was 49.33yrs, mean parity 2.4, mean duration of procedure 132.16 minutes& the length of hospitalization was 3.38 days. Fibroid uterus (46%) was the main indication in our study. Treatment resistant menorrhagia (33.7%) &Myoma uteri (27.7%) were main indication in another study[9.] In a multicentre study it was reported that vaginal and laparoscopic hysterectomy (LH) were more advantageous than abdominal hysterectomy and the patient recovered more rapidly, but bladder & ureter injury observed more frequently in patient underwent LH[10,] In our study, no bladder or ureter injury occurred. In one study, vascular complication was reported in 5 patient (1.39%)[11] . In our study, vascular complication in the form of hemorrhage were observed in 4 patient (8%). In study by Shenet al[12] intestinal complication observed in 6 patients. No intestinal complication was encountered in our study. Deviation of the surgical plan leading to conversion of technique was considered a complication[13]. Three patient (6%) needs conversion in this study.

Conclusion:

Total laparoscopic hysterectomy (TLH) is a preferable hysterectomy technique than abdominal hysterectomy for patients who cannot undergo vaginal hysterectomy. It is considered a safe surgical technique though duration of operation is longer. TLH increases patient's satisfaction in post operative days when expert surgical team performs the operation. To reduce the complication rate gynecologist should have appropriate training from specialized training centre. If uncontrollable and excessive haemorrhage or technical difficulties, conversion from laparoscopy to laparotomy should be done for the interest of patient's safety.

References:

1. Cohen SI, Vitonis AF, Einarsson JI. Updated hysterectomy surveillance and factors associated with minimally invasive hysterectomy. JSIS 2014: 18 (3).PMC4208898.

2. Cravello L, De Montgolfier R, D Ercole C, Roger V, Blanc B. Endoscopic surgery. The end of classic surgery? Eu J obstet Gynaecol Reprod Biol. 1997;75: 103-106.

3. Sutton C. Hysterectomy; a historical perspective; BailliersClinObstetGynaecol. 1997;11:1-22.

4. Reich H,DeCaprio J, Mc Glynn F. Laparoscopic hysterectomy. J Gynaecolsurg. 1989;5: 213-6.

5. AAGL Advancing Minimally Invasive Gynecology worldwide. AAGL position statement: Route of hysterectomy to treat benign uterine disease. J Minim Invasive Gynaecol. 2011;18(1): 1-3.

6. Mahendru R Malik S, Rana S, Gupta S. Hysterectomy through mini laparotomy for benighgynaecological conditions: A vaild option. J Turk Ger Gynaecol Assoc. 2009;10:208-12.

7. Nieboer TE, Johnson N, Lethaby A, Tavender E, Curr E, Garry R et al. Surgical approach to hysterectomy for benign gynaecological disease. Cochrane Database of systemic review. 2009; 8: CD003677 (Pub med-19588344)

8. Davis A, Magos AL. Indications and alternative to hysterectomy, Bailliers clin Obstet Gynaecol. 1997; 11:61-75.

9. Salman S, Ayanoglu, YT, Bozkurt M, Kumbasar S, Kavsi B, Sertoglu E et al. Total laparoscopic Hysterectomy. JAREM. 2015; 5: 10-3.

10. Johnson N, Barlow D, Lethaby A, Tavender E, Curr L, Garry R. Methods of hysterectomy systemic review and meta analysis of randomised controlled trials BMJ 2005; 330: 1478.

11. Nezhat F, Nezhat CH, Admon D, Gordon S, Nezhat C. Complications and results of 361 hysterectomies performed at laparoscopy. J Am CollSurg 1995; 180: 307-16.

12. Shen CC, Lu HM, Chang SY. Characteristics and management of large bowel injury in laparoscopic assisted vaginal hysterctomy. J Am assocGynaecolLaparosc 2009;9:35-9.

13. Albright BB, Witte T, Tofte AN, Chou J, Black JD, Desai VB et al. Robotic versus Laparoscopic Hysterectomy for Benign Disease: A systematic review and meta analysis of randomized trials. J Minim Invasive Gynaecol. 2016; 23 (1): 18-27.

Original Article

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Clinical and Etiological Evaluation of Raised Serum Alanine Aminotransferase (ALT) Level in Newly Detected Type 2 Diabetic Patients

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Abstract:

Background: Patients with diabetes mellitus have an increased risk of chronic liver disease. Objective: To find out the association between raised serum ALT level and body mass index (BMI) among patients with type 2 DM. Methods: This was a cross sectional study done among patients with type 2 DM at BIRDEM. Eighty patients were selected according to selection criteria. Purposive sampling technique was adopted. Results: Mean age was 42.44±11.67 (SD) years. Mostly the study subjects were sedentary worker (93.8%) and more than half had family history of DM (57.5%). Less than one third study subjects had history of hypertension (21.2%) and past history of jaundice (15.0%). Majority of the patients had non specific symptoms e.g. weakness, fatigability poor appetite etc. Mean body mass index was 25.65 ± 3.88 and mean waist hip ratio was 0.97 ± 0. 07. Average ALT was 109.41±63.14 u/L. Mean value of triglyceride, total cholesterol, LDL cholesterol (LDL-c) and HDL cholesterol (HDL-c) was found 199.20 ± 92.41, 196.71 ± 44.66, 124.25±37.37, 36.84 ±8.35 respectively. Serum ALT level was <2 times upper limit of normal in 68.2% patients with age less than 35 years, 63.4% patients with age 35 to 50 years and 76.5% patients with age 51 years or more. The association between age and raised serum ALT was significant (P <0.05). Of the the study subjects with fatty liver disease, 59.4% patients had serum ALT level <2 times upper limit of normal. Among the study subjects with normal liver on USG, 54.5% patients had serum ALT level >2 times upper limit of normal. Among the study subjects with normal weight, 58.3% patients had serum ALT level <2 times upper limit of normal. Conclusion: Raised serum ALT level has significant relation with age and Nonalcoholic fatty liver disease (NAFLD) is the most common etiological factor.

Keywords: Raised ALT, diabetes mellitus, NAFLD

Introduction:

Persistently raised serum ALT level in patients with type 2 DM is a predictor of chronic liver disease. It has a significant clinical impact in terms of morbidity and mortality from chronic liver disease. As majority of the diabetic patients remain asymptomatic for raised serum ALT, they are often inadequately investigated. It may miss an opportunity to identify the cause and treat specifically to prevent further progression of chronic liver disease. When detailed investigations were carried out in asymptomatic patients with elevated serum alanine aminotransferase (ALT), non-alcoholic fatty liver disease (NAFLD) was most common diagnosis, ranging from 64 to 90% in different studies. It is much more frequent among people with diabetes (50%) and obesity (76%), and almost universal among diabetic people who are morbidly obese[1,2,3]. Though NAFLD was unnoted in the metabolic field for a long period of time, it has emerged as a hepatic component of metabolic syndrome and as an independent predictor of mortality. A strong association found between chronic hepatitis C and diabetes mellitus in several studies. Another study

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shown that the prevalence of DM was not significantly different between patients with chronic hepatitis B and chronic hepatitis C. So, raised serum alanine aminotransferase (ALT) may be a marker for chronic viral hepatitis-B or C or other etiology of chronic hepatitis. So, this study is designed to find out any possible association between the clinical profile of newly detected diabetics IGT patients with raised ALT with a search to reach other possible etiology and to find out any associated biochemical abnormality that may adversely affect liver function.

Methods and Materials:

This study was a cross-sectional study, conducted during the period of 2014 in the Medicine out-patient department (OPD) of BIRDEM General Hospital. Newly detected type 2 diabetic patients having raised serum ALT level ≥ two times upper limit of normal (ULN)at medicine out-patient department (OPD) of BIRDEM general hospital were the study population. Inclusion criteria were: newly detected type 2 diabetic patients with age >18 years. Exclusion criteria were: known case of chronic liver disease, history of acute hepatitis/documented jaundice within the last six (06) months, patients with congestive cardiac failure, regular alcoholconsumption (>21 units/week in woman, >28units/week in man for more than 5 years), history of regular intake of hepatotoxic drugs. Purposive sampling technique was used in this study. Due to the time constraint, 80 samples were taken.

A semi-structured questionnaire was developed. The questionnaire was developed using the selected variables according to the specific objectives. The questionnaire contained questions related to: 1) socio-demographic characteristics, and 2) illness characteristics and other relevant information. Data were collected by face-to-face interview, document review and observation by clinical examination. Analysis was performed using SPSS (Statistical Package for Social Science) version 12. Data were expressed as mean, standard deviation (SD), range, percentage, and 95% confidence interval (CI) for a continuous variable. Chi-square test (x^2) was used for the comparison of qualitative data. Results are considered statistically significant at $p<0.05$. Statistical analysis for association between elevated serum alanine aminotransferase (ALT) and clinical, biochemical and ultrasonographic findings of hepatobilliary system was performed initially using univariate analysis with SPSS windows program.

Ethical consideration:

After getting the approval of the research proposal from Ethical Review Committee for data collection, all the study subjects was informed verbally about the study design, the purpose of the study, and their right to withdraw from the project at any time, for any reason, whatsoever.

Results:

Majority of the study subjects were 30 to 39 years age group (33.8%) and were male (58.8%). More than one third was from middle class (48.8%). Mostly the study subjects were sedentary worker (93.8%). More than half of the study subjects had family history of DM (57.5%).

Table 1: Socio demographic characteristics of the study subjects (N=80)

Characteristics	Frequency n(%)
Age (Years)	
20-29	7(8.8)
30-39	27(33.8)
40-49	25(31.2)
50-59	13(16.2)
60 and above	8(10.0)
Sex	**Frequency n(%)**
Male	47 (58.8)
Female	33 (41.2)
Socio-economic Condition	**Frequency n(%)**
Rich	10(12.5)
Middle	39(48.8)
Lower	31(38.8)
Physical activity	**Frequency n(%)**
Sedentary to light exercise	75(93.8)
Moderate to heavy exercise	5 (6.7)
Family history of DM	**Frequency n(%)**
Present	46 (57.5)
Absent	34 (42.5)

More than half of the cases the diagnosis of DM was incidental (56.2%). Among the study subjects classical symptom present in 33.8% cases and atypical symptom present in 12.5% cases. Less than one third study subjects had history of hypertension (21.2%) and past history of jaundice (15.0%) and blood transfusion (8.8%). More than one third of the study subjects had weakness (40.0%). On the other hand, 11.2% was fatigue, 2.5% had poor appetite, 3.8% had yellow coloration of eye/urine, and 1.2% had right upper quadrant pain and lump.

Table 2: Clinical presentation of the study subjects (N=80)

Presentation	Frequency (%)
Weakness	32(40.0)
Fatigue	9(11.2)
Poor appetite	2(2.5)
Yellow coloration of eyes/urine	3(3.8)
Right upper quadrant pain	1(1.2)
Right upper quadrant lump	1(1.2)
Past history of jaundice	12(15.0)
Past history of blood transfusion	7(8.8)
Incidental diagnosis of DM	45(56.2)
Classical symptoms of DM	27(33.8)
Atypical symptoms of DM	10(12.5)
History of hypertension	17(21.2)

Average age was 42.44 ± 11.67 (SD) years and body weight were 64.48 ± 11.01 (SD). Mean body mass index of the study subjects was 25.65 ± 3.88 (SD) Kg/m^2. Mean systolic and diastolic BP of the study subjects was observed 122.50 ± 13.14 (SD) and 79.19 ± 7.04(SD) respectively.On average waist and hip circumference of the study subjects was 88.97 ±9.44(SD) cm and91.61 ±6.68 (SD) cm respectively. Mean waist hip ratio of the study subjects was 0.97± 0. 07 (SD).

Table 3: Clinical characteristics of the study subjects (N=80)

Clinical characteristics	Mean ± SD
Age (years)	42.44 ± 11.67
Body weight (Kg)	64.48 ± 11.01
BMI	25.65 ± 3.88
SBP mmHg	122.50 ± 13.14
DBP mmHg	79.19 ± 7.04
Waist circumference (cm)	88.97 ± 9.44
Hip circumference (cm)	91.61 ± 6.68
Waist-hip ratio (WHR)	0.96 ± 0.07

Mean fasting plasma glucose level was 12.06 ± 4.46 (SD); and 2 hours after glucose meal, it was 19.50 ± 6.64 (SD) mmol/L. Mean ALT was 109.41 ± 63.14 (SD) u/L. Mean value of triglyceride, total cholesterol, LDL cholesterol (LDL-c) and HDL cholesterol (HDL-c) was found 199.20 ± 92.41 (SD), 196.71 ± 44.66 (SD), 124.25±37.37(SD), 36.84 ±8.35 (SD) respectively. Mean value of albumin was 43.29 ± 5.69 (SD).

Table 4: Bio-chemical characteristics of the study subjects (N=80)

Bio-chemical parameters	Mean ± SD
FPG (mmol/L)	12.06 ± 4.46
2-HAG (mmol/L)	19.50 ± 6.64
ALT (u/L)	109.41 ± 63.14
Total cholesterol (mg/L)	196.71± 44.66
Triglyceride (mg/L)	199.20 ± 92.41
HDL-c (mg/L)	36.84 ± 8.35
LDL-c (mg/L)	124.25± 37.37
Albumin (gm/L)	43.29 ± 5.69

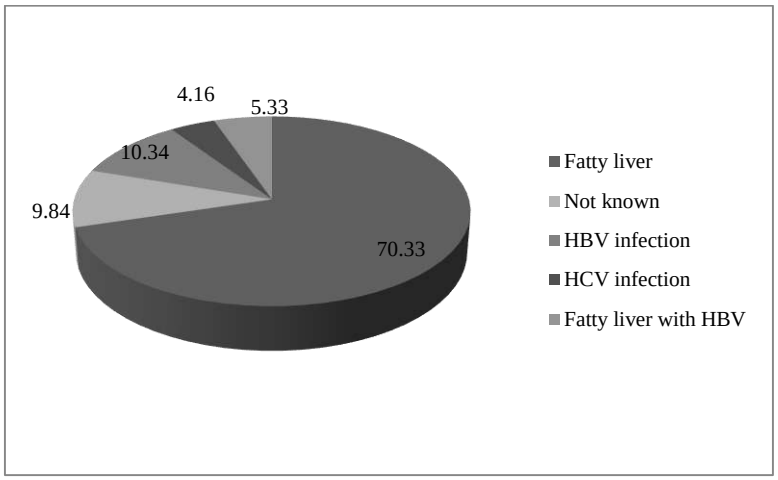

Figure 1: Aetiology of raised ALT (N=80)

Aetiology of raised ALT among the study subjects shown that fatty liver was 70.33%.

Among the study subjects of age less than 35 years, 31.8% patients had serum ALT level less than two times upper limit of normal and 68.2% patients had serum ALT level more than two times upper limit of normal. In the age range between 35 to 50 years, 63.4% patients had serum ALT level less than two times upper limit of normal and 36.6% patients had serum ALT level more than two times upper limit of normal. In the study subjects of age 51 years or more, 76.5% patients had serum ALT level less than two times upper limit of normal and 23.5% patients had serum ALT level more than two times upper limit of normal. The association between age and raised serum ALT was significant (P <0.05).

Table 5: Relation of age with raised serum ALT (N=80)

Grouping of age	Grouping of ALT		P value
	< 2 x ULN	> 2 x ULN	
< 35 years	7 (31.8%)	15 (68.2%)	0.011
35-50 years	26(63.4%)	15 (36.6%)	
≥ 51years	13 (76.5%)	4 (23.5%)	

The proportion of male study subjects (59.6%) was more who had serum ALT level less than two times upper limit of normal and 40.4% male had serum ALT level more than two times upper limit of normal. Among the female 54.5% had serum ALT level less than two times upper limit of normal and 45.5% female had serum ALT level more than two times upper limit of normal. But these differences were statistically insignificant(p=0.654).

Table 6: Relation of sex and raised serum ALT (N=80)

Grouping of sex	Grouping of ALT		P value
	< 2 x ULN	> 2 x ULN	
Sex			
Male	28 (59.6%)	19 (40.4%)	0.654
Female	18 (54.5%)	15 (45.5%)	

On the basis of ultrasonographic (USG) findings of hepatobiliary system- the study subjects with fatty liver disease, 59.4% patients had serum ALT level less than two times upper limit of normal and 40.6% patients had serum ALT level more than two times upper limit of normal. On the other hand, the study subjects of normal liver on USG, 45.5% patients had serum ALT level less than two times upper limit of normal and 54.5% patients had serum ALT level more than two times upper limit of normal. The association between raised serum ALT level and fatty liver disease was not statistically significant (P =0.384).

Table 7: Association of raised serum ALT with fatty liver disease (N-80)

Fatty liver on USG	Raised ALT		P value
	< 2 x ULN	> 2 x ULN	
Fatty liver	41 (59.4%)	28 (40.6%)	0.384
Normal liver	5 (45.5%)	6 (54.5%)	

Among the study subjects with normal weight, 58.3% patients had serum ALT level less than two times upper limit of normal and 41.7% patients had serum ALT level more than two times upper limit of normal. Among overweight patients, 56.2% had serum ALT level less than two times upper limit of normal and 43.8% patients had serum ALT level more than two times upper limit of normal. Patients with obesity, 60.0% had serum ALT level less than two times upper limit of normal and 40.0% patients had serum ALT level more than two times upper limit of normal. The association between raised serum ALT level and BMI was not statistically significant (P= 0.055).

Table-8: Association of raised serum ALT with BMI (N-80)

Body mass index (BMI)	Raised ALT		P value
	< 2 x ULN	> 2 x ULN	
18.5 – 24.9 (Normal weight)	21 (58.3%)	15 (41.7%)	
25.0 – 29.9 (Overweight)	18 (56.2%)	14 (43.8%)	0.055
≥ 30 (Obese)	6 (60.0%)	4 (40.0%)	

Discussion:

Diabetes mellitus is a metabolic disorder resulting from absolute or relative insulin deficiency producing an altered scenario of carbohydrate (primarily), protein and fat metabolism. Abnormal liver function test is a common as well as easily overlooked investigation findings among diabetic population which are often inadequately investigated and may miss an opportunity of identifying and treating the patients with significant liver disease in early stage. The prevalence of abnormal liver function tests among asymptomatic patients varies according to the population studied. Kenneth (2009) stated that approximately 70% of patients with type 2 diabetes mellitus have nonalcoholic fatty liver disease (NAFLD) in his review work[4].

Clark et al. (2003) showed that the prevalence of aminotransferase elevation in the United States was 7.9%. It was unexplained in the majority cases (69.0%). Currently, liver biopsy is recommended for all individuals with persistent, unexplained elevated aminotransferase levels for diagnosis, as well as for grading and staging of liver disease. In the study, aminotransferase elevation was more common in men compared to women.

In both men and women, unexplained aminotransferase elevation was significantly associated with higher body mass index, waist circumference, triglycerides, and lower HDL; and with type 2 diabetes and hypertension in women[5].

West et al. (2006) explored that the prevalence of elevated ALT is 9.5% in type 1 and 12.1% in type 2 diabetic patients[6]. BMI more than 25 kg m^{-2} and poor diabetic control (fasting blood glucose >11.88 mmol L^{-1}) were the most significant clinical variables associated with elevated ALT[7]. Meybodi et al. (2008) explored that the prevalence of elevated ALT was 10.4% of type 2 diabetic patients. Mean age of patients was 58.8 ± 11.5 years. 90% of patients had ALT less than 40 U L^{-1} and 9.2% had ALT between 40-80 U L^{-1} and only 0.09% had ALT more than twice the upper limit of normal range. Although the prevalence of elevated ALT increased with increasing age in subjects, but it was not statistically significant. The risk of elevated ALT increased with increasing triglyceride, but it was not significant at 5% level. BMI is divided in three subgroups: less than 25, 25-30 and over 30 kg m^{-2}, Mean ALT levels were not different in the subgroup of BMI. There was negative correlation between ALT and age[8].

Ahmed et al. (2008) selected 101 patients with type 2 diabetes mellitus who had persistently raised ALT for more than eight weeks. Of them, 68% were female. Mean age 49.09 years with a median at 49 years. BMI of patients ranged between 19.8 kg/m2 to 40.9 kg/m2 with a mean value of 29.04 and median at 29.0 kg/m2. In 33.7% patients the BMI was between 25 and 29.9 kg/m2, 46.5% were obese, having a BMI greater than 30 kg/m2 and 4% were morbidly obese, i.e., BMI greater than 40 kg/m2. Overall about 80% of the patients were over-weight or obese. 84% patients had serum ALT value below 100u/l and 14% had serum ALT between 100 to 220 u/l. Serum anti-HCV antibodies were present in about 22% of the patients and HBsAg in only two patients (2%). Ultrasonography of upper abdomen suggested fatty liver in 60.4% of patients, 29.7% had unremarkable ultrasonographic appearence of the liver and 9.9% of the patients showed some evidence suggestive of chronic liver disease. Majority of the patients showed a poor control of diabetes as suggested by their fasting plasma glucose values. Mean plasma glucose was 8.76 mmol/l and median was at 7.90 mmol/l. Serum triglycerides value varied between 0.7 mmol/l to 2.8 mmol/l with a mean value of 1.62 and median at 1.6 mmol/l. 42% of patients had a serum triglyceride value greater than 1.7 mmol/l, which is a cut off value for inclusion criteria of metabolic syndrome. On discussion, the authors noticed that about 80% of the patients with type 2 diabetes mellitus with mild to moderate elevation of ALT were over-weight or obese, 42.6% had a fasting triglyceride value greater than 1.7 mmol/l, both are component of metabolic syndrome. Sixty percent (60%) of patients showed fatty liver a common laboratory abnormality in patients with nonalcoholic fatty liver disease (NAFLD)[9]. In the United States, NAFLD is replacing alcoholic hepatitis and viral hepatitis as the most common etiology of chronically elevated LFTs, in

both diabetic and non-diabetic individuals, and 60-95% of them are obese[10]. Hepatitis C virus (HCV) is a known independent predictor of type 2 diabetes, the commonest endocrine disease, even in patients without cirrhosis[11]. About 22% of the patients were positive for anti-HCV antibodies, and 10% showed some evidence of chronic liver disease on abdominal ultrasonography. In conclusion the authors said that mild to moderate elevation of ALT is commonly encountered in patients of type 2 diabetes mellitus. Most of these individuals are over-weight or obese and/or having fatty liver on ultrasonography. HCV infection seems to be the next important cause of raised ALT.

Bayramer et al. (2001) studied seventy-four type 1 and 2diabetic patients to see the prevalence of hepatitis B and hepatitis C. The study showed that the frequency of HBs Ag and anti HCV was found to be 4 % and 4% respectively. It was seen that anti HCV seropositivity in diabetic patients is higher than normal population. The study also showed that there was no statistical relationship between the hepatitis B and C markers positivity and age, duration of diabetes mellitus[12]. Li-Ng (2007) explored that the prevalence of diabetes mellitus in patients with hepatitis B virus was significantly higher than in those without hepatitis B virus among Asians but not in Pacific Islanders. Among the 390 subjects who were tested for both hepatitis B virus and hepatitis C virus, the prevalence of diabetes mellitus was 29.4% in uninfected subjects, 44.4% in patients with hepatitis B virus mono-infection, 47.2% in patients with hepatitis C virus mono-infection and 85.0% in patients with hepatitis B virus and hepatitis C virus co-infection[13].

In our study Majority of the study subjects were 30 to 39 years age group (33.8%) and were male (58.8%). More than one third was from middle class (48.8%). Mostly the study subjects were sedentary worker (93.8%). More than half of the study subjects had family history of DM (57.5%) and the diagnosis of DM was incidental (56.2%). Among the study subjects classical symptom present in 33.8% cases and atypical symptom present in 12.5% cases. Less than one third study subjects had history of hypertension (21.2%) and past history of jaundice (15.0%) and blood transfusion (8.8%). More than one third of the study subjects had weakness (40.0%). On the other hand, 11.2% was fatigue, 2.5% had poor appetite, 3.8% had yellow coloration of eye/urine, and 1.2% had right upper quadrant pain and lump.

Average age were 42.44 ± 11.67 (SD) years and body weight were 64.48 ± 11.01 (SD). Mean body mass index of the study subjects was 25.65 ± 3.88 (SD) Kg/m^2. Mean systolic and diastolic BP of the study subjects was observed 122.50 ± 13.14(SD) and 79.19 ± 7.04(SD) respectively. On average waist and hip circumference of the study subjects was 88.97 ± 9.44(SD) cm and 91.61 ± 6.68 (SD) cm respectively. Mean waist hip ratio of the study subjects was 0.97 ± 0. 07(SD).Mean fasting plasma glucose level was 12.06 ± 4.46 (SD); and 2 hours after glucose meal, it was 19.50 ± 6.64 (SD) mmol/L. Mean ALT was 109.41 ± 63.14 (SD) u/L. Mean value of triglyceride, total cholesterol, LDL cholesterol (LDL-c) and HDL cholesterol (HDL-c) was found 199.20 ± 92.41 (SD), 196.71 ± 44.66 (SD), 124.25±37.37(SD), 36.84 ±8.35 (SD) respectively. Mean value of albumin was 43.29 ± 5.69 (SD).

Among the study subjects of age less than 35 years, 68.2% patients had serum ALT level more than two times upper limit of normal. In the age range between 35 to 50 years, 63.4% patients had serum ALT level less than two times upper limit of normal and 36.6% patients had serum ALT level more than two times upper limit of normal. In the study subjects of age 51 years or more, 76.5% patients had serum ALT level less than two times upper limit of normal and 23.5% patients had serum ALT level more than two times upper limit of normal. The association between age and raised serum ALT was significant ($P < 0.05$). The proportion of male study subjects (59.6%) was more who had serum ALT level less than two times upper limit of normal. Among the female 54.5% had serum ALT level less than two times upper limit of normal. But these differences were statistically insignificant ($p=0.654$).

On the basis of ultrasonographic (USG) findings of hepatobiliary system- the study subjects with fatty liver disease, 59.4% patients had serum ALT level less than two times upper limit of normal and 40.6% patients had serum ALT level more than two times upper limit of normal. On the other hand, the study subjects of normal liver on USG, 45.5% patients had serum ALT level less than two times upper limit of normal and 54.5% patients had serum ALT level more than two times upper limit of normal. The association between raised serum ALT level and fatty liver disease was not statistically significant (P =0.384).Among the study subjects with normal weight, 58.3% patients had serum ALT level less than two times upper limit of normal and 41.7% patients had serum ALT level more than two times upper limit of normal. Among overweight patients, 56.2% had serum ALT level less than two times upper limit of normal and 43.8% patients had serum ALT level more than two times upper limit of normal. Patients with obesity, 60.0% had serum ALT level less than two times upper limit of normal and 40.0% patients had serum ALT level more than two times upper limit of normal. The association between raised serum ALT level and BMI was not statistically significant (P= 0.055).

Majority of the study subjects with metabolic syndrome (62.1%) had raised ALT less twice the upper limit. On the other hand less than half of the patients without metabolic syndrome (45.1%) had raised ALT level more than twice the normal level. But statistically these differences were not significant (p=0.533).

Limitations of the study:

The study was conducted in a selected hospital. So the study population might not represent the whole community. Probability sampling technique could not be employed to recruit the study unit; they were selected purposively due to time constraints. As a result, there might be some selection bias. A larger sample size would have given a better result.

Conclusion:

Mild to moderate elevation of serum ALT level is a common scenario in type II DM. Most of the patients remain asymptomatic or had non-specific symptoms. Inadequate physical exercise may accompany the condition. This group of patients is mostly overweight to obese and has central (abdominal) obesity and raised waist hip ratio. Raised serum ALT level has significant relation with age. Nonalcoholic fatty liver disease (NAFLD) is the most common etiological factor. NAFLD has significant relation with waist hip ratio and obesity.

References:

1. Bellentani S, Saccoccio G, Masutti F, Croce LS, Brandi G, Sasso F. Prevalence of and risk factors for hepatic steatosis in northern Italy. Ann Intern Med 2000;132: 112-117.

2. Gupte P, Amarapurkar D, Agal S, Baijal R, Kulshrestha P, Pramanik S. Nonalcoholic steatohepatitis in type II diabetes mellitus. J GastroenterolHepatol 2004; 19: 854-8.

3. Del Gaudio A, Boschi L, Del Gaudio GA, Mastrangelo L, Munari D. Liver damage in obese patients. ObesSurg 2002;12: 802-804.

4. Kenneth C. Nonalcoholic fatty liver disease in type 2 diabetismellitus. Currentopinion in Endocrinology, Diabetes and Obesity 2009; 16: 141-149.

5. Clark JM, Brancati FL, Diehl AM. The prevalence and etiology of elevated aminotransferase levels in the United States. Am J Gastroenterol 2003; 98: 960-967.

6. West J, Brousil J, Gazis A, Jackson L, Mansell P, Bennett A, Aithal GP. Elevated serum alanine transaminase in patients with type 1 or type 2 diabetes mellitus QJM 2006; 99(12): 871-876.

7. Salmela PI, Sotaniemi EA, Niemi M, Maentausta O. Liver function tests in diabetic patients. Diabetes Care 1984; 7: 248-254.

8. Meybodi MA, Afkhami-Ardekani M, Rashidi M. Prevalence of abnormal serum alanine aminotransferase levels in type 2 diabetic patients in Iran. Pak. J. Biol. Sci.2008; 11:2274-2277.

9. Ahmed S, Ali N, Abdullah Z, Ilyas M, Naeem U. Study of raised alanine aminotransferase in patients of type 2 diabetes mellitus. Pakistan Armed Forces Medical Journal 2008; 58(3): 121-124.

10. Neuschwander-Tetri BA, Caldwell S. Nonalcoholic steatohepatitis: summary of AASLD single topic conference. Hepatology 2003; 37: 1202-19.

11. Knobler H, Schihmanter R, Zifroni A, Fenakel G, Schattner A. Increased risk of type II DM in non-cirrhotic patients with chronic hepatitis C virus infection. Mayo Clin Proc.2000; 75(4): 355-359.

12. Bayramer HF, Erdem I, Gündoğdu TT, Çınar Y, Barut Y, Demirtunç R. The prevalence of hepatitis B and hepatitis C virus in diabetic patients. Cilt 2001; 14:160-164.

13. Li-Ng M, Tropp S, DanoffA,Bini EJ. Association between chronic hepatitis B virus infection and diabetes among Asian Americans and Pacific Islanders. Digestive and Liver Disease 2007; 39(6): 549-556.

DCIMCJ

Original Article

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The Role of Prophylactic Intravenous Ondansetron for Prevention of Post-Spinal Shivering in Patients Undergoing Cesarean Section

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Abstract:

Background: Elective cesarean section is most commonly carried out under spinal anesthesia, which is commonly associated with shivering, both intra and postoperatively. Ondansetron has been shown to be effective for post-spinal shivering. In the present study, we tried to find out the efficacy of ondansetron to prevent post-spinal shivering (PSS) in parturients undergoing cesarean section under spinalanesthesia.Aim of the study:The primary aim of our study is to evaluate the efficacy of ondansetron in reducing the post-spinal shivering in pregnant patients undergoing elective lower segment cesarean section under spinal anesthesia. The secondary aim is to evaluate the effectiveness of ondansetron in reducing intraoperative nausea and vomiting.Materials and methods:This double-blinded, prospective, randomized trial included 80 parturients scheduled for cesarean section under spinal anesthesia. They were divided into two equal groups,40 patients in each group. Group-O (Ondansetron group) received 8 mgondansetron in 4 ml solution and group-S (Saline/control group)received 4 ml normal saline as placebo immediately before induction of spinal anesthesia. Post-spinal shivering at any time were recorded on a (0–4) scale and total pethidine dose required to treat shivering at score of 3 and 4 was also recorded. Maternal MAP assessed before spinal anesthesia, just after spinal and lateral tilt positioning, 2 min after positioning, 5 min after positioning, Just after delivery of the baby, at the end of surgery , together with total ephedrine required to treat any hypotension were recorded. Incidence of nausea and vomiting at any time during surgery was also recorded.Results:Grade 4 shivering was not observed in any patient. Grade 3 shivering was not found in ondansetron group but 6 patients (15%) had in placebo group. In ondansetron group 5 patients (12.5%) and in placebo group 18 patients (45%) experienced shivering ($p<0.05$). Grade 3 shivering during the perioperative period was treated with intravenous injection of 25 mg pethidine. One patient (2.5%) in ondansetron group and 12 patients (30%) in control group had nausea and vomiting ($P < 0.05$) and was treated with intravenous 10 mg metoclopramide. 1st and 5th min Apgar scores of neonates were not statistically different in the groups.Conclusion: Prophylactic intravenousondansetron 8 mg was effective in reducing post-spinal shivering in parturients undergoing elective cesarean section and decreasing the requirement ofpethidine and also with lower incidence of post-spinal hypotension and nausea-vomiting when compared to control group.

Keywords: Post-spinal shivering (PSS), ondansetron, cesarean section, spinal anesthesia

Introduction:

Elective cesarean section is most commonly carried outunderspinal anesthesia, which is commonly associated with shivering, both intra and postoperatively.

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The etiology of shivering is not clearly understood, it may involve a combination of mechanisms, including modulation of thermoregulatory thresholds, changes in body heat distribution, reduction in body temperature, and the cooling effect of the fluid infusion during surgery[1]. Shivering not only causes psychological stress to the patient but also physiologically leads to an increase in oxygen consumption by 200%–600% and increased carbon dioxide production, increased chances of myocardial ischemia, infection, bleeding, and increase in minute ventilation. It also produces hypoxemia, lactic acidosis, increased intraocular pressure,

intracranial pressure and interferes with patient monitoring such as electrocardiogram (ECG), noninvasive blood pressure (NIBP), and peripheral oxygen saturation (SpO_2). It may also cause maternal irritability and interfere with her ability to hold her baby[2].

Several drugs are effective in treating or preventing post-spinal shivering (PSS)[1] including pethidine, tramadol ketamine, clonidine etc. These drugs have adverse effects on the mother and fetus, including sedation, nausea, vomiting, bradycardia, and hypotension. These unwanted effects limit the use of such drugs before delivery, because of concerns about on the mother and the fetus[3].

The neurotransmitter pathways involved in the mechanism of shivering are complex and still poorly understood. Serotonin: 5-hydroxytryptamine ($5\text{-}HT_3$), a biologic amine found in the brain and spinal cord, plays a part in neurotransmission of shivering. Many studies explained that the serotonergic system plays an important role in the pathogenesis of perioperative shivering[4,5]. Serotonin antagonism seems to lower the human thermal set range thereby reducing metabolic cold defenses and discomfort associated with postoperative hypothermia. Ondansetron, $5\text{-}HT_3$ antagonist, is a widely used antiemetic drug. It can be used safely during pregnancy and surgery. Some studies showed its anti-shivering effect following both general and regional anesthesia[6]. It has a potential advantage in obstetric anesthesia because of its very low incidence of sedation, hypotension, bradycardia or risk to the neonate. The mechanism of action of ondansetron as anti-shivering is not clear, and it is proposed to act centrally at the level of the preoptic anterior hypothalamic region by inhibition of serotonin reuptake[7].

On the other hand, nausea and vomiting during spinal anesthesia for cesarean section are very common and unpleasant complications. During spinal anesthesia, ondansetron has been shown to be effective in the prevention of nausea and vomiting[8].

Materials and methods:

From April2017 to December 2017, at different private hospital in Dhaka city 80 female patients with written informed consent posted for elective cesarean section under spinal anesthesia were enrolled in this study.

Demographic data of all participants were collected preoperatively. Exclusion criteria included complicated pregnancy, preoperative use of ondansetronormeperidine, known allergy to the tested drug, preoperative shivering, preoperative fever, hypo- or hyperthyroidism, intraoperativeblood transfusion; or administration of opioids, clonidine, or vasodilator drugs. Exclusion criteria also included any contraindication to spinal anesthesia. Patients were randomly allocated into two equal groups. Group-O (Ondansetron group) received 8mg ondansetron in 4 ml solution and group-S (Saline/control group)received 4 ml normal saline as placebo immediately before induction of spinal anesthesia. These doses were prepared in a 5-mlsyringe by an independent anesthesiologist not involved in the rest of the study.

On arrival to the operating room, standardized monitoring was done throughout the perioperative period. Heart rate (HR), ECG, non-invasive blood pressure (NIBP), respiratory rate, SpO_2 and axillary temperature were recorded. Operation theatre temperature was maintained at 24°C by air-conditioning.

Peripheral intravenous access was secured using an 18-gauge cannula on the dorsum of the non-dominant hand. All patients were preloaded with warm Ringer's lactate solution of 7ml/kg before spinal anesthesia. Patients received respective drugs intravenously just before initiation of spinal anesthesia. All patients were blocked in the sitting position, in which a 25-gauge Quincke needle was inserted by midline approach into the L3–L4 or L4–L5 interspaces and after ensuring the correct position of the needle, 12.5 mg of hyperbaric 0.5% bupivacaine was injected.

Patients were immediately placed in the supine position after the block. Supplemental oxygen 3 L/min was applied through a nasal cannula till the end of the surgery. All patients were covered with one layer of surgical drape.

The level of sensory block, body temperature, shivering score, and presence or absence of nausea and vomiting during perioperative period, 1st and 5th min Apgar scores were recorded. Body temperatures were monitored just before intrathecal injection and then with every 15 min intervals up to 4 hours. Shivering was graded using a 5-item scale (Table I). Grades III and IV shivering for at least 3 min were considered positive, and prophylaxis was regarded as ineffective. An intravenous bolus of 25 mg pethidine was used as a rescue drug.

The incidence of hypotension, bradycardia, nausea and vomiting were recorded. Hypotension was managed by increasing intravenous fluid and increments of intravenous ephedrine 6 mg. Bradycardia was defined as a decrease in HR by 20% from the baseline value or an absolute HR <50 beats/min; which was managed by 0.4 mg intravenous bolus of atropine. Patients with refractory nausea or vomiting were treated with 10 mg metoclopramide intravenous as a rescue medication.

Statistical analysis:

According to the type of data it was represented as mean± standard deviation or percentages. Comparisons of the two studied groups were performed using either Student t-test or Chi-Square test as appropriate. In all tests results were considered statistically significant if p value was less than 0.05.

Table-I: Grading status of shivering:

- **Grade- 0:** No shivering observed.
- **Grade- 1:** One or more piloerection: peripheral cyanosis without other cause, but without visible muscular activity.
- **Grade- 2:** Visible muscle activity confined to one muscle group.
- **Grade- 3:** Visible muscle activity in more than one muscle group.
- **Grade- 4:** Gross muscular activity involving the entire body.

Results:

The demographic characteristics such as age, weight, ASA grade, and gestational age were comparable in both groups (P > 0.05) (Table II). There was no difference in baseline vital signs (HR, MAP and SpO_2). In addition, the preoperative body temperature was not statistically different between the study groups (Table II).

Duration of surgery was 42.7 ± 8.7 min in Group O and 43.2 ± 9.3 min in Group S and was comparable in both groups.(p>0.05).

Table-II: Demographic data and basal vital signs

Demographic data and basal vital signs	Group O (Ondansetron group)n=40	Group S (saline/control group)n=40
Age in years	25.4±3.2	26.2±3.8
Weight in kg	66.2±7.3	65.8±6.7
ASA I/II	36/4	37/3
Gestational age	38.3±1.4	38.5±1.1
Heart rate bpm	89.8±9.3	91.2±8.9
MAP mm Hg	93.7±12.4	94.8±11.8
SpO_2	99.1±0.8	99.2±0.6
Temperature degree C	36.6±0.2	36.8±0.3

Grade 4 shivering was not observed in any patient. Grade 3 shivering was not found in ondansetron group but 6 patients (15%) had in placebo group. In ondansetron group 5 patients (12.5%) and in placebo group 18 patients (45%) experienced shivering (p<0.05). Grade 3 shivering during the perioperative period was treated with intravenous injection of 25 mg pethidine (Table-III).

Table-III: Incidence and severity of shivering and incidence of nausea and vomiting

Variable	Parameter	Group O (ondansetron) %n=40	Group S (saline/control) %n=40	p value
Shivering	Yes	5 (12.5%)	18 (45%)	p<0.05
	No	35 (87.5%)	22 (55%)	p<0.05
Severity	Grade 0	35 (87.5%)	22 (55%)	p<0.05
	Grade 1	2 (5%)	8 (20%)	p<0.05
	Grade 2	3 (7.5%)	4 (10%)	p<0.05
	Grade 3	0	6 (15%)	p<0.05
	Grade 4	0	0	
Nausea and vomiting		3 (7.5%)	16 (40%)	p<0.05

None of the patients in both groups received atropine. Sixteen patients (40%) in the Group S and twelve patients (30%) in the Group O received the intravenous injection ephedrine 6 mcg for hypotension. There were no adverse effects of ondansetron on fetuses after delivery compared to the saline group regarding the Apgar scores.

Discussion:

The results of this prospective, randomized, double-blinded study demonstrate that statistically significant higher incidence of shivering was seen in Group S compared to Group O ($P < 0.05$). The incidence of maximum shivering score was also high in Group S compared to Group O. In addition, the incidence of nausea and vomiting was significantly high in Group S compared to Group O ($p<0.05$). 1st and 5th min Apgar scores of neonates in both groups were also not statistically significant.

In a double-blinded, placebo-controlled study by Powell and Buggy, two doses of ondansetron (4 mg vs. 8 mg) were compared with placebo for prevention of shivering after general anesthesia, in which 82 adult patients were randomized into three groups[9].Postanesthetic shivering was observed in 57% patients in group C compared with 33% inondansetron 4mg group and 15% patients in ondansetron 8mg group. This study is nearly comparable to our study where we found 45% had shivering in control group and 12.5% in ondansetron group.

Also, the results of the present study as regards reduction in the incidence of shivering was nearly similar with those of the work done by Kelsaka et al[10], who compared ondansetron and meperidine to saline as a preventive measure of shivering under spinal anesthesia and showed that both ondansetron and meperidinereduced shivering to 8% compared to the control group 38%. The difference in the degree of reduction in the incidence of shivering between this study 8% and the present study 12.5% may be rationalized by the facts that, Kelsaka et al[10], studied mostly males patients underwent orthopaedic surgeries and also, they pre-medicated their patients with diazepam 10 mg 45 min before anesthesia.

Again, the results of the present study were matched with those of the study done by Marashi et al[11], who studied two different doses of ondansetron 6 mg and12 mg compared to normal saline to attenuate spinal induced hypotension and shivering and showed that 17% of the control group patients experienced hypotension (MAP <80 mmHg) which was statistically higher than the ondansetron groups (p value = 0.04). Also, the incidence of shivering was statistically higher in the control group 45% compared to the ondansetron two groups (p value = 0.04), but still these results showed more reduction in the incidence of shivering in ondansetron 6 mg group 4% and 12 mg group 2% compared to the present study which showed 12.5% incidence of shivering. These differences may be attributed to the different shivering scoring system used byMarashiet al[11], which consisted shivering of 4 grades only.Also, the gender of the patients of the present study onlyfemale and the physiological changes of pregnancy with volume overload may affect the pharmacokinetics and pharmacodynamics of the studied drug.

The results of the present study as regards the lower incidence of hypotension in ondansetron group compared to the control group were supported by the results of the recently published work of Melissa Dawn Hudson et al[12], who retrospectively analyzed the charts of 46 parturients underwent cesarean sectionunder spinal anesthesia and found that, prophylactic ondansetronwas concomitant with more hemodynamic stability and reduced the incidence of vasopressor administration to 35.7% compared to 46.9% in those patients did not receive ondansetron. In our study it was 30% and 40% respectively.

Conclusion:

On the basis of our findings of the present study, we can conclude that ondansetron 8 mg intravenously is an effective prophylactic means of prevention of postspinal anesthesia induced shivering during lower segment cesarean section, with no effect on Apgar score. It is also very effective against nausea and vomiting. Intravenous ondansetron also reduces hemodynamic changes following spinal anesthesia.

References:

1. Crowley LJ, Buggy DJ. Shivering and neuraxialanesthesia. RegAnesth Pain Med. 2008;33:241–52.

2. Ostheimer G, Datta S. Observations in the postpartum recovery room after various local anesthetic techniques. RegAnesth 1981;6:13–7.

3. Mattingly JE, D Alessio J, Ramanathan J. Effects of obstetric analgesics and anesthetics on the neonate: a review. Paediatr Drugs 2003;5:615–27.

4. Tie HT, Su GZ, He K, Liang SR, Yuan HW, Mou JH. Efficacy and safety of ondansetron in preventing postanesthesia shivering: A meta-analysis of randomized controlled trials. BMC Anesthesiol. 2014;14:12.

5. Mohammadi SS, Jabbarzadeh S, Movafegh A. Efficacy of granisetron on prevention of shivering, nausea and vomiting during cesarean delivery under spinal anesthesia. J Obstet Anaesth Crit Care. 2015;5:22–6.

6. Shakya S, Chaturvedi A, Sah BP. Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. J Anaesthesiol Clin Pharmacol. 2010;26:465–9.

7. Asl ME, Isazadefar K, Mohammadian A, Khoshbaten M. Ondansetron and meperidine prevent postoperative shivering after general anesthesia. Middle East J Anaesthesiol. 2011;21:67–70.

8. Choi DK, Chin JH, Lee EH, Lim OB, Chung CH, Ro YJ, et al. Prophylactic control of post-operative nausea and vomiting using ondansetron and ramosetron after cardiac surgery. ActaAnaesthesiol Scand. 2010;54:962–9.

9. Powell RM, Buggy DJ. Ondansetron given before induction of anesthesia reducesshivering after general anesthesia. Anesth Analg. 2000;90:1423–7.

10. Kelsaka E, Baris S, Karakaya D, Sarihasan B. Comparison of ondansetron and meperidine for prevention of shivering in patients undergoing spinal anesthesia. RegAnesth Pain Med .2006;31:40–5.

11. Marashi SM, Soltani-Omid S, Soltani Mohammadi S, Aghajani Y, Movafegh A. Comparing two different doses of intravenous ondansetron with placebo on attenuation of spinal induced hypotension and shivering. Anesthesiol Pain Med. 2014; 4:e12055.

12. Hudson Melissa Dawn, Crogan Neva L, Bilsky Edward J. Efficacy of ondansetronas a prophylactic anti-hypotensive pharmacologic intervention among obese parturients undergoing spinal anesthesia for cesarean delivery. Anesthesia eJournal 2016;4(1):50–6.

Original Article

DCIMCJ

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Frequency and Predictors of Non-Urinary Infections among the Adult Patients with Sterile Pyuria

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Abstract:

Background: Urine analysis is a test commonly ordered, especially when the patient has a febrile illness. In most cases it provides useful information, but it can sometimes be misleading. A significant proportion of patients with acute febrile illness have transient pyuria without bacteuria. Identification and management of such cases could be improved by better predictive models. Objective: To determine predictors of non urinary infections in adult patients with sterile pyuria and to develop a preliminary predictive model. Methods: This cross sectional study was done in the department of Nephrology, BSMMU. All adult patients with sterile pyuria were included in the study. A total number of 233 cases who had urinary WBCs >5 per high power field (HPF) with a negative culture were selected as sample by convenient sampling technique. We performed detailed clinical and laboratory investigations to identify potential causes of the sterile pyuria. Patients were then divided into two groups, those with causative factors within the urinary tract and those with causative factors outside of the urinary tract. Results: Most 196(84.1%) patients were found to have disorders related to urinary tract (Group A) and 37(15.9%) patients had infections outside of the urinary tract (Group B). Significant proteinuria and urinary casts were more common in Group A, while urinary WBCs>30/hpf and microscopic hematuria were more common in Group(B). All of these differences were statistically significant (p<0.05). In the logistic regression model patients with sterile pyuria with fever (OR 32.9) and/or pyuria with urinary WBC>30/HPF (OR 2.14) were more likely to involvement outside of the urinary tract. Those with urinary tract symptoms (OR 0.28) and/or proteinuria (OR 0.20) were more likely to have renal and urinary tract involvement. Conclusions: In patients attended to the nephrology department, sterile pyuria was more likely to have its origin in the urinary tract if there were urinary tract symptoms and/or proteinuria and less likely if there was fever or urinary WBCs >30/hpf.

Keywords: Acute febrile illness, sterile pyuria, non urinary infections

Introduction:

The finding of white blood cells in a urinalysis in the absence of bacteria (a sterilepyuria or a pyuria without bacteriuria) can be a diagnostic challenge.

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The finding of leukocytes in the urine suggests an infectious or inflammatory process involving the genitourinary tract, either directly or indirectly[1]. Although the differential diagnosis for sterile pyuria includes these processes, a number of other diseases can result in this finding.

Urinalysis is a test commonly ordered at admission to a hospital, especially when the patient has a febrile illness. In most cases it provides useful information, but it can sometimes be misleading. It has observed that patients admitted to the hospital with acute infectious illnesses unrelated to the urinary tract frequently have pyuria, which can confuse the admitting physicians, who sometimes alter their antibiotic choice based on the abnormal urinalysis even when the evidence for urinary tract infection (UTI) is weak.

Others have documented that sterile pyuria can occur in both adults and children with pneumonia and other acute febrile illness, suggesting that some feature of these illnesses or fever itself might cause leakage of white blood cells (WBCs) into the urine[2,3,4,5,6].

However, the frequency, predictors and clinical implications of pyuria in patients admitted to the hospital with infections outside of the urinary tract have not been studied. Believing that more information about this phenomenon might help physicians make better initial antibiotic choices, we undertook this study to estimate the frequency of pyuria in patients with acute infections outside of the urinary tract and to gather information that could help clinicians make better initial evaluation and treatment decisions in such cases.

Methods:

This cross sectional study was done in the department of Nephrology, BSMMU, during the period of September 2016 to August 2017. All adult patients with sterile pyuria were included in the study. A total number of 233 cases who had urinary WBCs >5 per high power field (HPF) with a negative culture were selected as sample by convenient sampling technique. We performed detailed clinical and laboratory investigations to identify potential causes of the sterile pyuria. Patients were then divided into two groups, those with causative factors within the urinary tract and those with causative factors outside of the urinary tract. Logistic regression was used to create a model to predict causative group.

Results:

Table I: Diagnosis of the study population (n=233)

Diagnosis	Number of patients	Percentage
Disorders related to urinary tract (Group A)	196	84.1
Infections outside the urinary tract (Group B)	37	15.9

Table III shows diagnosis of the study patients, it was observed that 196(84.1%) patients was found disorders related to urinary tract (Group A) and 37(15.9%) was infections outside the urinary tract (Group B).

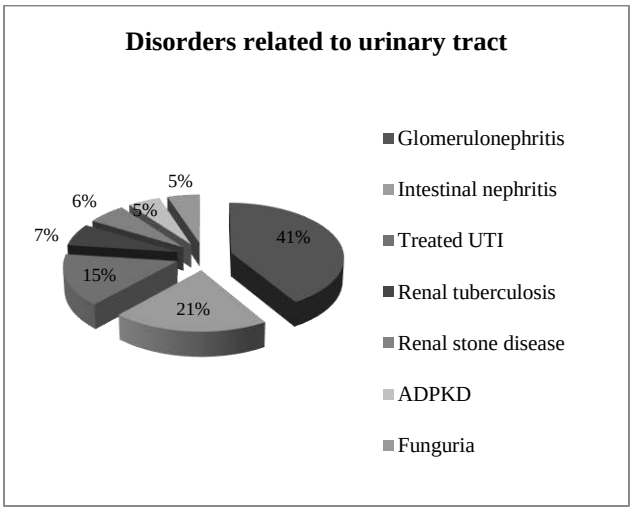

Figure- 2: Pie chart shows disorders related to urinary tract of the study patients

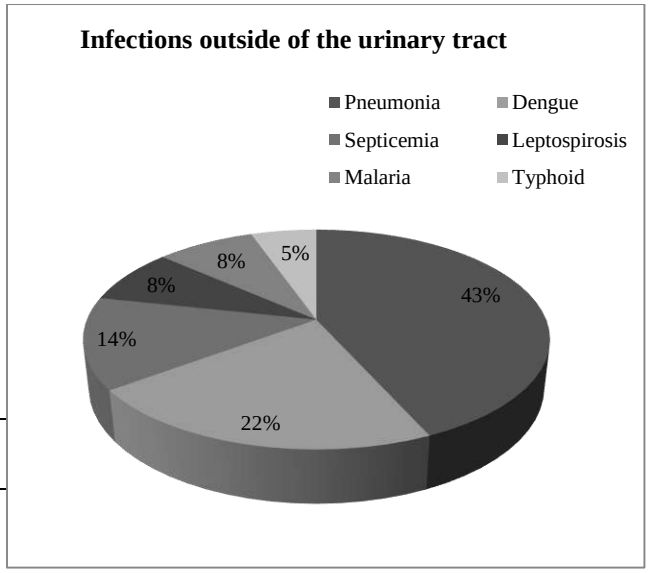

Figure 3: Pie chart shows infections outside of the urinary tract of the study patients.

Table II: Association between diagnosis with urinary characteristics (n=233)

Urinary characteristics	Diagnosis		P value
	Group A (n=196)	Group B (n=37)	
	n(%)	n(%)	
Protein			
Nil	75(38.3)	22(59.5)	
(+)	32(16.3)	7(18.9)	
(++)	26(13.3)	8(21.6)	0.002[s]
(+++)	42(21.4)	0(0.0)	
(++++)	21(10.7)	0(0.0)	
RBC			
0-5/hpf	118(60.2)	31(83.8)	
6-15/hpf	54(27.6)	6(16.2)	
15-30/hpf	5(2.6)	0(0.0)	0.032[s]
≥30 /hpf	19(9.1)	0(0.0)	
WBC			
≤30 /hpf	136(69.4)	19(51.4)	0.034[s]
>30/hpf	60(30.6)	18(48.6)	
Urinary cast	48(24.5)	3(8.1)	0.027[s]

s= significant
P value reached from chi square test

Group A= Disorders related to urinary tract
Group B= Infections outside of the urinary tract

Fourty two (21.4%) patients were +++ protein in group A and not found in group B. Majority 118(60.2%) patients had RBC 0-5/hpf in group A and 31(83.8%) in group B. In both groups, most of the patients had urinary WBC ≤30 /hpf which was 136(69.4%) in group A and 19(51.4%) in group B. Forty eight (24.5%) patients had urinary cast in group A and 3(8.12%) in group B. The difference were statistically significant ($p<0.05$) between two groups.

Table III: Association between diagnosis with hematological findings (n=233)

Hematological findings	Diagnosis		P value
	Group A (n=196)	Group B (n=37)	
	n(%)	n(%)	
Haemoglobin (gm/dl)			
Normal	65(33.2)	9(24.3)	0.289[ns]
Abnormal	131(66.8)	28(75.7)	
ESR (mm in 1st hour)			
Normal	29(14.8)	2(5.4)	0.094[ns]
Raised	167(85.2)	35(94.6)	
Total WBC count (/mm³)			
Normal	141(71.9)	23(62.1)	0.232[ns]
High	55(28.1)	14(37.8)	
CRP			
Normal	116(59.2)	14(37.8)	0.016[s]
Raised	80(40.8)	23(62.2)	

s= significant, ns= not significant
P value reached from chi square test

Group A= Disorders related to urinary tract
Group B= Infections outside of the urinary tract

Majority (59.2%) patients was found normal CRP in group A and 14(37.8%) in group B.Which was statistically significant ($p<0.05$) but other hematological findings were not statistically significant ($p>0.05$) between two groups.

Table IV: Association between diagnosis with renal function (n=233)

Renal function	**Diagnosis**		**P value**
	Group A (n=196)	**Group B (n=37)**	
	n(%)	**n(%)**	
Renal impairment in terms of serum creatinine (µmol/l)			
<130 (no renal impairment)	73(37.2)	13(35.1)	
130-173 (mild)	32(16.3)	0(0.0)	[a]0.001[s]
>173-300 (moderate)	44(22.4)	3(8.1)	
300 (severe)	47(24.0)	21(56.8)	
Serum creatinine (µmol/l)	247.7±218.6	301.8±260.5	[b]0.182[ns]
Range (min-max)	51-935	57-719	
BUN ((mmol/l)	24.4±33.7	25.9±42.7	[b]0.813[ns]
Range (min-max)	6.0-196.0	6-169	

s= significant, ns= not significant
[a]P value reached from chi square test
[b]P value reached from unpaired t-test

Group A= Disorders related to urinary tract
Group B= Infections outside of the urinary tract

Forty seven (24.0%) patients was found severe renal impairment in terms of serum creatinine in group A and 21(56.8%) in group B. Which was statistically significant ($p<0.05$) but other renal function werenot statistically significant ($p>0.05$) between two groups.

Table V: Association between diagnosis with serum albumin (n=233)

	Diagnosis		P value
	Group A (n=196)	Group B (n=37)	
	Mean±SD	Mean±SD	
Serum albumin (gm/l)	34.6±9.4	38.1±5.9	0.030[s]
Range (min-max)	13-50	29-47	

s= significant
P value reached from unpaired t-test

Group A= Disorders related to urinary tract
Group B= Infections outside of the urinary tract
Mean serum albumin was found 34.6±9.4 gm/l in group A and 38.1±5.9 gm/l in group B. The difference was statistically significant ($p<0.05$) between two groups.

Table VI: Multivariable logistic regression analysis for infections outside the urinary tract

	Adjusted OR	95% CI		P Value
		Lower	Upper	
Fever	32.90	10.57	99.96	0.001[s]
Urinary tract symptom	0.28	0.09	0.85	0.024[s]
Dysuria	0.10	0.02	0.47	0.003[s]
Frequency	0.32	0.06	1.60	0.165[ns]
Urgency	0.25	0.01	3.51	0.303[ns]
Flank pain	0.01	0.001	1.42	0.998[ns]
Abdominal pain	0.47	0.04	6.17	0.563[ns]
Renal impairment in terms of Serum creatinine (µmol/l)	5.96	0.65	54.28	0.133[ns]
Urinary cast	0.21	0.04	1.10	0.065[ns]
Proteinuria	0.20	0.05	0.77	0.019[s]
Urinary WBCs (>30/hpf)	2.14	1.05	4.37	0.036[s]
Serum albumin	1.22	0.35	4.32	0.758[ns]
CRP (Raised)	0.84	0.31	2.33	0.742[ns]

s=significant, ns= not significant
Multivariable logistic regression analysis was preformed

Patients having fever 32.9 (95% CI 10.57% to 99.96%) times more likely to developed infections outside of the urinary tract. Patients having urinary tract symptom 0.28 (95% CI 0.09% to 90.85%) times more likely to developed infections outside of the urinary tract. Patients having dysuria 0.10 (95% CI 0.02% to 0.47%) times more likely to developed infections outside of the urinary tract. Patients having proteinuria 0.20 (95% CI 0.05% to 0.77%) times more likely to developed infections outside of the urinary tract. Patients having urinary WBCs>30/hpf 2.14 (95% CI 1.05% to 4.37%) times more likely to developed infections outside of the urinary tract. Patients having fever, urinary tract symptom, dysuria, proteinuria, urinary WBC were statistically significant (P<0.05).

Discussion:

A total of 233 sterile pyuria patients attending in the Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, during the period from September 2016 to August 2017 were included in this study. Among 233 sterile pyuria patients were diagnosed into two groups, 196 patients with disorders related to renal & urinary tract as group A and 37 patients with infections outside of the urinary tract.

In this study it was observed that disorders related to urinary tract (Group A) was found in 196(79.7%) patients among them majority 81(32.9%) had glomerulonephritis, 40(16.3%) had interstitial nephritis, 30(12.2%) had treated UTI, 13(5.3%) had renal tuberculosis, 12(4.9%) had renal stone disease, 10(4.1%) had ADPKD and 10(4.1%) had funguria. Sterile pyuriamay be seen in tuberculosis, renal papillary necrosis, acute interstitial nephritis and glomerulonephritis[7]. Intrinsic urinary tract pathology leading to sterile pyuria include papillary necrosis secondary to obstructive uropathy, tubulointerstitial nephritis, glomerulonephritis, interstitial cystitis, renal transplant rejection, and urinary tract tumors[8] .Most patients with renal TB have sterile pyuria, which can be accompanied by microscopic hematuria[9] .

In this current study it was observed that infections outside of the urinary tract (Group B) was found in 37(15.0%) patients, among them majority 16(6.5%) had pneumonia, 8(6.5%) had dengue, 5(2.0%) had septicemia. In one study found pneumonia was 8.9%, septicemia 31.8% in infections outside of the urinary tract infection group[10]. Another study found sterile pyuriain patients of septicemia in 30.6% of cases[11].

In this series it was observed that 42 (21.4%) patients were +++ protein in group A and not found in group B. Majority 118(60.2%) patients had RBC 0-5/hpf in group A and 31(83.8%) in group B. Most of the patients had urinary WBC ≤30 /hpf which was 136(69.4%) in group A and 19(51.4%) in group B. Forty eight (24.5%) patients had urinary cast in group A and 3(8.12%) in group B. Which were statistically significant (p<0.05). A study also observed proteinturia in about 70% of our pyuria patients[12]. Another study found the absolute number of WBCs or red blood cells in the urine and the presence of casts, proteinuria, and leukocyte esterase were not associated with urinary tract disorder[10].

In this present study it was observed majority (59.2%) patients was found normal CRP in group A and 14(37.8%) in group B. Which was statistically significant (p<0.05). Haemoglobin, ESR and total WBC count were not statistically significant (p>0.05) between the groups. In one study observed the increased presence of band neutrophils accounting for >10% of the WBC count, hyperthermia or hypothermia, and a C-reactive protein level >100 mg/L[13].

In this current study it was observed that 47 (24.0%) patients was found severe renal impairment in terms of serum creatinine in group A and 21(56.8%) in group B. Which was statistically significant (p<0.05). Mean serum creatinine, sodium, potassium, chloride, TCO_2 and BUN were not statistically significant (p>0.05) between the groups. A study shows the mean BUN and creatinine levels were also somewhat higher in patients with sterile pyuria (means of 20.2 vs 17.1 and 1.25 vs 1.05, respectively), but these differences were not statistically significant[10].

In this current study it was observed that mean serum albumin was found 34.6±9.4 gm/l in group A and 38.1±5.9 gm/l in group B. Two (5.4%) patients was found blood culture in group B and not found in group A. Which were statistically significant ($p<0.05$) but other biochemical & microbiological findings were not statistically significant ($p>0.05$) between the groups. One study showed sterile pyuria was unrelated to reported serum albumin[10]. A study done by found blood culture was found in 29.0%[14].

In multivariate analysis in this study it was observed that patients having fever 32.9 (95% CI 10.57% to 99.96%) times, Patients having urinary tract symptoms 0.28 (95% CI 0.09% to 90.85%) times, dysuria 0.10 (95% CI 0.02% to 0.47%) times, proteinuria 0.20 (95% CI 0.05% to 0.77%) times and pyuria with WBC>30/hpf have 2.14 (95% CI 1.05% to 4.37%) times more likely to developed infections outside of the urinary tract. Patients having fever, urinary tract symptoms, dysuria, proteinuria, pyuria with WBC>30/hpfwere statistically significant ($P<0.05$).

Conclusions:

Among patients with culture negative pyuria, the frequency of non-urinary tract infections is not uncommon. Presence of fever, pyuria with urinary WBCs> 30/HPF were found to be more frequent in those with infections outside of the urinary tract and such symptoms and laboratory findings in a patient should prompt and warrant investigations to search for involvement of organ systems other than the renal system.

References:

1. Brenner BM, Rector FC (eds). The Kidney. 4th ed. Philadelphia: W.B. Saunders Co; 1991.
2. Turner, GM &Coulthard, MG 1995, Fever can cause pyuria in children, BMJ, vol. 311, p.924.
3. North AF. 1963 Bacteriuria in children with acute febrile illnesses. J Pediatr. 1963; vol. 63, pp.408–11.
4. Shike H, Kanegaye JT, Best BM, Pancheri J, Buns JC. Pyuria associated with acute Kawasaki disease and fever from other causes. Pediatr Infect Dis J. 2009; 28:440–3.
5. Hogg RJ. A search for the æclusive urinary tract infection in febrile infants. Pediatr Infect Dis J. 1987;6:233–4.
6. Wu CY, Chiou YH, Wang RS, Huang WC, Lee WY, Chiou CC. Prolonged fever and pyuria: a urinary tract infection presentation of incomplete Kawasaki disease. Acta Paediatr. 2005;94:375–7.
7. Schrier RW. Manual of Nephrology. 7th Edition Philadelphia: Lippincott Williams and Wilkins ;2008
8. Narita M. Sterile Pyuria . 2017Reprinted from www.antimicrobe.org
9. Daher EDF, da Silva GB Jr, Barros EJ. Renal tuberculosis in the modern era. Am J Trop Med Hyg, 2013; 88(1): 54-64.
10. Hooker JB, Mold JW, Kumar S. Sterile pyuria in patients admitted to the hospital with infections outside of the urinary tract. J Am Board Fam Med. 2014; 27:97- 103.
11. Yacoub R, Akl NK. Urinary Tract Infections and Asymptomatic Bacteriuria in Renal Transplant Recipients. J Glob Infect Dis. 2011;3(4):383–389.
12. Mahmud HM, Qureshi S, Kumar D, Farman S. Pyuric diabetic patients: A tertiary centre experience from Karachi. Pak J Med Sci. 2014; 30(1):77-80.
13. Chen CY, Chen YH, Lu PL, Lin WR, Chen TC, Lin CY. Proteus mirabilis urinary tract infection and bacteremia: Risk factors, clinical presentation, and outcomes. Journal of Microbiology, Immunology and Infection. 2012;45:228 -236.
14. Spoorenberg V, Prins JM, Opmeer BC, de Reijke TM, Hulscher ME, Geerlings SE. The additional value of blood cultures in patients with complicated urinary tract infections. ClinMicrobiol Infect. 2014;20(8): 476-9.

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Original Article

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One Year Case Study of Autopsy in Hanging Death at Dhaka South

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Abstract:

Hanging is one type of violent asphyxial death. Hanging is a common method of asphyxial suicide in many countries. All most all hangings are self suspension. This may be carried out by a wide variety of methods. Hanging is always suicidal in nature unless otherwise it is proved. There are two basic forms of hanging-complete & partial hanging. Of them partial hanging is more suicidal; that is there is no second thought. Blindness or age is no bar to hanging.There are more than 5 million people lived in Dhaka south. The one year case study shows that there are 90 hanging cases out of 501 post-mortem cases at Sir Salimullah Medical College morgue. All were suicidal Death.

Keywords: Post-mortem, hanging, suicidal, police station

Introduction:

Hanging may be defined as a form of violent asphyxia as a result of suspension of the body by a ligature around the neck, the constricting force being the weight of the body. The ligature constricts the neurovascular bundle of the neck and/or the upper airways.[1] Person can be 10-80years, more common in males. Point of suspension remains approachable to the suicider. Partial hanging is almost always suicidal in nature. A history of a previous attempt may be present and generally committed in a secluded place(victim's home is the most frequent site), suicidal note may be left behind. There should be a motive for committing suicide, Fibers of ligature material may be present in the clenched hand of the victim.[2] Hanging in its face value goes in a favour of suicidal in nature. Depending on the area of the country, hanging is either first or second most popular method of suicide.

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Materials and Method:

One year retrospective case study of hanging autopsy death at Sir Salimullah Medical College morgue is taken for analysis of data of Dhaka south Police stations. Notice that. Sir Salimullah medical college morgue was under 14 police stations during 2009. There were 90 autopsy of hanging cases held during one year out of 501 autopsy cases at Sir Salimullah Medical College morgue.

Statistical Analysis:

The post-mortem of SSMC comprises the Dhaka South; there are 12 police stations under it. The 12 police station are-Kotwali, South Keranigang, Dhohar, Kamrangirchar, Kadamtoli, Shampur, Lalbag, Nababgang, Hazaribag, Sutrapur, Demra and Jatrabari. There were more than 3million people reside there during this period. one year case study shows different trends of age distribution, monthly case distribution, gender distribution, Thana distribution and manner of death.

Results:

During this one year period 90 autopsy cases of hanging were held at Sir salimullah Medical College Morgue out of 501deaths. All cases of hanging deaths were dealing with suicidal cases. Of them 36 were male, 54 were female. 81 cases were Muslims whereas 09cases were Hindus. Most common age group was 15-25years. Out of 136 hanging deaths, 21 cases were coming from Keranigonj. Most common problem was the youth peoples were the main victim. Females are more common victim because they are most sensitive, social and family violence upon them. But in developed countries males are predominant than female. So it is one of the burden issues of Bangladesh.

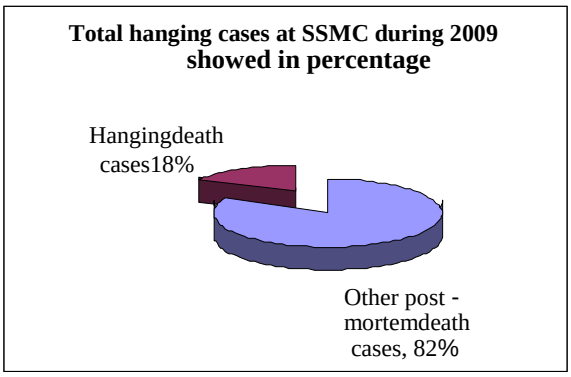

Fig 1: Statiscal data showning Hanging death during the year of 2009)

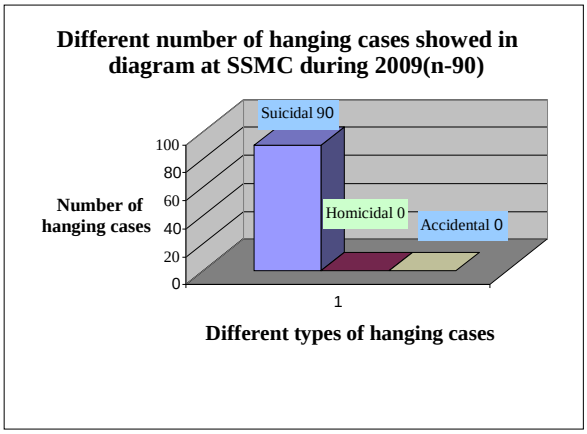

Fig 2: Manner of death of hanging cases

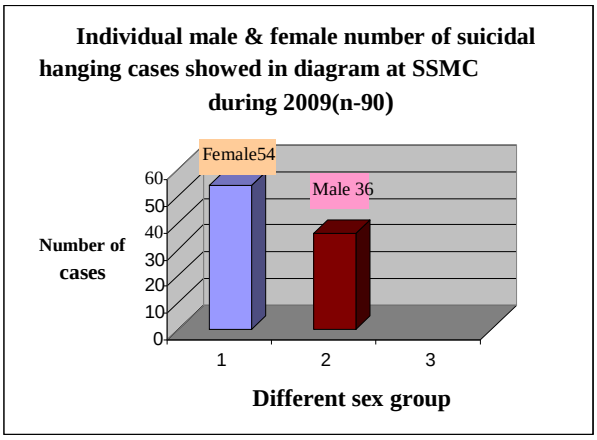

Fig 3: Sex distribution of hanging death.

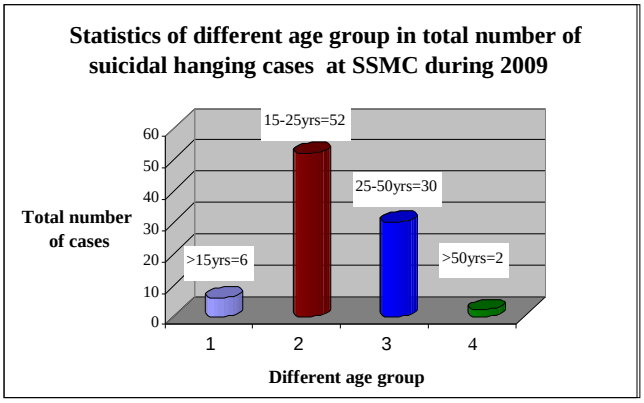

Fig 4: Age distribution pattern of hanging death

Age distribution states that Hanging victims are common among young adults. Most common victims are in 15-25 years. Female victims are more than male because our socio economic status against go for female in Bangladesh.

Police station	No of victim
South Keranigang	20
Kadamtali	12
Hazaribag	10
Jatrabari	08
Lalbag	08
Kamrangirchar	08
Kotwali	05
Dohar	05
Sutrapur	05
Demra	04
Shampur	02
Nababganj	02

Table shows one year case study of hanging cases in P.S level.

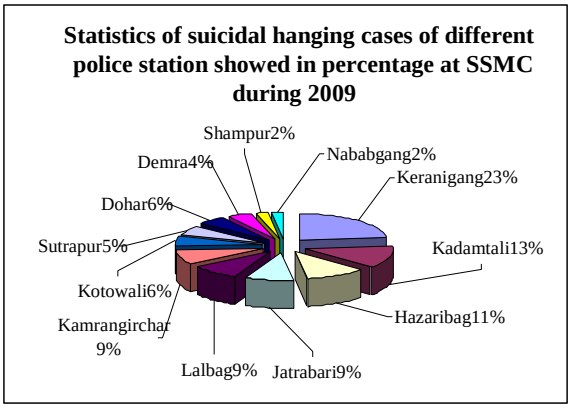

Fig 5: Thana distribution of hanging death

Notices that, table 1 showed most of the downing cases were coming from South keranigong Ps, On the other hand, less frequent in nababganj and shampurthana.

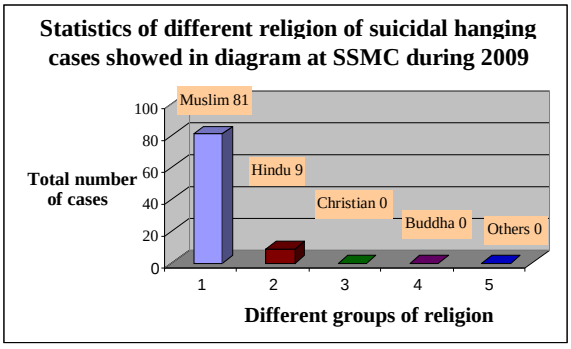

Fig 6:Different groups of religion of hanging death

Diagram shows that most victims were the muslims(81), then hindus (09). But there were no Cristian or Bhuddas. Because majority of the people of Bangladesh are muslims. Dowry is common in both muslim and hindu community, so family violence is more common among them.

Discussion:

Study shows that in the year 2009; there were 501post-mortem held at SSMC Morgue, of them 90 cases were hanging deaths. About 1/5 deaths were hanging cases. Study shows all hanging death were suicidal, no homicidal or accidental death. So it is proved that hanging is always suicidal in nature.

Hanging is one of the commonest methods of committing suicide. In general, hanging is suicidal in natural unless otherwise proved. Partial hanging is invariably suicidal except in masochistic accident (Sexual asphyxia).Sir JhonSibald has pointed out that a death by hanging can seldom be concealed and when known it can seldom be regarded as otherwise as suicide. This cannot be said of any other method. Suicide may be confirmed by the presence of suicide notes and of a platform such as chair, table used to affect suspension.. The ligature material was also available to the victim. The ligature mark was high up in neck, oblique, non-continuous. There was no sign of struggle or foul play. The victim was mentally depressed for loss of huge amount of money and was in financial crisis, which act as a factor for taking decision of self destruction.[3]

Homicidal hanging is extremely rare. It is difficult for a single assailant to carry it out; unless the victim becomes unconscious by injury or by a drug, or is taken unawares or is a child or a very weak person. In all doubtful cases circumstantial evidence is helpful to solve the problem.[4]

Methods of Hanging:

Most hangings are self suspension. This may be carried out by a wide variety of methods, but a typical method of self destruction is to attach a thin rope to a high point such as a ceiling beam or staircase, The lower end is formed into either a fixed loop or a slipknot, which is placed around the neck while the intending suicide stands on a chair or other support. On jumping & then suspended with all or most of his weight upon the rope. There are many variations of this involve either the ligature or the height of suspension, Wires, string, pyjama cords. Belts, braces (suspenders), scarves, neckties, stockings and numerous other devices may be used, depending on availability. In prison or police custody considerable ingenuity may be employed to defeat the efforts of the custodians to remove anything that could be used for self-destruction: shoelaces, stockings and torn bed-sheets have been used in prison cells.[5]

Motives behind hanging:

- Domestic troubles, worries and quarrels.[6]
- Poverty and financial loss.[6]
- Failure at examinations or scolding on that account by the guardians.[6]
- Disappointment in love.[6]
- Incurable disease & prolonged suffering from disease or mental illness.[6]

Legal aspects of hanging:

- Suicide means self committed murder. Acts or instances of taking one's own life voluntarily.[7]
- Attempted suicide is an offence under the Penal Code of Bangladesh (Section: 305,306,309.[7]

Section 305 BPC:

Punishment for abetment of suicide of a child under 18years of age or of an insane, idiot, delirious or intoxicated person may be death or imprisonment for life or imprisonment for a period not exceeding 10years with or without fine.

Section 306 BPC:

Punishment for abetment of suicide in any other case may extend up to 10years which may be either description (simple or rigorous), with or without fine.

Section 309 BPC

Attempt to commit suicide makes the person so attempted, liable to be punished with simple imprisonment for a period which may be extended for one year with fine.

Difficulties in diagnosis of death from hanging:

Following may be difficult to explain whenever encountered in a body found hanged;[8]

1. Ligature running around the neck; victim might be killed first by strangulation and then hanged to simulate suicidal hanging.
2. Presence of two ligature marks-it might be an ante-mortem hanging case, but after few minutes of hanging, if might have slipped further down producing second ligature mark.
3. Nail marks on the neck-it might look like manual strangulation (throttling), but possibilities are that, the victim after getting hanged, made efforts to release the ligature around the neck with his or her fingers and while doing so his or her own fingernails might produce nail marks.
4. Faint ligature mark-may be in dark skin complexion person.
5. Injuries on the body-victim while inducing hanging might have got injured himself or herself.

Social aspect of hanging:

Treatment and rehabilitation of victims of attempted suicide is an important social aspect. They need to be given proper psychotherapy and medication in a psychiatric centre under the expert management of a psychotherapist .Proper education; familial harmony and employment can cure this problem.[9]

Conclusion:

Excluding judicial hanging execution, hanging is commonly a suicidal act of males. Some cases are accidental and entanglement with cords and ropes can occur; amongst children, many tragedies have happened due to leather or plastic restraint harnesses getting around the necks of unattended infants. The tying of toys to the sides of cots results in several deaths of young children each year. Cases of suicidal death are increasing day by day in our country. Of them hanging death is the most common methods of suicides in both urban & rural area in Bangladesh. Most of the people of Bangladesh are very emotional especially female. Recent studies showed that provocative suicidal hanging increasing day by day among females. Proper education, psychotherapy, removal of predisposing factors- Eve teasing, family violence, removal of other provocating factors can improve this situation. Proper case study in our can also play a good role.

References:

1. Parikh CK. Parikh's Textbook of Medical Jurisprudence, Forensic Medicine and Toxicology. 6th ed. London: CBS Publishers; 2007.

2. Biswas G. Review of Forensic Medicine & Toxicology: Including Clinical and Pathological Aspects. 2nd ed. Delhi: Jaypee Brothers Medical Publishers;2012.

3. Taylor AS. The Principles and Practice of Medical Jurisprudence. Philadelphia: Henry C Lea; 1873.

4. Reddy KSN, Murty OP. The essentials of Forensic Medicine & Toxicology. 33rd edition. Delhi: Jaypee Brothers Medical Publisher;2014.

5. Saukko P, Knight B. Knightd's Forensic Pathology. 3rd ed. London: Hooder Arnold;2004.

6. The neuropsychological sequelae of attempted hanging.J of Neurology, Neurosurgery and Psychiatry, 1991; 54(6): 546-88.

7. Uddin MA. A short Textbook of Forensic Medicine. 1989.

8. Rao NG. Text book of Forensic Medicine & Toxicology. 2nd ed. New Delhi: Jaypee Brothers Medical Publisher;2010.

9. Wolfson AB, Hendey GW, Ling LJ, Rosen CL, Schaider JJ, Sharieff GQ, editors. Harwood-Nuss' the Clinical Practice of Emergency Medicine. 5th ed. Philadelphia: Lipppincott Williams & Wilkins;2009.

Original Article

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Multiple micronutrient supplementations during pregnancy in rural Bangladesh: Its impact in a GK project area

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Abstract:

Micronutrient deficiency is a widespread nutritional problem in Bangladesh. Iron deficiency is the primary underlying cause of anaemia in women. In an attempt to address the problem of micronutrient deficiency, GK, a local NGO started to deliver multiple micronutrient supplements to pregnant and lactating women. The objectives of this paper is to study the impact—the attitudes, knowledge of the micronutrients, purchasing and usage pattern and also to measure the prevalence of anaemia in the sample pregnant women (N=60). Both quantitative and qualitative methods have been used to collect information. Our study results indicate that supplementation does have a positive impact in so far as knowledge, attitude and usage patterns are concerned and we also found the incidence of anaemia to be low.

Keywords: Micronutrient deficiency, pregnant women, anaemia

Introduction:

Micronutrient deficiency or hidden hunger is a widespread nutritional problem in developing countries, including Bangladesh. Nutritional deficiency in iron, calcium, folic acid, vitamin A, vitamin C and other trace minerals are referred to as micronutrient deficiency whereas nutritional deficiency in carbohydrate, protein and fat are known as macronutrient deficiency. Nutritional deficiency anaemia occurs due to deficiency in iron, vitamin B_{12} and folic acid. Iron deficiency during pregnancy affects both the mother and the baby adversely. It causes pre term delivery, low birth weight of the newborn, poor neonatal health and higher maternal morbidity and mortality. In this paper, we will examine micronutrient deficiency with a special focus on anaemia of women in pregnancy. The materials for this paper are mainly derived from an in-depth cross sectional study of factors affecting malnutrition in pregnancy in rural Bangladesh.

In Bangladesh, as in other developing countries, iron deficiency is a major health problem Women suffer from iron deficiency anemia more than men because of their increased needs of iron during pregnancy and lactation. Nutritional anemia is widely prevalent in South Asia. According to a UNICEF published regional report, prevalence of nutritional anemia in Bangladesh is highest among the South Asian countries. Seventy percent of Bangladeshi women and 77% of the pregnant women suffer from nutritional anemia whereas 45% of the Sri Lankan women and 39% of the Sri Lankan pregnant women suffer from anemia[1].

Hyder et al[2]. cross sectional study of 214 women in rural Bangladesh found prevalence of anemia to be 50% but they found no incidence of severe anemia. Iron deficiency was found in 80% of women who had moderate anemia and 50% of women with mild anemia. Even non anemic women were found to have iron deficiency. Bhutta[3] studied the impacts of micronutrient supplementation in pregnant women in rural Bangladesh. Their results showed multiple micronutrient supplementations resulted in decrease

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of LBW babies. The positive impacts of micronutrient supplementation in pregnancy have been established in many studies. Ahmed et al's study is the only study which examined long term micronutrient supplementation once or twice weekly on adolescent girls. They found it to improve the micronutrient deficiency for the girls[4].

Bhargava et al's studied the relationship between socioeconomic factors and dietary intake and their association with hemoglobin concentration of Bangladeshi women. There was a close association between socioeconomic status and diet. Intake of iron from meat fish poultry and other animal sources was lower in low socioeconomic group. Their results showed increase in household income led to higher intake of iron from meat, fish and poultry.and other animal sources[5].

Materials and Methods:

This cross-sectional study was conducted in SavarGonoshasthaya Kendra (GK) project area of Dhaka district. GK is a national level NGO in Bangladesh. 60 pregnant women were conveniently selected for this study. Respondents were asked 4 specific questions regarding micronutrients.

1. If they bought the micronutrient supplements
2. If they knew the names of these supplements
3. If they knew for what purpose they were taking these supplements
4. If they were taking these supplements regularly

Both qualitative and quantitative information were collected from in-depth conversation with the pregnant women and observation of their daily life schedules. Information on incidence of anaemia in the sample women came from co-investigator and paramedics who routinely do clinical examination to check anaemia.

Results:

Since pregnant women suffer from multiple micronutrient deficiency in addition to iron, GK started providing micronutrient supplements as a part of its antenatal care services.

Table 1: Tablet which health worker brings was bought or not

Tablet bought	Frequency	Percent
Yes	48	80.0
No	9	15.0
Will buy	3	5.0
Total	60	100.0

Table -1: shows that the overwhelming majority of our sample women 48 (80%) were buying the micronutrient supplements. There were 12 (20%) pregnant women who did not buy recently. who said that they were taking it before but stopped it because they did not like the smell or the taste.

Table 2: Awareness of the names of these tablets

Awareness	Frequency	Percent
Yes	50	83.3
No	10	16.7
Total	60	100.0

In response to our question on if they knew the names of the supplements, we found 50 (83%) of our sample women knew the names of micronutrient supplements they were taking, only 10 women

(17%) could not recall all the names of the supplements (Table 2). They also knew that these supplements had beneficial effects on the mother and the unborn fetus.

Table 3: Regular intake of the tablets

Tablets intake	Frequency	Percent
Yes	44	73.3
No	15	25.0
Missing	1	1.7
Total	60	100.0

The overwhelming majority of our sample pregnant women were taking their micro-nutrient supplements twice a day as advised by the GK paramedics who provide antenatal care. Table 2 shows 44 (73%) of our sample women were taking the supplements regularly.

Table 4: Perception of pregnant women on food they should eat

Food Item	n=60	Percent of Cases
Fish	35	58.3%
Meat	26	43.3%
Egg	43	71.7%
Vegetables	42	70.0%
Fruits	31	51.7%
Rice	10	16.7%
Milk	47	78.3%
Nutritious food	5	8.3%
Don't know	2	3.3%
Missing	3	5.0%

Table- 4: shows that pregnant women should eat foods containing micronutrients include fish, poultry, meat, eggs, vegetables and leafy greens.

Table 5: Anaemia by clinical examination

Status of Anaemia	Frequency	%
Mildly anaemic	4	7
No anaemia	56	93
Total	60	100

Table 6: shows that only 4 women were diagnosed clinically as being mildly anemic.

Discussion:

In the GK project area, no field based study has been carried out to find out the impact of micro-nutrient supplements on anaemia status of women. Studies done in India, Nepal and other low income countries show micronutrient supplementation reduce/eliminate micro-nutrient deficiencies. In writing about intervention strategies for controlling micronutrient deficiency, Lindsay[6] states that most commonly used intervention strategies used in developing countries has been micro nutrient supplementation and fortification because they are cost effective and easy to deliver. Our study results show that village women's perceptions of micronutrient supplements have changed in the last few years. When GK introduced micronutrient supplements, the pregnant women were concerned about the possible negative effects on the unborn fetus.

Our in-depth cross sectional study of pregnant women's attitude towards multiple micro nutrient supplementations shows a positive attitude (Table 1, 2, and 3). Almost all the pregnant women commented that taking these supplements was good for both the mother and the unborn fetus. While all the pregnant women had a positive attitude, a few mentioned about not taking them regularly because they did not like the smell or the taste of the tablets (Table 3). A study conducted by Phuong H et al's found that

micronutrient intakes in Northern Vietnam are sub-optimal, where iron intake was 38%[7].

Bhutta ZA et al[8] mentioned that micronutrient supplementation and food fortification are recommended in the Millennium Development Goals to eradicate poverty, decrease the rate of child mortality, and improve maternal health status. There is no doubt that a food based approach is a long term sustainable solution to meeting micronutrient deficiency. The question is how do we ensure that the pregnant women will be taking sufficient amount of micronutrient rich foods? First, we need to make micronutrient rich foods available and affordable for the poor women who are more vulnerable to micronutrient deficiencies. Foods containing micronutrients include fish, poultry, eggs, vegetables and leafy greens. All of these foods are available but with the exception of vegetables and leafy greens, other micronutrient rich foods are too expensive for the poor pregnant women. While doing antenatal check up, the paramedics tell the mothers to eat vegetables and greens.

Nutrition advice given by GK paramedics and electronic media (television and radio) has made women aware of the health benefits of eating fish, meat, vegetables and greens (Table 4). In a rice based meal, greens and vegetables are used as fringe foods mainly to flavor the rice—the core food. So, the quantity of greens and vegetables remain less than the required amount. As in other parts of rural Bangladesh, in our study area, rice supply 70-80% of the calories and rice is the medium through which other foods are enjoyed. What has prevented the pregnant women from consuming adequate amounts of micronutrient rich vegetables and greens? It is not lack of knowledge, there exists no cultural prohibition against eating vegetables and greens during pregnancy. In the local classification of foods all green color vegetables and most leafy greens are considered to be "cool" (neither hot nor cold) so appropriate for consumption at all times. Nag's review of traditional beliefs and practices about food during pregnancy found vegetables and fruits were viewed as cold therefore suitable in pregnancy –a cold state[9]. The price of vegetables and leafy greens is affordable compared to other micronutrient rich foods. We believe reasons for not having fruits are both cultural and economic. The lower intake of vegetables has to do with the age old habit of eating these foods as flavoring foods- a food habit deeply embedded in the Bangali food culture.

Since only four cases of anemia was detected in our sample by the paramedics' clinical examination, it can be safely assumed that provision of micronutrients at the doorstep of village women have had a positive impact on the pregnant women's health (Table 5). Menendez C et al[10] found that iron supplementation led to a significant reduction in the prevalence of anaemia.

Conclusion:

GK's strategy of delivering micronutrient supplements to address the problem of micro nutrient deficiency in pregnant women has produced positive impacts. Our study results show overwhelming majority of the sample pregnant women (n=60) are aware of the beneficial effects of the supplements on both the mother and the baby, they purchase the supplements and also take them regularly. The incidence of anaemia as detected by the paramedics using clinical symptoms is low. From this small sample study we cannot infer that provision of supplements have drastically reduced the incidence of anaemia.

References:

1. UNICEF. Report on anaemia prevalence survey of urban Bangladesh & rural Chittagong hill tracts 2003. Bangladesh Bureau of Statistics.2004: 26-28.

2. Hyder SM, Persson LA, Chowdhury M, Lonnerdal Bq, Ekstrom BC, Anaemia and Iron Deficiency during Pregnancy in rural Bangladesh. Public Health Nutrition. Dec 2004, 7(8): 1065-70.

3. Haider BA, Bhutta ZA (October 2006). Multiple micronutrient supplementation for women during pregnancy. Cochrane Database of Systematic Review. Issue 4. Art. No. :CD004905. DOI: 10.1002/14651858. CD004905. pub2. [Date accessed: 26.2.17]

4. Ahmed F, Khan MR, Akhtaruzzaman M, Karim R, Williams G , Torriese H, Darnton-Hill I. (October 2010). Long term intermittent multiple micronutrient supplementation enhances hemoglobin and micronutrient status more than iron+folic acid supplementation in Bangladeshi rural adolescent girls with nutritional anaemia. J of Nutrition. 140(10) :1879-86.

5. Bhargava A, Bois HE, Scrimshaw NS (March 2001). Dietary Intakes and Socioeconomic Factors Are Associated with the Hemoglobin Concentrationof BangladeshiWomen. J of Nutrition. [online] 131(3) :758-64. Available fromhttp://jn.nutrition.org/content/131/3/758. Full" \l "fn-1" [Date accessed 26.2.17]

6. Lindsay HA. Anaemia and Iron Deficiency: Effects on pregnancy outcome. American J of Clinical Nutrition. 2005; 71(5): 1280-1284.

7. Phuong H. Nguyen, Hieu Nguyen, Ines Gonzalez-Casanova, Erika Copeland, Garrett Strizich, Alyssa Lowe et al (February 2014). [Online] available from http://dx.doi.org/ 10.1371/journal.pone.0089504 [accessed 25-02-2017]

8. Bhutta ZA, Ahmed T, Black RE, Cousens S, Dewey K, et al. (2008). What works? Interventions for maternal and child under nutrition and survival. Lancet 371: 417–440.

9. Nag M (September 1994). Beliefs and Practices about Food during Pregnancy. Economic and Political Weekly. [online] 29(37); 2427-2438. Available from http://www.jstor.org/ stable/ 4401755. [Date accessed 26.2.17]

10. Menendez C, Todd J, Alonso PL, Francis N, Lulat S, Ceesay S et al (September-October 1994). The effects of iron supplementation during pregnancy, given by traditional birth attendants on the prevalence of anaemia and malaria. Medicine and Hygiene. 88(5); 590-593.

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Hyponatraemia: Diagnosis and Management

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Abstract:

Hyponatraemia is the most common disorder of electrolyte balance encountered in clinical practice. It can lead to a wide spectrum of clinical symptoms, from subtle to severe or even life threatening and is associated with increased morbidity and mortality. Although classically defined as a condition with low serum Sodium levels, hyponatraemia in a true sense is primarily a disorder of water balance, with a relative excess of body water compared to total body sodium content. A number of conditions can lead to this imabalance, which include some endocrine diseases also. Hyponatremia has been classically divided into hypovolemic, euvolemic and hypervolemic types depending on the volume status, and hypotonic, isotonic and hypertonic types depending on plasma osmolality. This review focuses on clinical and pathophysiological aspects of hyponatremia with special attention on endocrine disorders.

Keywords: Hyponatremia, SIADH

Background:

Hyponatraemia, defined as a serum sodium concentration <135 mmol/L, is the most common disorder of electrolyte balance encountered in clinical practice. Hyponatraemia ispresent in 15–20 % of emergency admissions to hospital and occurs in up to 20 % of critically ill patients[1]. It can lead to a wide spectrum of clinical symptoms, from subtle to severe or even life threatening and is associated with increased mortality, morbidity and length of hospital stay in patients presenting with a range of conditions[2,3]. Even mild hyponatraemia may have detrimental effects on patients, although it is generally thought of as an asymptomatic condition[4,5]. Hyponatremia is important clinically because: 1) acute severe hyponatremia can cause substantial morbidity and mortality; 2) adverse outcomes, including mortality, arehigher inhyponatremic

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patients with a wide range of underlying diseases; and 3) overly rapid correction of chronic hyponatraemia can cause severe neurological deficits and death[6].

Although classically defined as a condition with low serum Sodium levels, hyponatraemia in a true sense is primarily a disorder of water balance, with a relative excess of body water compared to total body sodium content[7]. A number of conditions can lead to this imabalance, which include some endocrine diseases also. This review focuses on clinical and pathophysiological aspects of hyponatremia with special attention on endocrine disorders.

Table-1: Selected terminology for hyponatraemia[7]

Definition of hyponatraemia based on biochemical severity	
Mild	Serum Sodium 130 to <135 mmol/L*
Moderate	Serum Sodium 125 to <130 mmol/L*
Severe	Serum Sodium <125 mmol/L*
Definition of hyponatraemia based on time of development**	
Acute	Hyponatraemia that is documented to exist <48 hours
Chronic	Hyponatraemia that is documented to exist for at least 48 hours
Definition of hyponatraemia based on symptoms	
Moderately symptomatic	Any biochemical degree of hyponatraemia in the presence of- • Nausea without vomiting • Confusion • Headache
Severely symptomatic	Any biochemical degree of hyponatraemia in the presence of- • Vomiting • Cardiorespiratory distress • Abnormal and deep somnolence • Seizures • Coma (Glasgow Coma Scale <8)

* Measured by ion-specific electrode.

** If hyponatraemia cannot be classified, it should be considered as chronic, unless there is clinical evidence of the contrary.

Pathophysiology:

Under normal conditions, renal handling of water is sufficient to excrete as much as 15-20 L of free water per day. Further, the body's response to a decreased osmolality is decreased thirst. Thus, hyponatremia can occur only when some condition impairs normal free water excretion[8].. An exception to this rule is acute primary polydipsia (acute water intoxication) in which the excessive water intake can overwhelm even the normal excretory capacity[9]. Generally, hyponatremia is of clinical significance only when it reflects a drop in the serum osmolality (ie, hypotonic hyponatremia), which is measured directly via osmometry or is calculated as- [2(Na) mEq/L + serum glucose (mg/dl)/18 + BUN (mg/dl)/2.8]. Urea is not an effective osmole, so when the urea levels are very high, the measured osmolality should be corrected for the contribution of urea.

Taking into account that the suppression of arginine vasopressin (antidiuretic hormone (ADH) secretion is essential for the excretion of any water load, the presence of high serum concentrations of ADH is a condition sine qua non for the development and maintenance of hyponatremia. Virtually all the causes of hyponatremia (except for renal failure, primary polydipsia, beer potomania, and low dietary solute intake) are characterized by an excess of ADH (despite the presence of hypotonicity) most frequently due to the syndrome of inappropriate ADH secretion (SIADH) or to depletion of effective circulating volume, which is a normal stimulus to ADH secretion (i.e. appropriately raised ADH levels)[10].

Hypovolemic Hyponatremia:

Hypovolemia causes a markedneurohumoral activation, increasing circulating levels of ADH, which in turn helps preserve blood pressure via vascular and baroreceptor V_{1A} receptors and increases water reabsorption via renal V_2 receptors. Activation of V_2 receptors leads to hyponatremia in the setting of increased free water intake. In nonrenal causes of hypovolemic hyponatremia (GI loss, sweating, burns), urine Na+ concentration is typically <20 mmol/L in the absence of adequate oral

replacement. These patients may be mistakenly classified as euvolemic, with only the reducedurinary Na+ concentration to indicate the cause of their hyponatremia.

The renal causes of hypovolemic hyponatremia share an inappropriate loss of Sodium in the urine, leading to volume depletion and an increase in circulating ADH; urine Na^+ concentration is typically >20 mmol/L. Aldosterone deficiency can lead to hyponatremia in primary adrenal insufficiency and other causes of hypoaldosteronism. Salt-losing nephropathies may lead to hyponatremia when sodium intake is reduced, due to impaired renal tubular function. Thiazide diuretics cause hyponatremia via a number of mechanisms, including polydipsia and diuretic-induced volume depletion. Thiazides do not inhibit the renal concentrating mechanism, such that circulating ADH retains a full effect on renal water retention. In contrast, loop diuretics, which are less frequently associated with hyponatremia, inhibit Na^+-Cl^- and K^+ absorption, blunting the countercurrent mechanism and reducing the ability to concentrate the urine. Increased excretion of an osmotically active nonreabsorbable or poorly reabsorbable solute can also lead to volume depletion and hyponatremia; important causes include glycosuria, ketonuria, and bicarbonaturia (e.g., in renal tubular acidosis or metabolic alkalosis). The syndrome of "cerebral salt wasting" is a rare cause of hypovolemic hyponatremia, encompassing hyponatremia with clinical hypovolemia and inappropriate natriuresis in association with intracranial disease; associated disorders include subarachnoid hemorrhage, traumatic brain injury, craniotomy, encephalitis, and meningitis. Distinction from the more common syndrome of inappropriate antidiuresis is critical because cerebral salt wasting will typically respond to aggressive Na^+-Cl^- repletion[11].

Hypervolemic Hyponatremia:

Patients with hypervolemic hyponatraemia develop an increase in total-body sodium that is accompanied by a proportionately greater increase in total-body water, leading to a reduced plasma Na^+ concentration. The causative disorders can be separated by the effect on urine Na^+ concentration, with acute or chronic renal failure uniquely associated with an increase in urine Na^+ concentration. The pathophysiology of hyponatremia in congestive heart failure, cirrhosis, and nephrotic syndrome is similar to that in hypovolemic hyponatremia, except that arterial filling and circulatory integrity is decreased due to the specific etiologic factors. Urine Na+ concentration is typically very low, i.e., <10 mmol/L, even after hydration with normal saline[11].

Euvolemic Hyponatremia:

The syndrome of inappropriate antidiuresis (SIADH) is the most frequent cause of euvolemic hyponatremia. The generation of hyponatremia in SIADH requires an intake of free water, with persistent intake at serum osmolalities that are lower than the usual threshold for thirst. Four distinct patterns of AVP secretion have been recognized in patients with SIAD, independent for the most part of the underlying cause. Type 1 shows erratic excess ADH secretion, unrelated to plasma osmolality. It is the commonest of all types (40%), mostly associated with tumours. In type 2 there is 'reset osmostat'; patientsautoregulate around a lower serum osmolality. This type is mostly found in chest and CNS disease. Type 3 denotes 'leaky osmostat', i.e.-normal osmoregulation until plasma hypotonicity develops when vasopressin secretion continues. In case of type 4 SIADH there is normal osmoregulated vasopressin secretion; hyponatraemia occurs possibly due to receptor defect, or alternative ADH[12].

Strictly speaking, patients with SIADH are not euvolemic but are subclinically volume-expanded, due to AVP-induced water and sodium retention. Serum uric acid is often low (<4 mg/dL) in patients with SIADH, consistent with suppressed proximal tubular transport in the setting of increased distal tubular Na^+-Cl^- and water transport; in contrast, patients with hypovolemic hyponatraemia will often be hyperuricemic, due to a shared activation of proximal tubular Na^+-Cl^- and urate transport[11].

Euvolemichyponatremia can occur in moderate to severe hypothyroidism, with correction after achieving a euthyroid state. The proposed mechanisms by which hypothyroidism induces hyponatremia in patients with normal fluid intake are-

a. The inability to maximally suppress ADH, partly due to a reduced cardiac output, which can lead to the release of ADH via the carotid sinus baroreceptors[13].

b. The glomerular filtration rate has been reported to be decreased in hypothyroidism, which leads to diminished water delivery to the diluting segments and subsequently diminished free water excretion[14].

The net effect of the impaired water excretion is retention of ingested water and dilutionalhyponatremia.

Severe hyponatremia can also be a consequence of secondary adrenal insufficiency due to pituitary disease; whereas the deficit in circulating aldosterone in primary adrenal insufficiency causes hypovolemic hyponatremia, the predominant glucocorticoid deficiency in secondary adrenal failure is associated with euvolemichyponatremia. Hyponatremia can occur in hypocortisolism due to-

a. Inappropriately excess secretion of ADH because of hypocortisolism[15] (Ishikawa 1982). Hypersecretion of ADH in cortisol deficiency may also be due to the reductions of systemic blood pressure and cardiac output[16].

b. Hypocortisolism mediated altered renal sensitivity to ADH, as suggested by aquaporin-2 water channel up-regulation in glucocorticoid-deficient rats[17].

c. ADH-independent factors, such as impaired renal hemodynamicsand decreased distal fluid delivery to the diluting segments of the nephron[18].

d. In Addison's disease, not only cortisol deficiency but aldosterone deficiency also contributes to hyponatraemia by causing sodium wasting and hypovolemia[19].

e. There may be concomitant primary (due to Hashimoto's thyroiditis) or secondary hypothyroidism with Addison's disease and hypopituitarism, respectively contributing to hyponatremia[20].

Pseudohyponatremia:

Marked elevations of either lipids or proteins in plasma can cause artifactual decreases in serum sodium because of the larger relative proportion of plasma volume that is occupied by the excess lipids or proteins. Because the increased protein or lipid will not appreciably change the total number of solute particles in solution, the directly measured plasma osmolality will be normal in such cases and, therefore, the patient will be isotonic rather than hypotonic[6].

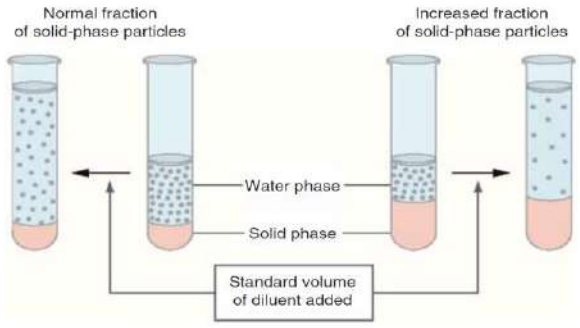

Figure-1: Pseudohyponatremia.

Normally, serum contains 7% solids by volume. To reduce the volume of blood needed for analysis, serum is frequently diluted before the obtaining the actual measurement. The same volume of diluent is always used, and the degree of dilution is estimated under the assumption that the serum contains 7% solid-phase particles. When the fraction of solid-phase particles is increased (e.g.- Hyperlipidemia), the same amount ofdiluent results in a greater dilution, which the laboratory personnel is not aware of (right side of figure). Consequently, the calculation

of an ion level with the use of a degree of dilution that is based on the incorrect fraction of solid-phase particleswilllead to an underestimate. (Adapted from Turchinet al[21])

Table-2: Important causes of hyponatremia

	Hypovolaemic	Renal sodium losses • Diuretic therapy (especially thiazides) • Adrenocortical failureGastrointestinal sodium losses • Vomiting • DiarrhoeaSkin sodium losses • Burns
Hypotonic (Plasma osmolality<280 mOsm/Kg)	**Euvolaemic**	SIADH Primary polydipsia Hypothyroidism Excessive electrolyte-free water infusion
	Hypervolaemic	Congestive cardiac failure Cirrhosis Nephrotic syndrome Chronic renal failure (during free water intake)
Isotonic (Plasma osmolality 280 to 295 mOsm/Kg)		Hyperglycemia Hyperlipidemia Hyperproteinemia
Hypertonic (Plasma osmolality >295 mOsm/Kg)		Severe hyperglycemia with dehydration Mannitol

Table-3: Causes of Syndrome of Inappropriate ADH secretion[22]

Malignant Neoplasia
Carcinoma: bronchogenic, pancreatic, duodenal, ureteral, prostatic, bladder Lymphoma and leukemia Thymoma and mesothelioma
Central nervous System Disorders
Trauma Infection Tumors Porphyria

Table-3: (Continued)

Pulmonary Disorders
Tuberculosis
Pneumonia
Fungal infections
Lung abscesses
Mechanical positive-pressure ventilation
Drug Induced
Carbamazepine
Desmopressin
Oxytocin
Vinca alkaloids
Alkylating agents/antimetabolites
Interferons
Anticonvulsants
Antipsychotic agents
Nicotine
Cyclophosphamide
Morphine
Amitriptyline
Selective serotonin reuptake inhibitors
3-4-Methylenedioxymethamphetamine (Ecstasy)

Clinical Features:

Acute Hyponatremia:

Symptoms of acute hyponatremia primarily occur with sudden and marked reductions in the serum sodium concentration and reflect neurologic dysfunction induced by cerebral edema and adaptive responses of brain cells to osmotic swelling. The major clinical manifestations of acute hyponatremia include[23,24,25]:

- Nausea and malaise (earliest findings, may be seen when the serum sodium concentration falls below 125 to 130 meq/L).
- Headache, lethargy, obtundation, seizures, coma, and respiratory arrest can occur if the serum sodium concentration falls below 115 to 120 meq/L.
- Noncardiogenic pulmonary edema.

Acute hyponatremic encephalopathy may be reversible, but permanent neurologic damage or death can occur, particularly in premenopausal women[23,24].

Chronic Hyponatraemia:

Due to the cerebral adaptation in chronic hyponatraemia, many patients may remain asymptomatic despite a serum sodium concentration below 120 mmol/L. When symptoms do occur, they are relatively nonspecific[26]:

- Fatigue
- Nausea
- Dizziness
- Gait disturbances
- Forgetfulness
- Confusion
- Lethargy
- Muscle cramps

Seizures and coma are uncommon and often reflect an acute exacerbation of the hyponatremia.

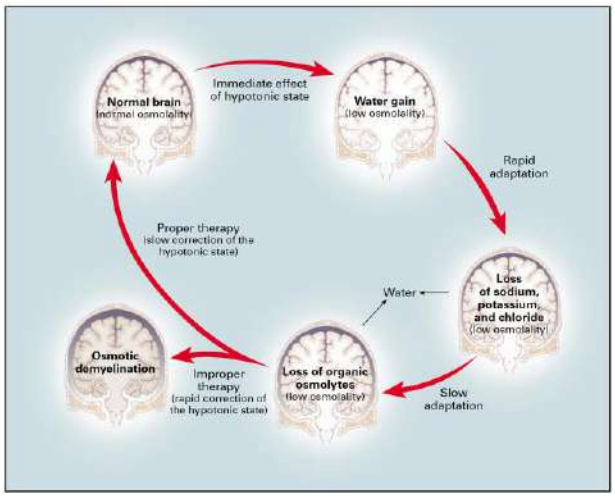

Figure-2: Effects of Hyponatremia on the Brain and Adaptive Responses (Adapted from Adrogueet al[27])

Diagnostic evaluation:

To diagnose and manage a case of hyponatraemia, we have to answer some questions:

1. Whether it is true hyponatraemia or pseudohyponatremia?
2. Whether the condition is acute or chronic?
3. What is the volume status of the patient?
4. What is the urinary osmolality and urine sodium level?
5. What is the underlying cause?

Acute vschronichyponatraemia:

For practical purposes, we can define acute hyponatraemia as low serum sodium documented to be of less than 48 hours duration. If the duration is documented to be >48 hours, or if exact duration isnot known, it is said to be chronic (Table-1)[7].

Determination of volume status:

Although it seems easy to assess volume status by checking blood pressure, postural hypotension, jugular venous pressure and peripheral edema, in practice it is very difficult. If the volume status is unclear, an infusion of normal saline (e.g. 1 L over 12 h) as a therapeutic trial will often reveal the true situation. Hypovolaemic patients will respond well (typically serum sodium will rise > 5 mmol/L), whereas patients with SIADH will often not improve and may experience a worsening of hyponatraemia. It is imperative that serum sodium is rechecked 6 h after the infusion is started[28].

Detailed clinical and laboratory workup:

Apart from assessment of volume status, the physician should search for a history of gastrointestinal fluid loss, detailed drug history, clinical features consistent with consistent one of the causes of SIADH, such as small cell carcinoma or central nervous system disease, and symptoms and signs suggestive of adrenal insufficiency or hypothyroidism.

The most important investigations to find out the cause of hyponatraemia include serum osmolality, urine osmolality and urine sodium, potassium, and chloride concentrations.

Serum osmolality:

Ideally, in the face of hyponatraemia, serum osmolality should be decreased (<275 mOsm). If the serum osmolality is high or 'inappropriately' normal, one should think of marked hyperglycemia, severe azotemia, and alcohol intoxication. Less common causes of this condition includes infusion or absorption of solutions containing sugars, systemic absorption of irrigant solutions containing glycine, sorbitol, or mannitol (e.g.- during transurethral resection of prostate), and pseudohyponatremia due to hyperlipidemia or hyperproteinemia.

Urine osmolality:

In patients with hyponatremia and a low plasma osmolality, urine osmolality should be high (>100 mOsm/Kg) in most of the cases (SIADH, true hypovolemia, heart failure, and cirrhosis). If urine osmolality is <100 mOsm/Kg, it indicates primary polydipsia, beer potomania syndrome and reset osmostat.

Urine sodium and chloride:

In hypovolemic hyponatraemia, urine sodium excretion is <20 meq/L. If it is >20 meq/L, one should think of renal salt-wasting (e.g.- diuretic therapy, adrenal insufficiency, cerebral salt-wasting syndrome).

Similarly in hypervolemic patients with low effective circulating volume (e.g.- heart failure, cirrhosis, nephritic syndrome), urine sodium excretion is <20 meq/L. When it goes >20 meq/L, acute or chronic renal failure is suspected.

The urine sodium concentration is usually above 20 meq/L in patients with SIADH, hypothyroidism and other causes of euvolemichyponatraemia. In SIADH, typically urine sodium is >40 meq/L.

Urine chloride is important in hypovolemic hyponatremic patients who have metabolic alkalosis caused by vomiting, where the urine sodium concentration may be > 25 meq/L, but the urine chloride concentration will be low (less than 25 meq/L).

Other investigations:

- Renal function tests
- Serum potassium- High in adrenal insufficiency, renal failure. Low or low-normal in SIADH.
- Blood glucose and blood lipids (to exclude pseudohyponatremia)
- Serum uric acid (<4 mg/dl in SIADH)
- Thyroid, adrenal and pituitary hormone evaluation
- Radiography of chest and CNS in suspected cases of SIADH.

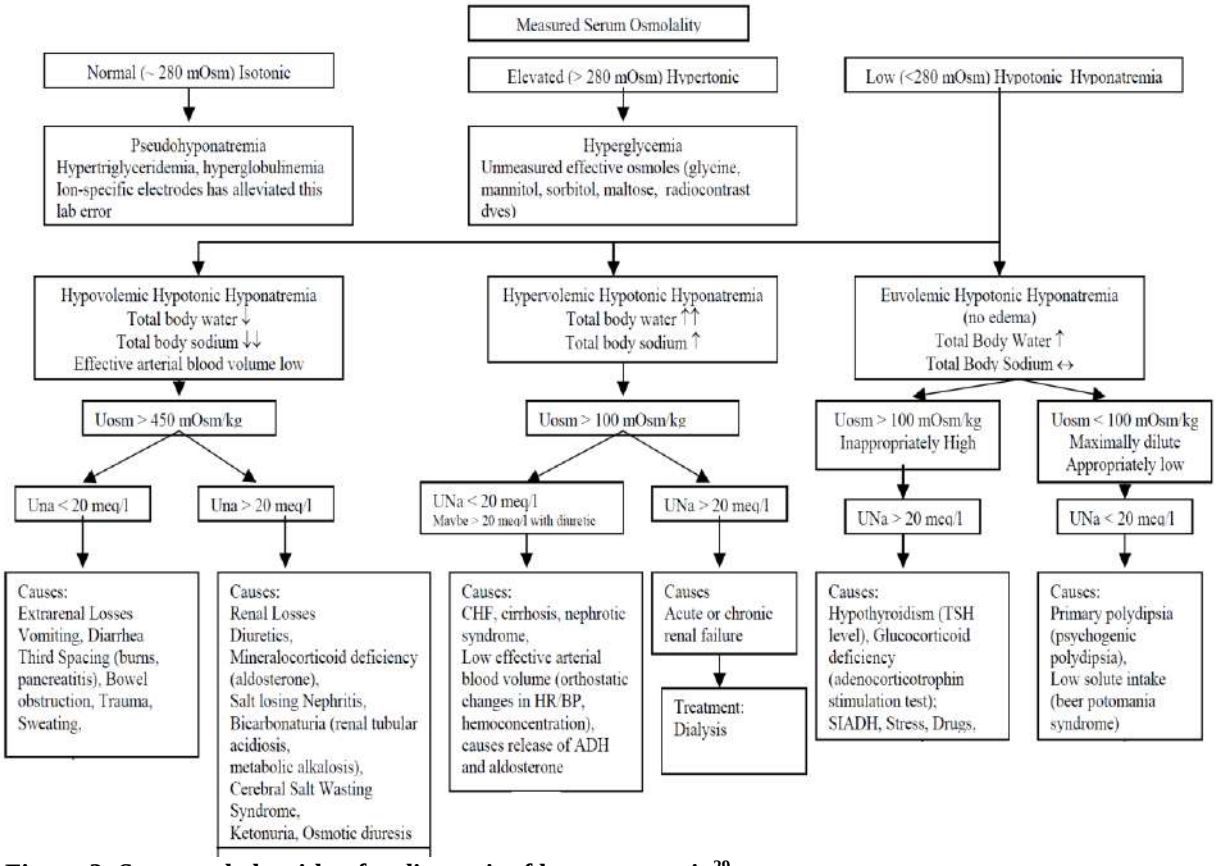

Figure-3: Suggested algorithm for diagnosis of hyponatraemia[29]

Syndrome of inappropriate ADH secretion:

SIADH is the most important cause of euvolemichyponatraemia. It can be diagnosed by using predefined criteria (Table-4). Important differential diagnoses are hypothyroidism, hypoadrenalism and true hypovolemia including cerebral salt wasting (CSW). Indeed, it may be very difficult to distinguish SIADH from CSW.

Table-4: Diagnostic criteria of SIADH[30]

Essential features	Supplemental features
• Decreased effective osmolality (<275 mOsm/kg) • Urinary osmolality >100 mOsm/kg • Clinical euvolemia • No clinical signs of volume depletion of extracellular fluid • No orthostasis, tachycardia, decreased skin turgor, or dry mucous membranes • No clinical signs of excessive volume of extracellular fluid • No edema or ascites • Urinary sodium >40 mmol/liter with normal dietary salt intake • Normal thyroid and adrenal function • No recent use of diuretic agents	• Plasma uric acid <4 mg/dl • Blood urea nitrogen <10 mg/dl • Fractional sodium excretion >1%; fractional urea excretion >55% • Failure to correct hyponatremia after 0.9% saline infusion • Correction of hyponatremia through fluid restriction • Abnormal result on test of water load (<80% excretion of 20 ml of water perkg of body weight over a period of 4 hours), or inadequate urinary dilution (<100 mOsm/kg of water) • Elevated plasma AVP levels, despite the presence of hypotonicity and clinical euvolemia

Table 5: Differences between SIADH and cerebral salt wasting[7]

	SIADH	Cerebral salt wasting
Serum urea	Low normal	High normal
Serum uric acid	Low	Low
Urine volume	Low normal	High
Urine sodium	>40 mmol/L	Usually >100 mmol/L
Blood pressure	Normal	Orthostatic hypotension
Central venous pressure	Normal	Low

Management of hyponatraemia:

Acute hyponatraemia:

Treatment of severe acute symptomatic hyponatremia should include hypertonic 3% saline (513 mmol/L) to acutely increase plasma Na+ concentration by 1–2 mmol/h to a total of 4–6 mmol/L; this modest increase is typically sufficient to alleviate severe acute symptoms, after which corrective guidelines for chronic hyponatremia are appropriate. The traditional approach is to calculate an Na^+ deficit, where the Na^+ deficit = 0.6 × body weight × (target plasma Na+ concentration – starting plasma Na+ concentration), followed by a calculation of the required rate. A practical approach can be an infusion of 150 ml of 3% NaCl over a period of 20 minutes, followed by checking the serum sodium concentration while repeating an infusion of 150 ml 3 % hypertonic saline or equivalent over the next 20 min. This procedure can be repeated twice or until a target of 5 mmol/L increase in serum sodium concentration is achieved[7]. (Spasovski 2014). For mild to moderate symptoms, the rate of infusion of 3% saline should be 0.5-2 ml/kg/hour[6]. Regardless of the method used to determine the rate of administration, the increase in plasma Na^+ concentration can be highly unpredictable during treatment with hypertonic saline, due to rapid changes in the underlying physiology. Therefore, plasma Na^+ concentration should be monitored every 2–4 h during treatment, with appropriate changes in therapy based on the observed rate of change. AVP antagonists do not have an approved role in the management of acute hyponatremia[11].

Chronic hyponatraemia:

Treatment of underlying cause:

In addition to the specific therapies described below that are aimed at correcting the hyponatremia, therapy should also be directed at the underlying disease. This includes administration of saline to patients with true volume depletion, administration of glucocorticoids to patients with adrenal insufficiency, thyroid hormone replacement in patients with hypothyroidism and reversing the cause of SIADH.

Fluid restriction:

Fluid restriction to below the level of urine output is indicated for the treatment of symptomatic or severe hyponatremia in edematous states (such as heart failure and cirrhosis), SIADH, and advanced renal failure. Restriction to 50-60% of daily fluid requirements may be required to achieve the goal of inducing negative water balance[27]. Fluid restriction is also warranted in hyponatremic patients with primary polydipsia in whom increased fluid intake is the primary problem.

Sodium chloride administration:

Sodium chloride, usually as isotonic saline or increased dietary salt, is given to hyponatremic patients with true volume depletion and/or adrenal insufficiency and to some patients with SIADH. Salt administration is generally contraindicated for chronic therapy in edematous patients.

Administration of hypertonic saline is primarily limited to patients with symptomatic or severe hyponatremia or, occasionally, to patients with SIADH and a highly concentrated urine.

Vasopressin receptor antagonists (Vaptans):

The vasopressin receptor antagonists produce a selective water diuresis (aquaresis) without affecting sodium and potassium excretion. The ensuing loss of electrolyte-free water will tend to raise the serum sodium in patients with SIADH and may improve mental status in patients with a serum sodium under 130 meq/L. Thirst increases significantly with these agents, which may limit the rise in serum sodium. They are used in cases of SIADH and hypervolemic hyponatremias[31,32].

Table-6: Osmotic demyelination syndrome during correction of chronic hyponatraemia[6]

Factors associated with high risk of developing the osmotic demyelination syndrome

- Serum sodium concentration 105 mmol/L
- Hypokalemia
- Alcoholism
- Malnutrition
- Advanced liver disease

Measures to take for avoiding osmotic demyelination syndrome

Goal:

- Minimum correction of serum [Naþ] by 4-8 mmol/L per day, with a lower goal of 4-6 mmol/L per day if the risk of ODS is high.

Limits not to exceed:

- For high risk of ODS: 8 mmol/L in any 24-hour period;
- For normal risk of ODS: 10-12 mmol/L in any 24-hour period; 18 mmol/L in any 48-hour period.

Table-7: Recommendations for the use of vaptans in the treatment of hyponatraemia

Hyponatraemia classification	Expert panel recommendation[6]	European Clinical Practice guidelines[7]
Hypovolemic	Not recommended	Not recommended
Euvolemic		
Asymptomatic	Recommended	Not recommended
Moderate to severe CNS symptoms	Not recommended	Not recommended
Hypervolemic		
Asymptomatic	Recommended (except patients with liver disease)	Not recommended
Moderate to severe CNS symptoms	Not recommended	Not recommended

Conclusion:

The diagnosis and management of hyponatraemia is challenging even for the expert physician. When there is no apparent feature of GI or urinary loss, one should meticulously search for other causes including drugs. In cchronic cases, slow correction is better than rapid correction, and oral correction is better than parenteral correction. The primary treatment measure for mild symptoms is water restriction. A decision to correct serum sodium more rapidly depends on the chronicity of the hyponatremic state and whether the patient is symptomatic. Drug treatment causing or contributing to hyponatremia should be carefully monitored at the onset of symptoms. Proper monitoring, awareness of optimal treatment modalities, and active management ensure that a good outcome is likely in all mild cases and in most of the more serious cases of hyponatremia.

References:

1. Funk GC, Lindner G, Druml W. Incidence and prognosis of dysnatremias present on ICU admission. Intens Care Med 2010; 36:304–311.

2. Beukhof CM, Hoorn EJ, Lindemans J, Zietse R. Novel risk factors for hospital-acquired hyponatraemia: a matched case-control study. ClinEndocrinol 2007; 66:367–372.

3. Upadhyay A, Jaber BL, Madias NE. Epidemiology of hyponatremia. SeminNephrol 2009; 29:227–238.

4. Renneboog B, Musch W, Vandemergel X, Manto MU, DecauxG. Mild chronic hyponatremia is associated with falls, unsteadiness, and attention deficits. Am J Med 2006; 119:71 e 1–8.

5. Corona G, Giuliani C, Parenti G, Norello D, Verbalis JG, Forti G et al. Moderate hyponatremia is associated with increased risk of mortality: evidence from a meta-analysis. PLoS One 2013; 8: e80451.

6. Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, Thompson CJ. Diagnosis, Evaluation, and Treatment of Hyponatremia: Expert Panel Recommendations. The American Journal of Medicine 2013; 126: S1-S42.

7. Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, Decaux G, Fenske W, Hoorn EJ, Ichai C, Joannidis M, Soupart A, Zietse R, Haller M, Van der Veer S, Van Biesen W, Nagler E, on behalf of the Hyponatraemia Guideline Development Group. Clinical practice guideline on diagnosis and treatment of hyponatraemia. European Journal of Endocrinology 2014; 170: G1–G47.

8. Singhi S, Jayashre M. Free water excess is not the main cause for hyponatremia in critically ill children receiving conventional maintenance fluids. Indian Pediatr. 2009; 46(7):577-83.

9. Milionis HJ, Liamis GL, Elisaf MS. The hyponatremic patient: a systematic approach to laboratory diagnosis. CMAJ. 2002;166:1056–62.

10. Liamis GL, Milionis HJ, Elisaf MS. Endocrine disorders: Causes of hyponatremia not to neglect. Annals of Medicine, 2011; 43: 179–187.

11. Mount DB. Fluid and Electrolyte Disturbances. In: Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J, Eds. Harrison's Principles of Internal Medicine. 19thed. New York: The McGraw Hill Companies. 2015: 295-312.

12. Wass J, Owen K, Turner H, Eds. Oxford Handbook of Endocrinology and Diabetes. 3rd ed. Oxford: Oxford University Press. 2014: 220-221.

13. Hanna FW, Scanlon MF. Hyponatraemia, hypothyroidism, and role of arginine-vasopressin. Lancet. 1997; 350:755 – 6.

14. Schmitz PH, de Meijer PH, Meinders AE. Hyponatremia due to hypothyroidism: a pure renal mechanism. Neth J Med. 2001;58:143 – 9.

15. Ishikawa S, Schrier RW. Effect of arginine vasopressin antagonist on renal water excretion in glucocorticoid and mineralocorticoid deficient rats. Kidney Int. 1982; 22: 587-593.

16. Schrier RW. Body water homeostasis: clinical disorders of urinary dilution and concentration. J Am SocNephrol. 2006; 17:1820-1832.

17. Saito T, Ishikawa SE, Ando F, Higashiyama M, Nagasaka S, Sasaki S. Vasopressin-dependent upregulation of aquaporin-2 gene expression in glucocorticoid-deficient rats. Am J Physiol Renal Physiol. 2000; 279: F502 – F508.

18. Raff H. Glucocorticoid inhibition of neurohypophysial vasopressin secretion. Am J Physiol. 1987; 252: R635 – 644.

19. Oelkers W. Adrenal insufficiency. N Engl J Med. 1996; 335: 1206 – 12.

20. Michels AW, Eisenbarth GS. Immunologic endocrine disorders. J Allergy ClinImmunol. 2010;125: S226 – 237.

21. Turchin A, Seifter JL &Seely EW. Clinical problem-solving. Mind the gap. N Engl J Med 2003; 349: 1465–1469.

22. Slotki I, Skorecki K. Disorders of sodium and water homeostasis. In: Goldman L, Schafer AI, Eds. Goldman-Cecil Medicine. 25th ed. Philadelphia: Saunders. 2016: 741-755.

23. Ayus JC, Wheeler JM, Arieff AI. Postoperative hyponatremic encephalopathy in menstruant women. Ann Intern Med 1992; 117:891.

24. Ayus JC, Varon J, Arieff AI. Hyponatremia, cerebral edema, and noncardiogenic pulmonary edema in marathon runners. Ann Intern Med 2000; 132:711.

25. Moritz ML, Ayus JC. The pathophysiology and treatment of hyponatraemic encephalopathy: an update. Nephrol Dial Transplant 2003; 18:2486.

26. Chow KM, Kwan BC, Szeto CC. Clinical studies of thiazide-induced hyponatremia. J Natl Med Assoc 2004; 96:1305.

27. Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med 2000; 342 (21): 1581-1589.

28. Grant P, Ayuk J, Bouloux PM, Cohen M, Cranston I, Murray RD, Rees A, Thatcher N, Grossman A. The diagnosis and management of inpatient hyponatraemia and SIADH. Eur J Clin Invest 2015; 45 (8): 888–894.

29. Hyponatraemia algorithm: Stellaris Health. Available from: https://www.stellarishealth.org/ PDFs/Hyponatremia_Algorithm.pdf.Accessed on 30 June 2017.

30. Ellison DH, Berl T. The Syndrome of Inappropriate Antidiuresis. N Engl J Med 2007;356:2064-72.

31. Greenberg A, Verbalis JG. Vasopressin receptor antagonists. Kidney Int 2006; 69:2124.

32. Schrier RW, Gross P, Gheorghiade M, et al. Tolvaptan, a selective oral vasopressin V2-receptor antagonist, for hyponatremia. N Engl J Med 2006; 355:2099.

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Case Report

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Conservative Management of Single Fetal Demise in Twin Pregnancy in Dhaka Bangladesh: A Case Report

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Abstract:

Introduction: In twin pregnancy, the demise of a twinduring the second or third trimester is an infrequent obstetric problem. This can cause management dispute to the obstetrician. It is a source of enormous anxiety and emotional strain to the parents, as well as probable difficulties to the mother and the surviving twin. Bangladesh has lower twinning rates in the world, very few case reports on twinning and its complications exist in the literature. Case: Presented is a 20 year old, booked, third gravida Bangladeshi woman who had intrauterine fetal death of the second twin at 17+ week's gestation. She was admitted at Dhaka Central International Medical College and Hospital, Dhaka. She was managed conventionally with close fetal monitoring and serial valuation of her clotting report. She went through successful caesarian operation at 36+ weeks with delivery of a live female baby, its birth weight was 3.02 kg. The dead second twin was fetus papyraceous and was lying in the same cavity with the live fetus. Discussion: Rare incidences have been stated in other parts of the earth. The type of delivery in most cases being caesarean section. Conclusion: to make a diagnosis in time to prevent severe complications. Patient assurance is critical in expectation of normal ending in maximum instances. Delivery should be scheduled at a tertiary center if possible.

Keywords: Conservative management, single intrauterine fetal demise, fetus papyraceous

Introduction:

Intrauterine fetal death of one twin in a multiple gestation is a multifaceted clinical condition. Chorionicity, age at gestation at diagnosis, pregnancy problems, and patient's mental necessities could influence supervision. Strategies to enhance consequences might comprise a multidisciplinary group method and fetal monitoring. One needs to understand the adverse fetal and neonatal consequences related to intrauterine fetal death of one twin, the potential maternal impact, and the strategies to probably avoid unfortunate endings.

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Also, even the maximum attentive supervision might not elude hostile sequelae of a risk-pregnancy. Single intrauterine fetal demise (sIUFD) happens in approximately 3.7 – 6.8 % of twin pregnancies[1-3]. Death might happen at any given time and it rises mortality and morbidity of the surviving twin secondary to the cause of death of the co-twin, to preterm labor, or both. sIUFD in twin pregnancy therefore creates more problems to an already hazardous situation and has diverse outcomes in fetofetal effects and fetomaternal problems unlike to a singleton pregnancy. sIUFD may be triggered by genetic and anatomical anomalies, abruption, placental deficiency, absolute or relative (discordant) growth constraint, cord anomalies, infection, and maternal disease (e.g. diabetes and hypertension)[4]. The incidence of twinning varies from place to place, being 26.0 – 40.2 for each 1000 deliveries in Nigeria[5,6] and 6.0 – 9.0 for each 1000 deliveries in South and South-East Asia[7]. The death of a twin during the second and third trimester of pregnancy is

a rare obstetric complication. This might pose management challenge to the obstetricians. It is a cause of tremendous worry and psychological anxiety to the patient and her relatives. Informed cases of single fetal demise in twin gestations vary from 0.5 – 6.8%[8]. An elevated occurrence was observed in Beijing where 13 of 99 incidences of twin pregnancies reviewed had a lone intrauterine fetal death, giving a prevalence of 13.1% [9]. Maximum of these cases are monochorionic twin gestation and can happen at any age of gestation [8].

The occurence of numerous pregnancy has risen recently owing to misuse of ovulation stimulation medicines and aided reproductive methods[10]. The demise of single twin happens after 24 weeks of gestation in 1.1% dichorionic twin in contrast to 3.6% of monochorionic twins. Causes of fetal death may include placental deficiency, discordant lump, congenital deformity, twin-twin transfusion syndrome, placental abruption, direct abdominal wound, etc[11]. The brutality of problems after the demise death of a twin is dependent on the age of gestation and the chorionicity at which it happened [10,12,13]. Fetal demise of a twin through the first trimester is not a rare occurrence and does not appear to damage the growth of the second twin[14]. Fetal demise in second or third trimester might elevate the chance of microcephaly, cerebral encephalomalacia, pre-eclampsia, preterm labor, and perinatal mortality [10,15-17]. Fetal demise in first trimester has less complications as the dead fetus might be completely absorbed and it is called 'vanishing twin'. But the complications are more if demise occurs during second or third trimester, especially DIC and neurological complications [12]. In majority of cases, it is difficult to know the exact time of fetal demise in utero. If the fetal death happens in the first trimester, the hazard of difficulties results is much lesser than in cases in which it happens in the second or third trimester because the demised fetus might be completely absorbed keeping no additional proof of twinning or hazard of dispersed intravascular coagulopathy, subsequent ultrasonographic test might uncover a single fetuswhich is named as the "vanishing twin syndrome" [12]. It is also a reason of notable worry and psychological anxiety to the couple. Maternal coagulopathy has been stated to happen in 3-5 weeks following fetal death[13]. Therefore, maternal clotting profile should be reassessed every 2-3 weeks when the fetal demise occurs after first trimester[18]. When intrauterine death occurs in first trimester, vanishing twin syndrome occurs and the mother may develop only minor cramping and bleeding from vagina. If this event occurs in second trimester the dead fetus becomes compressed between the developing fetus and uterine wall. Thin mummified fetus is called fetus papyraceous (FP) which may be found within the membrane or in the placenta after delivery[18]. These incidents are documented due to infrequency, best result and the ethical concerns needed during management.

Case Report:

A 20 years old woman Bristi from Keranigonj Dhaka who is in 8 weeks of pregnancy with slight lower abdominal pain came at a nearby private clinic. It was her spontaneous pregnancy without any ovulation induction or any other procedure. She had previously two missed abortions both within first trimester. Her USG was confirmed by Ultrasonogram (USG) taken on 25th November, 2017 which shows early live twin pregnancy of about 9 weeks duration and expected date of delivery given by USG on 24th June, 2018. Since then she was on regular antenatal checkup. She was advised for all antenatal investigations and took antenatal medications like folic acid, iron, and calcium supplements. Her investigations report was on normal value according to twin pregnancy. She was non-hypertensive, non-diabetic, thyroid was normal. Her Hemoglobin was 14.2 g/dl and blood group O positive.

Her antenatal period was uneventful. On 20th February, 2018 she did USG of pregnancy profile as a routine checkup but surprisingly it showed, Fetus-1: BPD- 56 mm, FL- 38 mm, AC- 182 mm, Est. fetal weight: 531 gm ± 78 gm; calculated average gestational age- about 22 weeks and 5 days. Presentation- cephalic at present. Fetus-2: Dead and

demise. BPD- 46 mm, FL- 32 mm, AC- 162 mm. Est. fetal weight: 370 gm ± 54 gm. Average gestational age of dead fetus- about 20 weeks and 3 days. Presentation- cephalic. So, ultimate impression was: Diamniotic twin pregnancy Fetus-1 is alive and about 23 weeks while F-2 was dead and demise of about 20 weeks. Expected delivery date given by USG as 21st June, 2018.

Then she came over to a tertiary care center Dhaka Central International Medical College and Hospital and consulted with her new physician (1st author). She was advised to do CRP, coagulation profile (including Blood CBC, APTT, PT, Fibrin Degradation Product (FDP), D-Dimer, S. fibrinogen level) and gave all medical support whereas there was chance of DIC (Disseminated Intravascular Coagulopathy). On 1st March, 2018 she brought all her investigations. Her hemoglobin was 11.2 g/dl. FDP 3.32 pg/ml, Fibrinogen level 326 mg/dl, Prothrombin Time (PT) 12 seconds and all other investigations were within normal level. Then her physician assured her nothing to be worried and she could continue her pregnancy. Mrs. Bristi followed her physician regularly for check up with coagulation profile and was closely monitored. She was on steroid and her dose was completed on 29th week pregnancy. Her final USG was done on 27th May, 2018, it showed twin pregnancy Fetus-1 is alive and about 36^{+} weeks. Cephalic presentation, Estimated fetal weight 3024 gm ± 442 gm while Fetus-2 was dead and demise of about 17^{+} weeks. Placental maturity Grade III.

Due to alternation of her coagulation profile (D-Dimer 3.08 µg/mL: ref range <0.5 µg/mL; FDP 14.10 pg/mL: ref range <5.0 pg/mL) her physician decided to terminate her pregnancy on 30th May, 2018 by caesarean section. On 30th May, 2018 early morning Mrs. Bristi delivered two female babies.

One baby was healthy,butanother was dead **(Figure- 1).**

Figure- 1: Pictures of newborn healthy baby and the dead fetus.

After delivery both mother and baby was in good health, had progressive recovery and was discharged after three days. The patient was counseled for postnatal checkup at 6 weeks. The infant was systematically tested by pediatrician and has been completely normal. All investigations were done on the infant including sepsis screening. Immunization are being done according to national immunization schedule.

Discussion:

Demise of a twin shows a management test to the obstetrician and has medicolegal consequences therefore precaution should be taken in deciding to provide conservative management. However, it is important that the mode of treatment offered be individualized and the hazard of conservative management must be done with the risk of preterm birth. Other investigations that could be done include fetal blood sampling which may be a useful diagnostic tool in identifying those fetuses that are not anemic and hence unlikely to be at danger of evolving a cerebral lesion especially in cases in which twin-twin transfusion syndrome is suspected [21]. There is no particular contraindication to vaginal delivery after demise of a twin.

However, some incidences may indicate caesarean section and the frequency differs significantly varying from 19 – 92%[25]. In some instances, delivery was by caesarean section, the indication in most cases being fetal heart rate irregularities[21-23]. Cord defect was detected in some of these fetuses and may have produced intrauterine hypoperfusion causing in the demise of a twin. Only an incident of one fetal decease of a twin had been stated in Nigeria in literature in spite of the high incidence of twinning. This was an instance of fetus papyraceous accidently revealed during scheduled test of the placenta and membranes after spontaneous vaginal delivery of a low birth weight (but healthy normal) infant to a primigravid mother[19]. Similar cases had been stated in other countries which were also managed conservatively until delivery[20-23].

A twin demise in the first trimester seldom makes the pregnancy complicated. The etiology of death of one fetus in twin include twin-twin transfusion syndrome, cord problems (30%), congenital anomalies (25%), growth discordance (11-12%) and placental insufficiency[18]. A twin demise in second or third trimester is an uncommon incidence and may be associated with high fetal and maternal complications[26]. Fetus papyraceous can happen in both uniovular and binovular twins which may be due to twin-twin transfusion syndrome, cord problems, placental deficiency and congenital anomalies[27]. Chief worry of fetus papyraceous is its influence on mother and living co-twin which depends on gestational age. Maternal problems comprise of preterm labor, infection from a retained fetus, severe puerperal hemorrhage, consumptive coagulopathy and hindered labor by a low-lying fetus papyraceus instigating dystocia leading to cesarean delivery. The effects on living twin comprise hazard related to cerebral palsy, congenital abnormalities (e.g. neural tube defects, optic nerve hypoplasia, unilateral absence of kidney, microcephaly, hypoxic ischemic lesions of white matter, post hydrocephalus, bilateral renal cortical necrosis, hemifacialmicrosomia, gastrointestinal tract atresia, gastroschisis, aplasia cutis)[28]. The surviving twin may be in difficult situation due to twin embolization syndrome. The emboli effects from placental and fetal thromboplastin or necrosed fragments of the deceased placenta triggering dispersed intravascular coagulation which can harm organs like brain, kidney and cause intrauterine death or premature birth [29]. However, the incidence of this complication is very low for twin pregnancies[30]. Even when it is a dichorionic placentation, microvascular connections between the two placentae cannot be totally cut off, therefore intimate fetal monitoring should be done for conservative management.

If fetus papyraceous is diagnosed antenately, then serial assessment of the living fetus (by sonography, biophysical profile, doppler and maternal coagulation factors) must be performed successively. Zygosity and chorionocity assessment must be done antenately. The scheduling and procedure for the ending the pregnancy with a living twin are decided mainly by the maturity of the fetus and kind of placenta. For dizygotic twin, danger to the surviving twin is not enhanced and impulsive start of labor at tenure can be expected by intimately supervising of maternal and fetal parameters. For monochorionic twin, hazard to living twin is substantially raised through shunt communications which can direct to DIC induced demise and organ damage[31,32]. Okamura et al.[33] found out that survival difference due to chorionocity is because of frequency of vascular connections (85-98%) in monochorionic placenta. Close supervision of the condition of the mother and surviving child is essential and the mother should be let in hospital for this purpose if required [34].

Determination of zygosity is crucial in multifetal gestation, as the danger to the fetus varies with zygosity. Incidence of death of single fetus in twin gestation in uterus is 2.7% (second trimester) and 6.7% (third trimester)[10, 35]. The fetal problems are extra for monozygotic twins[10,12-13]. A particular problem in zygosity is unusual vascular interaction, which is observed in monochorionic placenta. Not often, substantial pushes between fetuses happen

directing to acardiac twin to twin transfusion syndrome. Other complications associated with vascular communication are cerebral palsy, microcephaly, multicysticencephalomalacia caused by ischemic necrosis, leading to brain damage because of hypotension and demise of a single fetus[10]. The incidence of FP is reported as one in 17000 to 20000 pregnancies [18, 36].

The surviving co-twin however may suffer from some type of neurological damage even when findings on close fetal surveillance has been normal, hence it is advisable to perform a thorough neonatal assessment in the living twin to detect anomalies in the renal, circulatory and central nervous systems [25]. Consequences of dead fetus on the living twin are unlikely in dichorionic gestation[10]. Adverse consequences of dead fetus on the mother are rare if death occurs before 34 weeks. From dead fetus fibrin and thromboplastin are released in circulation causing DIC which is lethal for both the mother and the fetus[17]. The incidence of DIC is 25%[36]. So mother is assessed at regular interval and when pregnancy has reached up to 34 weeks, delivery should be planned[10]. Psychological support for the patient and her spouse is very important because death of a twin is a cause of great anxiety to the patient and her family. The patient remains under constant threat of the possibility of the surviving twin dying.

Here, we presented a case of intrauterine single fetal demise discovered during second semester. It was a dichorionicdiamniotic pregnancy. Both our patient and her spouse were counseled from time to time until delivery and discharge to allay their anxiety and fears. In our case the relatives were counseled and wanted to continue pregnancy. We closely monitored the patients with clotting profile and USG for fetal surveillance. The patient had completed dose of steroid. Steroid prophylaxis must be given when gestational age is less than 34 weeks to induce lung maturation. There was no cord defect seen in this case. Our patient had twice weekly biophysical profile and daily fetal kick chart to supervise the health of the living twin. In our case the surviving twin was healthy with goodbirth weight of 3024 grams. In our case, fetal death occurred in early second trimester and a thin, mummified fetus papyraceous was found attached to placenta. Placental insufficiency may be the cause in both the cases although exact cause was not possible to determine. There were noticeable musculoskeletal deformities in the deceased fetus, which may have caused from lengthy soaking and compression in utero. This case was managed conservatively up to 36+ weeks of gestation with appropriate evaluation, consultation with medicine specialist, neonatologist and counseling to the relatives. The patient was effectively supervised with superior maternal and fetal ending.

Conclusion:

Fetal death in a multiple pregnancy with one or more usually living fetus is uncommon. It is vital for reassurance to the patient that in maximum instances there is expectation of normal outcome. When patient is kept on conservative management, the intimate observation of both mother and fetus must be done. Fetal monitoring and sonographic determination of chorionocity are mandatory. It is challenging for the obstetricians to decide appropriate time and mode of delivery. It is worth-while employing conservative management after the demise of a twin. This preferably should be in a tertiary center and a multidisciplinary method should be used. Proper counseling and management can result in successful outcome.

Conflict of interest:

The author declares that there is no conflict of interest.

References:

1. Enbom JA. Twin pregnancy with intrauterine death of one twin. Am J Obstet Gynecol. 1985; 152: 424 – 429.

2. Kilby MD, Govind A, O' Brien PM. Outcome of twin pregnancies complicated by a single intrauterine death: a comparison with viable twin pregnancies. Obstet Gynecol. 1994; 84:107 – 109.

3. Woo HH, Sin SY, Tang LC. Single foetal death in twin pregnancies: review of the maternal and neonatal outcomes and management. Hong Kong Med J. 2000; 6:293 – 300.

4. Blickstein I and Perlman S. Single fetal death in twin gestations. J. Perinat. Med. 2013; 41:65–69.

5. Abasiattai AM, Umoiyoho AJ, Utuk NM, Shittu DG. Incidence and mode of delivery of twin pregnancies in Uyo, Nigeria. Niger Med J. 2010; 51:170 –172.

6. Akinboro A, Azeez MA, Bakare AA. Frequency of twinning in south-west Nigeria. Indian Journal of Human Genetics. 2008; 14(2):41 – 47.

7. Smits J, Monden C. Twinning across the developing world. PLOS ONE. 2011; 6(9): e25239.

8. Kursheed R, Ahmed A, Parveen K. Foetuspapyraceous in twin pregnancy – A case report. The Internet Journal of Gynaecology and Obstetrics. 2009; 11(2):1-3.

9. Juntao L, Jiaxin Y, Xuming B, Yu Z. Conservative management of twin pregnancy with single fetal death. Clin Med Sci J. 2000; 15(2):103 – 106.

10. Kunaal S, Bangal VB, Sai B, Rashmi S. Intrauterine Fetal Demise of Co-Twin in Multifetal Pregnancy. International Journal of Biomedical Research. 2012; 3(1):52-55.

11. Szpera-Gozdziewicz A, Dera A, Breborowicz GH. Twin Pregnancy Complicated by Intrauterine Death of One Fetus. Archives of Perinatal Medicine. 2012; 18(4):210-213.

12. Babah OA, Olamijulo A, Ayanbode OS, Sanusi MM. Conservative management of single fetal death in twin pregnancy at a tertiary health institution in southern Nigeria: a case report. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2014; 13(3): Ver. IV:79-83.

13. Divya J, Purohit RC. Review of Twin Pregnancies with Single Fetal Death: Management, Maternal and Fetal Outcome. The J Obstetgynecol India. 2014; 64(3):180-183.

14. Enbom JA. Twin Pregnancy with Intrauterine Death of One Twin. Am J Obstet Gynecol. 1985; 152:424-429.

15. Landy HJ, Weingord AB. Management of Multiple Gestation Complicated by an Antepartum Fetal Demise. ObstetGynecolSurv. 1989; 44:171-176.

16. Fusi L, Gordon H. Twin Pregnancy Complicated by Single Intrauterine Death. Problems and Outcome with Conservative Management. Br J Obstet Gynecol. 1990; 97:511-516.

17. Sonneveld SW, Correy JF. Antenatal Loss of One of Twins. Aust NZ J Obstet Gynecol. 1992; 32:1-10.

18. Haque R, Rahman MM, Akhter K. Intrauterine Single Fetal Demise in Twin Pregnancy. Delta Med Col J. Jan 2018; 6(1):53 – 57.

19. Airede LR, Ahmed Y. Fetus papyraceous: A case report. Annals of African Medicine. 2005; 4(3):136 – 138.

20. Chen CD, Ko TM, Hsieh FJ, Huang SF. Intrauterine death of co-twin in the third trimester: a case report of twin to twin transfusion syndrome and cord accident. J Formos Med Assoc. 1993; 92(7):665 – 667.

21. Preis K, Ciach K, Kowalewska-Wlas A, Wojcik D, Swiatkowska- Freundi M, Klasa-Mazurkiewicz D. Twin pregnancy with single fetal death due to triploidy – a case report. Ginekol Pol. 2005; 76(8):648 – 651.

22. Fleisch MC, Hoehn T. Intrauterine fetal death after multiple umbilical cord torsion – complication of a twin pregnancy following assisted reproduction. J Assist Reprod Genet.2008; 25(6):277 – 279.

23. Athwal S, Mallard K, Lakhoo K. Twin reversed arterial perfusion (TRAP) sequence in association with VACTERL association: a case report. Journal of Medical Case Reports. 2010; 4: 411.

24. Senat MV, Bernard JP, Loizeau S, Ville Y. Management of single fetal death in twin to twin transfusion syndrome: a role for fetal blood sampling. Ultrasound Obstet Gynecol. 2002; 20(4):360 – 363.

25. Woo HHN, Sin SY, Tang LCH. Single fetal death in twin pregnancies: review of the maternal and neonatal outcomes and management. HKMJ. 2000; 6(3):293 – 300.

26. Sahin Z, Sahin HG, Surucu R, KamaciM.Intrauterine Death of One Twin: Case Report. J Turkish German Gynecol Assoc. 2003; 4:63-65.

27. Karl WM. Intrauterine death in a twin: implications for the survivor. In: Multiple pregnancy. Ward RH, Whittle M (Eds.), RCOG Press: London. 1995;218-230.

28. Akbar M, Ikram M, Talib W, Saeed R, Saeed M. Fetus papyraceous; demise of one twin in second trimester with successful outcome of second twin at term. Professional Med J. 2005; 12:351-353.

29. Enbom JA (1985) Twin pregnancy with intrauterine death of one twin. Am J Obstet Gynecol. 1985; 152:424-429.

30. Malinowski W, Janowski J, Lokociejewski J, Rozewicki K, Tomala J. Intrauterine death of one twin in the third trimester. Ginekol Pol. 2003; 74:135-143.

31. Hagay ZJ, Mazor M, Leiberman JR. Multiple pregnancy complicated by a single intrauterine fetal death. Obstet Gynecol. 1985; 66:837-838.

32. Hagay ZJ, Mazor M, Leiberman JR, Biale Y. Management and outcome of multiple pregnancies complicated by the antenatal death of one fetus. J Reprod Med. 1986; 31:717-720.

33. Okamura K, Murotsuki J, Tanigawara S, Uehara S, Yajima A. Funipuncture for evaluation of hematologic and coagulation indices in the surviving twin following co-twin's death. Obstet Gynecol. 1994; 83:975-978.

34. Rahman H, Pathak R, Dubey S, Chavan P, Sharma BK, et al. Fetus Papyraceous in Uniovular Twin; Death of One Twin in Early Third Trimester and Successful Outcome of Other Twin at Term: A Rare Case Report. Gen Med (Los Angel). 2013; 1(4): 118.

35. Bajoria R, Kingdom J. A Case for Routine Determination of Chorionicity and Zygosity in Multiple Pregnancies. PrenatDiagn. 1997; 17:1207-1225.

36. Bozkurt M, Kara D. Fetus Papyraceus in a Twin Pregnancy: a Case Report without Any Maternal and Fetal Complications. Proceedings in Obstet and Gynecol. 2013; 3(2): 1

DCIMCJ

Case Report

DCIMCJ 2018 July;5(2):112-116

Bronchogenic Cyst in a 20-Months- Old Male Child Causing Diagnostic Dilemma: A Case Report

Islam MF[1], Chowdhury SMMH[2], Islam MN[3], Mia MMR[4], Adhikary AB[5]

Abstract:

Bronchogenic cysts of the mediastinum are congenital abnormalities that can occur in infants, children, and also in adults and are considered to be rare. It shows varying degree of presentation and occasionally may even cause death in early life by compression of the trachea or main bronchi. A case of bronchogenic cyst was incidentally detected by computed tomography scan in a 20-months-old male presenting with cough and dyspnea. The case is reported here to give an emphasis on its presentation which sometimes causes dilemma and its surgical treatment accordingly.

Keywords: Bronchogenic cyst, mediastinal mass

Introduction:

Bronchogenic cysts result from the abnormal or late budding of the ventral lung bud or the tracheobronchial tree during the process of the development. Most of the bronchial branches are formed within the 15th week of development in fetal life, but they continue to divide and completed in eighth year.[3]so a vast majority of the mediastinal cysts are congenital in origin[1]. Some arise from the developmental aberration of the primitive foregut. Cysts arising from the respiratory system are usually known as bronchogenic cysts. Those derived from the digestive tract are termed esophageal or gastric. There is no sharp line of distinction between the bronchogenic cysts and those arising from the digestive tube. Bronchogenic cyst is usually an incidental finding, so in most of the cases are asymptomatic. The cyst appears to have a well-defined margin, no enhancing with occasional calcifications. Mediastinal tumors comprise a heterogeneous group and are rarely met in clinical practice. They can be classified according to their location (Table 1) and nature. Majority of them originates from the antero-superior mediastinum (50–60%) followed by posterior (20–25%) and medial mediastinum (15–20%)[2]. Most frequently occurring are the lymphomas, which typically involve myocardium and pericardium along with neighboring tissues.

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Table- 1: Classification of mediastinal tumors according to their location [3]

Anterior mediastinum	Medial mediastinum	Posterior mediastinum
Thymomas	Cysts (bronchial, pericardial, primitive gut tube)	Neurogenic tumors
Lymphomas	Lymphomas	Esophageal tumors
Neuroendocrine tumors (goiter, parathyroid tumors)	Granulomas	
Germ cell tumors – dermoid cysts, teratomas	Metastatic tumors of lymph nodes	
Mesenchymal tumors	Castelman's disease (non - cancerous proliferation the lymphatic system cells)	
	Vascular tumors	

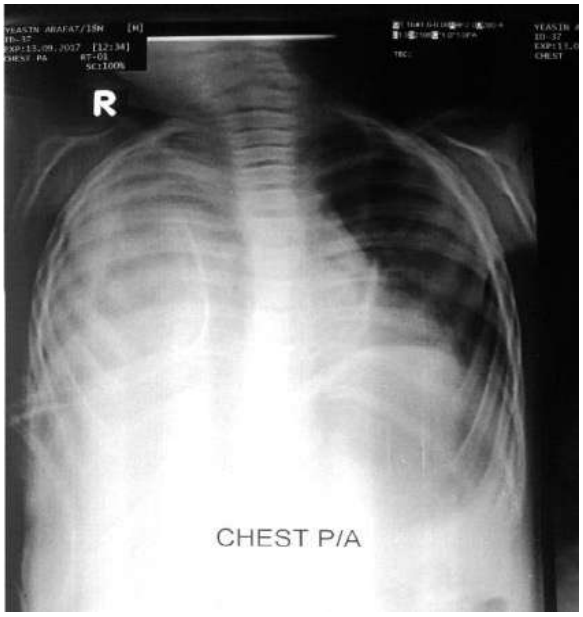

Figure-1: Pre-operative CXR giving the impression of thickened pleura with chest drain in situ.

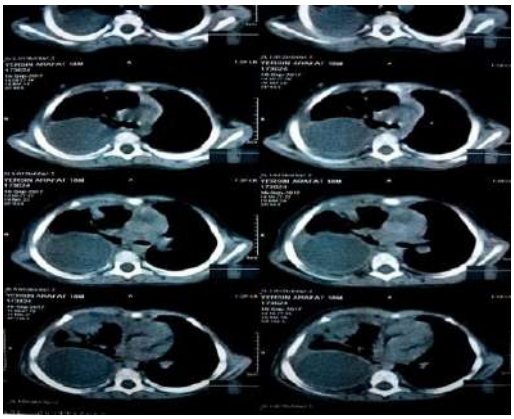

Figure-2: Encysted pleural effusion with thickened pleura

Mediastinal type bronchogenic cysts are classified into five types: paratracheal, carinal, hilar, paraoesophageal, or miscellaneous[4]. The paratracheal or carinal types can produce symptoms such as dyspnea or chest pain, due to compression of the trachea or bronchi. A giant carinal type of

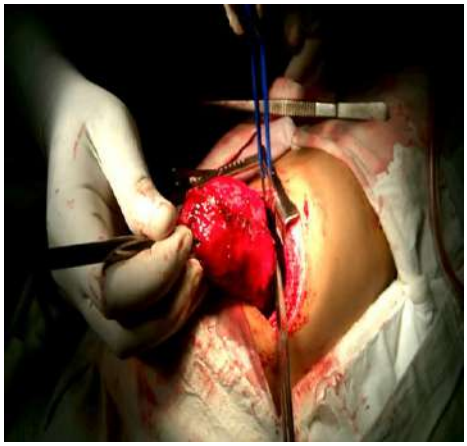

Figure- 3: Bronchogenic cyst being removed from the chest cavity.

mediastinal type bronchogenic cysts can compress the left atrium of heart due to its proximity to the heart. The cyst is lined by the ciliated, secretory respiratory epithelium with cartilage, smooth muscle, fibrous tissue and mucous glands. The bronchogenic cyst may be filled with fluid or air or both according to the communication with the tracheobronchial tree[5].

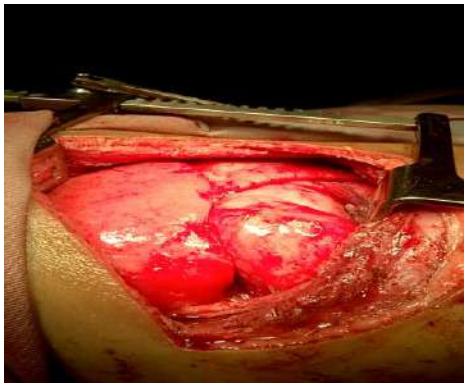

Figure- 4: Satisfactory expansion of the lung after removal of the bronchogenic cyst

Case report:

In November 2017, a 20 months old male child presented at thoracic surgery department of National Institute of Diseases of the Chest and Hospital with Cough and dyspnea for the last 3 months. Prior to admission, he was admitted at Chittagong Medical College hospital with the complaints of cough and fever for 7 days. At that time the cough was mostly dry with a few occasions of sputum production, no diurnal variation, the cough did not intensify with change of posture or subjected to dust or pollen. There was also history of fever with the highest recorded temperature of 102^0 F. The fever was not associated with chills and rigor and subsided with taking paracetamol. While examining the patient they found the vocal fremitus, vocal resonance and breath sounds to be diminished on the right side, percussion note was dull. Needle aspiration was done on September 2017 and 60 ml of turbid colored fluidcame out. So the diagnosis was made as right sided empyema thoracis.As no more collection came and with no satisfactory CXR improvement. Then the diagnosis was made, right sided encysted pleural effusion withthickened pleura and referred to NIDCH for further management. CXR gives the impression of thickened pleura [Figure 1] and CT scan of chest showed Encysted pleural effusion with thickened pleura. [Figure 2] He underwent operation in December 2017, Standard postero-lateral thoracotomy incision through right 5^{th} ICS.

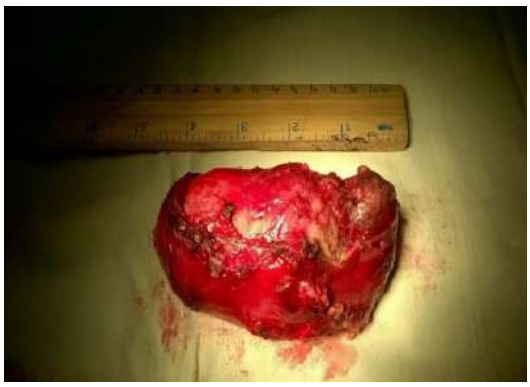

Figure -5: Excised bronchogenic cyst

A 10 x 5 cm cystic mass was found occupying the posterolateral aspect of the right chest wall separated from lung tissue. The mass compressed the right lung antero-medially. The whole pleural cavity was found sterile with no collection. Careful dissection surrounding the mass was done. The mass was found closely related to the esophagus. (esophagus confirmed by NG tube). But not connected to esophagus.

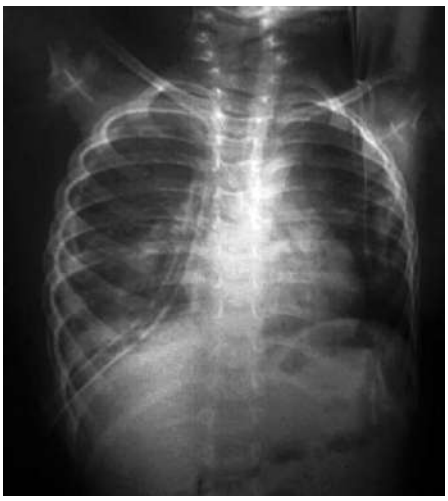

Figure 6: Post-operative CXR

Then the mass was excised and removed. [Figure 3, 4, 5] The right lung was checked for expansion. Whole of the lung expanded except part of the right lower lobe. Wedge resection of the non-expanded part was done. Thorough pleural toileting done with povidone iodine and normal saline.

A 24 Fr chest tube kept in situ. Wound closed in layers. Resected mass cut open for histopathology. Pus came out and sent for culture and sensitivity. [Figure 5]

Histopathology:

Cyst lined by pseudostratified ciliated columnar epithelium with focal ulceration. The cyst wall is made up of fibromascular tissue.

Diagnosis:

Bronchial mediastinal cyst.

Discussion:

The initial workup of a mediastinal mass includes chest x rays, CT of the chest with iodinated contrast medium in patients with normal renal function. Other examinations, such as barium swallow, CT angiography, magnetic resonance imaging (MRI), can also be used to further characterize a mediastinal mass.

Bronchogenic cysts result from abnormal budding from the perimeter of the trachea after it has differentiated from the foregut. They are the most frequent cysts of the mediastinum, accounting for approximately 60% of these lesions. Male are more frequently affected than female (1:0.75). They usually affect infants, children, or young adults but can also be found in older individuals. They may be hilar, attached to a lobar bronchus, and occasionally they are intrapulmonary or may also be situated below the diaphragm or in the parasternal subcutaneous tissue, skin, or pericardium[6].

In our case, the mass was para esophageal, situated at the posterolateral aspect of the right chest wall, separated from esophagus. The cyst is commonly unilocular and usually measure 2 to 10 cm. The cyst we operated measured approx. 10 x 5 cm and also unilocular. The presentation of the bronchogenic cyst is variable, making pre-operative diagnosis difficult. Majority of them are either asymptomatic or discovered incidentally. The most common presenting symptoms are cough, fever and dyspnea like in our patient which is also supported by study of others.

Chest X-ray usually shows homogenous opacity in the middle and lower zones which supports our findings. CT typically demonstrates a round, smoothly marginated, homogeneous lesion with imperceptible walls. The CT scan density is variable, reflecting the composition of the cyst content, which may be serous, hemorrhagic, or highly viscous. Approximately half are filled with serous fluid and therefore have characteristic water attenuation (0-20 HU). Cysts containing proteinaceous fluid may be difficult to differentiate from a solid mass on CT[7].

The cystic nature may be demonstrated on CT by the lack of enhancement after IV administration of contrast. MRI is indicated in those cases in which the cystic nature cannot be determined on CT scans or IV iodine contrast is contraindicated[8]. Our patient showed features suggestive of right sided Encysted pleural effusion in CT scan. MRI was not performed. The differential diagnosis of bronchogenic cyst includes foregut or pericardial cysts, encysted pleural effusion, pulmonary sequestrations, teratoma, hemangioma, hamartoma and neurogenic tumors.

We prepared the patient for operation keeping these differential diagnoses in mind, with encysted pleural effusion, mediastinal cyst and neurogenic tumors were top of the list. Bronchogenic cysts should be excised completely, if possible. If there is a stalk, it is ligated, and the bronchial defect is repaired. Asymptomatic cysts should be removed for diagnosis and to prevent complications associated with the natural history of these cysts, including perforation, hemorrhage, enlargement, infection, and malignant degeneration[9].

In children, the airways are pliable and much more susceptible to life-threatening compression by an enlarging cyst. In this patient the mass was excised as a whole, no definitive stalk was found but a rudimentary connection with lung tissue seen without any bronchial defect. A part of right lower lobe was

non-expanded by PPV and wedge resection of the non-expanded part was done. Histologically, Bronchogenic Cysts are lined by ciliated pseudostratifid columnar epithelium interspersed with goblet cells which is consistent with our histological finding. They may also contain normal bronchial elements, including cartilage and smooth muscle.

Malignant degeneration has been reported, including an adenocarcinoma in an 8 ½ year-old girl, incidence altogether is very rare[10]. No malignant changes were seen in histological findings. The patient had an uneventful intra operative and postoperative period with symptomatic improvement. He was shifted from post-operative ward to general ward on the 4th post-operative day and currently recovering as expected.

Conclusion:

The bronchogenic cysts are rare mediastinal mass which are very much important, in treatment point ofview. The diagnosis itself is quite arbitrary and often poses a diagnostic dilemma. The patient was subjected to tube thotacostomy twice owing to such conditions. Any encysted collection in young patients should be considered congenital along with other infective causes as differential diagnosis. Surgical option should be exercision as a definitive procedure in all cases of bronchogenic cysts to avoid development of complications.

References:

1. Carlson, H, A Congenital Cysts of the Mediastinum. J. Thoracic Surg. 1943;12: 376.
2. Jablonski S, Brocki M. Guzysrodpiersia (online) Wielkainterna –pulmonologia.
3. Schmidt FE, Drapanas T. Congenital cystic lesions of the bronchi and lungs. Ann ThoracSurg, 1972 ;14(6):650-7.
4. Mawatari T, Itoh T, Hachiro Y, et al. Large bronchial cyst causing compression of the left atrium. Ann Thorac Cardiovasc Surg. 2003 ;9(4):261-3.
5. Harvey S. Mediastinum. In: Computed Body Tomography with MRI correlations (Joseph KT., Lee MD, et al, eds). Lippincott Williams and Wilkins, Philadelphia. 1998;271-72.
6. Sellke FW, del Nido PJ: Mediastinum. Sabiston& spencer, Surgery of the chest, 9th ed:697-745.
7. Patterson GA, Cooper JD, Deslauriers J: Pearson's thoracic & esophageal surgery, 3rd ed:1497-1503.
8. Bolton JW, Shahian DM: Asymptomatic bronchogenic cysts: what is the best management? Ann ThoracSurg. 1992; 53(6):1134–1137.
9. Suen HC, Mathisen DJ, Grillo HC, et al: Surgical management and radiological characteristics of bronchogenic cysts. Ann ThoracSurg. 1993; 55(2):476–481.
10. Duwe BV, Sterman DH, Musani AI: Tumors of the mediastinum. Chest. 2005; 128:2893-2909.

DCIMCJ

Case Report

DCIMCJ 2018 July;5(2):117-119

Takayasu'sArteritis Presenting as Ischaemic Stroke in a 17-Year- Old Girl

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Abstract:

Takayasu's Arteritis is a large vessel vasculitis that primarily affects aorta and its branches[1]. Stroke as the initial presentation in patients with Takayasu's arteritis is rarely reported. Here we report the case of a 17 years old girl presented with ischaemic stroke with right sided hemiparesis with aphasia . Her left sided radial pulse was absent and blood pressure could not be measured in left upper limb.Ischemic stroke due to Takayasu's arteritis was diagnosed on the basis of acute phase response, microcytic hypochromic anemia, CT head and CT angiogram of aortic arch and its branches.

Keywords: Takayasu's arteritis, stroke, vasculits

Introduction:

Takayasu's arteritis is a rare, systemic, inflammatory large-vessel vasculitis of unknown aetiology that most commonly affects women of childbearing age[1]. It is defined as granulomatous inflammation of the aorta and its major branches[2]. It is most commonly seen in Japan, Southeast Asia, India and Mexico. It predominantly affects women in their second to third decade of life1[2]. During the progressive phase with fibrosis and thickening of the arterial wall, transient ischemic attack and stroke occur in 10 to 20% patients[1].

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Case report:

A 17– year- old girl presented with history of sudden onset right-sided weakness and inability to talk. She had no history of headache or trauma. There was no history of rheumatic fever or valvular heart disease. On examination there was pallor, right carotid bruit, expressive aphasia, right hemiparesis, hyperreflexia and extensor plantar response on the right. Base line investigations revealed mild microcytic hypochromic anemia, high erythrocyte sedimentation rate (ESR), C reactive protein(CRP). CT head showed left middle cerebral artery territory infarct .The echocardiogram was normal but duplex study of left upper limb showed 70-80 % stenosis of left subclavian artery and an adherent thrombus . Duplex study of both carotid artery revealed 60-70% stenosis of left common carotid artery . CT angiogram of arch of aorta and its major branches showed complete occlusion of Ist part of subclavian artery and 6.7 cm occlusion of left common carotid artery. She was treated withanoxaparin, warfarin, steroid and azathioprine. She was under regular physiotherapy. She improved clinically after 7 days.

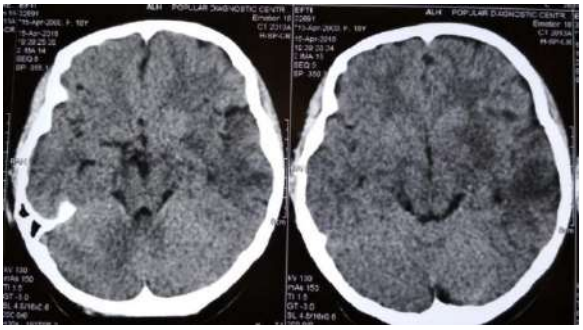

Figure- 1: CT head revealed hypodensity at the left middle cerebral artery territory

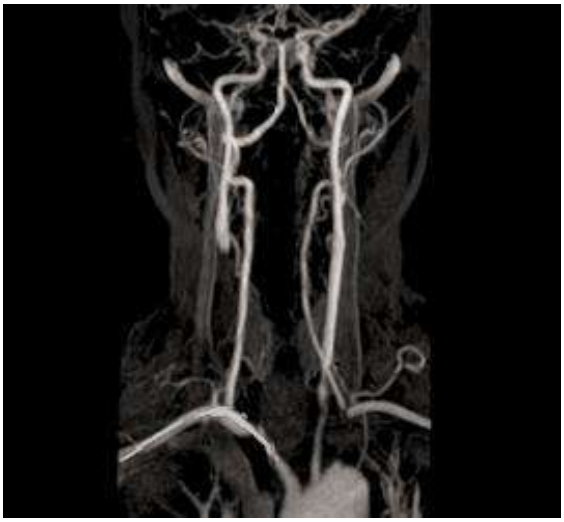

Figure-2: Magnetic resonance angiography revealed occlusion of left common carotid and left subclavian artery

Discussion:

Takayasu's arteritis is achrionic granulomatous vasculitis that primarily affects the aorta and its main branches[1].Vascular inflammation can cause stenosis,occlusion and aneurism formation[2].It is a rare disease and was first reported in 1905 by Mikito Takayasu[3]. It is most common in Japan[4]. Women are most commonly affected and it occurs in the second and third decades of life. Diminished or absent pulses and hypertension arecommon.

Most patients initially present with non-specific symptoms, such as fever, malaise and arthralgia[5]. Neurological manifestations are common in the chronic phase. It includes dizziness, visual disturbance, headache, transient ischemic attack, ischemic stroke, seizures[4]. Stroke as the initial presentation is rarely described in the literature the exact aetiology of ischemic stroke in Takayasu's arteritis remains unclear. Reduced cerebral blood flow from the stenotic or occlusive lesion in the aortic arch and its main branches may be responsible for ischaemic stroke in most patients[2]. Most of the lesions were located at middle cerebral artery territory[5]. Several criteria for the diagnosis of Takayasu's arteritis were proposed by the American College of Rheumatology in 1990. Six criteria were selected: age of onset less than 40 years, claudication of an extremity, decreased brachial artery pulse, >10 mm Hg difference in systolic blood pressure between arms, a bruit over the subclavian arteries or the aorta, and arteriographic evidence of narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities[6]. The presence of three of the six criteria is required. However, because of the rarity of Takayasu's arteritis, the diagnosis and treatment may be delayed, especially when neurological manifestation such as stroke occurs as an initial presentation[7]. A high index of suspicion should arise when stroke develops in young patients with asymmetrical pulses and blood pressure, and there is presence of systemic symptoms, claudication of limbs, and elevated ESR,CRP[8,9]. In our patient, asymmetry of blood pressure in the upper limbs and the lack of pulse at the distal arteries were seen. Steroid is the mainstay of treatment for Takayasu's arteritis[10]. Cytotoxic drugs, including cyclophosphamide, azathioprine, and methotrexate have been used to treat such patients[11]. However, when acute vascular compromise such as stroke occurs, thrombolytic, surgical or interventional revascularization can be considered[12].

References:

1. Kerr GS, Hallahan CW, Giordano J, Leavitt RY, Fauci AS, Rottem, et al. Takayasus Arteritis. Ann Intern Med. 1994;120:919-29.

2. Jain S1, Kumari S, Ganguly NK, Sharma BK. Current status of Takayasu Arteritis in India. Int J Cardiol. 1996;54: 111-16.

3. Park KC, Kim JH, Yoon SS, Heo SH. Takayasu's disease presenting with atherothrombotic ischaemic stroke. NeurolSci. 2008;29:363-6.

4. Klos K, Flemming KD, Petty GW, Luthra HS. Takayasu's arteritis with arteriographic evidence of intracranial vessel involvement. Neurology. 2003;60:1550-1.

5. Khealani BA, Baig SM. Takayasu's arteritis presenting as ischemic stroke--case report. J PakMedAssoc 2002;52:263-5.

6. Sikaroodi H, Motamedi M, Kahnooji H, Gholamrezanezhad A, Yousefi N. Stroke as the first manifestation of Takayasu's arteritis. ActaNeurol Belg. 2007;107:18-21.

7. Numano F, Okawara M, Inomata H, Kobayashi Y.Takayasu's arteritis. Lancet. 2000;356:1023-5.

8. Arend WP, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum. 1990;33:1129-34.

9. Li-xin Z, Jun N, Shan G, Bin P, Li-ying C. Neurological manifestations of Takayasuarteritis.Chin Med Sci J. 2011;26:227-30.

10. Cantu C, Pineda C, Barinagarrementeria F, Salgado P, Gurza A, Paola de Pablo, et al. Noninvasive cerebrovascular assessment of Takayasu arteritis. Stroke. 2000;31:2197-202.

11. Hoffmann M, Corr P, Robbs J. Cerebrovascular findings in Takayasu disease. J Neuroimaging. 2000;10:84-90.

12. Hwang J, Kim SJ, Bang OY, Chung CS, Lee KH, Kim DK, et al. Ischemic stroke in Takayasu's arteritis: lesion patterns and possible mechanisms. J ClinNeurol. 2012;8:109-15.

Medical Quiz

DCIMCJ 2018 July; 5(2):120-121

Medical Quiz: Images

Mamun KAA[1]

A 12 years old boy presented with unsteady gait, slurred speech, headache, poor school performance, epilepsy and involuntary movement in the form of tremor . He was suggested CT head and EEG.

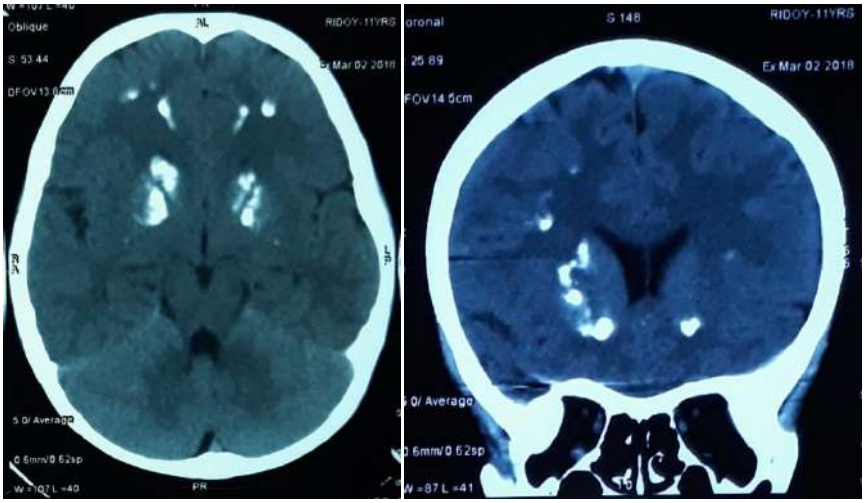

Figure 1: CT Head

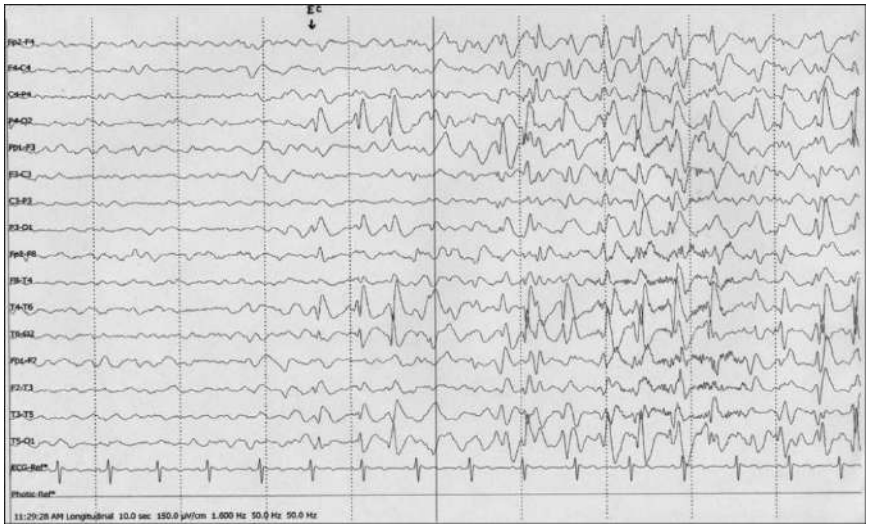

Figure 2:EEG

- **Q1. Mention abnormal findings in CT head.**
- **Q2. Mention abnormal findings in EEG.**
- **Q3. What other investigations should be done?**
- **Q4. What is the diagnosis?**
- **Q5. What are the differential diagnosis?**

Answer to Medical Quiz: Images:

1. This is CT head showing bilateral extensive calcifications in basal ganglia and subcortical white matter .
2. EEG shows focal epileptiform discharge with secondary generalization.
3. Serum calcium, phosphate and parathormone level.
4. Fahr's disease.
5. Differentials include hypoparathyroidism, pseudohypoparathyroidism and hyperparathyroidism.

Idiopathic basal ganglia calcification, also known as Fahr's disease, is a rare, autosomal dominant, neurologicaldisorder characterized by abnormal calcifications primarily in the basal ganglia and in other areas of cerebral cortex.[1] The disease usually manifests in the third to fifth decade but may appear in childhood or later in life.[2]It usually presents with clumsiness, unsteady gait, slow or slurred speech,headache, involuntary movement and seizures[1] . Neuropsychiatric symptoms may range from mild difficulty with concentration and memory , changes in personality andbehaviour, to psychosis and dementia.[2] However, the sites of calcification are not specific and a similar pattern may be found in hypoparathyroidism, pseudohypoparathyroidism and hyperparathyroidism.[3] Normal calcium, phosphate and parathormone levels in Fahr's disease aid in diagnosis.[1,2] There is currently no cure for Fahr's Syndrome. The available treatment is directed towards symptomatic control[2]. If parkinsonian features develop, there is generally poor response to levodopa therapy. Haloperidol or lithium carbonate may be used for psychosis and anticonvulsants are used for seizure control[4].

References:

1. Sinha R, Sodhi K, John BM, Singh D et al. Fahr's Disease: A Case Report. Nepal Paed Society J.2010 ;30(1)44-45 .
2. Ghormode D, Maheshwari U, Kate N, etal. Fahs disease and psychiatric syndromes: a case series. Ind Psychiatry J 2011;20:136–8.
3. Hegde AN, Mohan S, Lath N, et al. Differential diagnosis for bilateral abnormalities of the basal ganglia and thalamus. Radiographics 2011;31:5–30.
4. Chiu HF, Lam LC, Shum PP, Li KW. Idiopathic calcification of the basal ganglia. Postgrad Med J. 1993; 69 (807): 68–70.