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Editor-in-Chief, Journal of Bangladesh College of Physicians and Surgeons, BCPS Bhaban, 67, Shaheed Tajuddin Ahmed Sarani
Mohakhali, Dhaka-1212, Tel : 8825005-6, 8856616, 9884189, 9884194, 9891865 Ext. 124, Fax : 880-2-8828928,
E-mail : <bcps@bcps-bd.org> Editor's e-mail: journal.bcps@gmail.com

Journal of Bangladesh College of Physicians and Surgeons (JBCPS)

INFORMATION FOR AUTHORS

MANUSCRIPT PREPARATION AND SUBMISSION

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Editor-in-Chief
Prof. Khan Abul Kalam Azad
BCPS Bhaban
67 Shaheed Tajuddin Sarani
Mohakhali, Dhaka 1212,
BANGLADESH
Phone: +8802-8825005 +8802-8825005
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The **cover letter** should include the corresponding author's full address and telephone/fax numbers and should be in an e-mail message sent to the editor, with the file, whose name should begin with the first author's surname, as an attachment.

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Article Types

FIve types of manuscripts may be submitted:

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

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

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Review Process:

All manuscripts are initially screened by editor and sent to selective reviewer. Decisions will be made as

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I. A. Preparing a Manuscript for Submission to JBCPS

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

Conditions for submission of manuscript:

- All manuscripts are subject to peer-review.
- Manuscripts are received with the explicit understanding that they are not under simultaneous consideration by any other publication.
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- Permission of the patients and/or their families to reproduce photographs of the patients where identity is not disguised should be sent with the manuscript. Otherwise the identity will be blackened out.

Preparation of manuscript:

Criteria: Information provided in the manuscript are important and likely to be of interest to an international readership.

Preparation:

1. Manuscript should be written in English and typed on one side of A4 (290 x 210cm) size white paper.
2. Margin should be 5 cm for the header and 2.5 cm for the remainder.
3. Style should be that of modified Vancouver.
4. Each of the following section should begin on separate page :
   - o Title page
   - o Summary/abstract
   - o Text
   - o Acknowledgement
   - o References
   - o Tables and legends.

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

I. A. 1. a. General Principles

- The text of observational and experimental articles is usually (but not necessarily) divided into the following sections: Introduction, Methods, Results, and Discussion. This so-called "IMRAD" structure is a direct reflection of the process of scientific discovery.
- Long articles may need subheadings within some sections (especially Results and Discussion) to clarify their content. Other types of articles, such as case reports, reviews, and editorials, probably need to be formatted differently.
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- Double-spacing all portions of the manuscript—including the title page, abstract, text, acknowledgments, references, individual tables, and

legends—and generous margins make it possible for editors and reviewers to edit the text line by line and add comments and queries directly on the paper copy.

- If manuscripts are submitted electronically, the files should be double-spaced to facilitate printing for reviewing and editing.
- Authors should number on right upper all of the pages of the manuscript consecutively, beginning with the title page, to facilitate the editorial process.

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

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- Structured abstracts are essential for original research and systematic reviews. structured abstract means introduction, methods, results and conclusion in abstract
- Should be limited to 250 words
- The abstract should provide the introduction of the study and blinded state and should state the study's purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect sizes and their statistical significance, if possible), principal conclusions. It should emphasize new and important aspects of the study or observations. Articles on clinical trials should contain abstracts that include the items that the CONSORT group has identified as essential (http:// www.consort-statement.org).
- Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to be careful that they accurately reflect the content of the article

I. A. 5. Introduction

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

I. A. 6. Methods

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

I. A. 6. a. Selection and Description of Participants

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

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

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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).
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- Present results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Please keep the result the sequence of specific objective selected earlier.
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- Emphasize the new and important aspects of the study and the conclusions that follow from them in the context of the totality of the best available evidence.
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- Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses when warranted, but label them clearly as such.

I. A. 9. References

I. A. 9. a. General Considerations Related to References

- Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible.
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- References should be numbered consecutively in the order in which they are first mentioned in the text.
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- Tables capture information concisely and display it efficiently.

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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 abbreviations in footnotes, and use the following symbols, in sequence:

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

Check Lists

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

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2. Authorship and conflicts of interest form
3. Manuscript
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- General outline for article presentation and format
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    - Δ Font size should be 12 in arial
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    - Δ Title page contains all the desired information (vide supra)
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    - Δ Complete title of your article
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  - Δ Do not use subheadings in the abstract
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  - Δ Key words provided – arrange them in alphabetical order (three – five)
- **Introduction**
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  - Δ Pertinent information only
- **Material and Methods**
  - Δ Study Design
  - Δ Duration and place of study
  - Δ Ethical approval
  - Δ Patient consent
  - Δ Statistical analysis and software used.
- **Result**
  - Δ Clearly present the data
  - Δ Avoid data redundancy
  - Δ Use table information at the end of the sentence before full stop between the small bracket
- **Discussion**
  - Δ Avoid unnecessary explanation of someone else work unless it is very relevant to the study
  - Δ Provide and discuss with the literatures to support the study
  - Δ Mention about limitation of your study
- **Conclusion**
  - Δ Give your conclusion
  - Δ Any recommendation
- **Acknowledgement**
  - Δ Acknowledge any person or institute who have helped for the study
- **Reference**
  - Δ Abide by the Vancouver style
  - Δ Use reference at the end of the sentence after the full stop with superscript
- **Legends**
  - Δ Table
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Vol. 35, No. 1, Page 1-47 **January 2017**

CONTENTS

EDITORIAL

Treatment of Hypertension in Adults Above the Age of 60

Treating hypertension is a day to day duty of any physician. But when it comes to treat hypertension in elderly patients, especially above the age of 60, achieving the target BP becomes difficult. Because of multiple co-morbidities and use of concomitant different kind of medications, very often, a single anti-hypertensive agent often fails to achieve the goal. Joint National Committee (JNC) publishes the guideline for hypertension management for several years and the latest one in JNC 8. In that also, the difficulty of treating hypertension in elderly patients have been mentioned.

In this editorial, we intend to focus on the latest updates as well as the modified target BP for elderly patients. — The American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) have published an evidence-based clinical practice guideline on the appropriate systolic blood pressure target for adults 60 years old and older with hypertension very recently[1].

Hypertension, an elevation of systemic arterial blood pressure, is one of the most common chronic diseases in the United States. About 65 percent of adults in the U.S. over the age of 60 have hypertension, and the disease affects about 29 percent of all adults in the nation. We have no such national data in our country. ACP and AAFP recommend that physicians initiate treatment in adults aged 60 years old and older with persistent systolic blood pressure at or above 150 millimeters of mercury (mm Hg) to achieve a target systolic blood pressure of less than 150 mm Hg to reduce the risk of mortality, stroke, and cardiac events. Most benefits of targeting of less than 150 mm Hg apply to individuals regardless of whether or not they have diabetes. Appropriate management of hypertension reduces the risk for cardiovascular disease, renal disease, cerebrovascular disease, and death. However, determining the most appropriate BP targets, particularly for adults aged 60 years or older, has been controversial. Debate about the goal for systolic BP (SBP) among adults treated for hypertension has intensified, especially in light of recent recommendations. In addition, when selecting BP targets for adults aged 60 years or older, clinicians need to consider comorbid conditions that could affect treatment choice. Treatments for hypertension include lifestyle modifications, such as weight loss, dietary modification, and increased physical activity, and antihypertensive medications, which commonly include thiazide-type diuretics, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin-receptor blockers (ARBs), calcium-channel blockers, and β-blockers.

JNC 8 also suggested in patients 60 years or over, start treatment in blood pressures >150 mm Hg systolic or >90 mm Hg diastolic and treat to under those thresholds[2].

The ACP/AA FP guideline notes that some patients may have falsely elevated readings in clinical settings ("white coat hypertension"). Therefore, it is important for physicians to ensure that they are accurately measuring blood pressure before initiating or changing treatment for hypertension. The most accurate measurements come from multiple blood pressure measurements made over time. These may include multiple measurements in clinical settings or ambulatory or home-monitoring.

The guideline emphasize on two recommendations:
ACP and AAFP recommend that physicians consider initiating or intensifying drug therapy in adults aged 60 years old and older with a history of stroke or transient ischemic attack to achieve a target systolic blood pressure of less than 140 mm Hg to reduce the risk of recurrent stroke.

ACP and AAFP recommend that physicians consider initiating or intensifying pharmacological treatment in some adults aged 60 years old and older at high cardiovascular risk, based on individualized assessment, to achieve a target systolic blood pressure of less than 140 mm Hg to reduce the risk of stroke or cardiac events.

Increased cardiovascular risk includes all people with known vascular disease and among others, is defined as most patients with diabetes, individuals with chronic kidney disease with estimated glomerular filtration rate (eGFR) <45 mL/min/per 1.73 m2, metabolic syndrome (abdominal obesity, hypertension, diabetes, and dyslipidemia), and older age.

Whatever the guidelines describe every patient has separate merit in elderly as because of their co morbid conditions. A physician should weigh the risk versus benefit in all case management of treating hypertensive patients.

(J Bangladesh Coll Phys Surg 2017; 35: 1-2)

Prof. Quazi Tarikul Islam
Professor of Medicine
Popular Medical College

Referrences:

1. Qaseem A ,Wilt TJ, Ritch R , Humphrey LL et al. A clinical practice guideline from American College of Physicians and American Academy of Family Physicians; *Ann Intern Med* ,144(2):2017
2. JNC 8 Guidelines for the Management of Hypertension in Adults. *Am Fam Physician*. 2014 Oct 1;90(7):503-504

Effect of Low Dose Oral Contraceptive Pill on Coagulation Status in Women with Normal and Low Body Mass Index

SB KASEM[a], TA CHOUDHURY[b], SA RAZZAQUE[c], F BEGUM[d], R ADIBA[e], S ANIKA[f]

Summary:

Background: Oral contraceptive pill (OCP) is widely used by millions of women of various socioeconomic conditions.Use of low dose oestrogen and newer progesterone in OCP now associated with less thromboembolic and cardiovascular risk. The safety aspects of these pills had not been investigated in details in malnourished women of developing countries. In the present study the effects of the pillson coagulation status have been studied.

Objective: To explore the effect of the most widely used low dose OCP (Shukhi) on coagulation status of Bangladeshi women with normal and low BMI(Body Mass Index).

Materials and Methods: The study population group (n=29) comprised of women with normal BMI and the underweight group (n=11,BMI<18.5). Both groups use low dose OCP(30µg ethinyl estradiol and 150µg levonorgestrel) for 6-60 months.

The coagulation status were assessed as follows: Plasma Fibrinogen, Prothrombin time and Platlete aggregation and Anticoagulation statuseg: AntithrombinIII (ATIII).

Result:Coagulation status showed no significant difference in platelet aggregation between the groups. Plasma fibrinogen median value (450mg/dl) just exceeded the upper limit of reference range (normal range: 200-400mg/dl) in normal BMI. In contrast, the corresponding value in the low BMI (318mg/dl) group was almost at the middle of the reference range. A significantly prolonged prothrombin time (13.80 seconds) was found in the low BMI group (p=0.058); values were still within the reference range (10-14 seconds). No significant correlation existed between plasma fibrinogen, prothrombin time and platelet aggregation in normal BMI or low BMI groups. Antithrombin IIIactivity in normal BMI group was 108% and in low BMI group it was 105%. Atendency of positive correlation existed between antithrombin III activity and BMI in low BMI pill users (r=0.591,p=0.072).

Conclusion:The study suggested that a) Reported risk of procoagulant or thromboembolic changes in pill users is lower in low BMI &normal BMI and b) Low BMI users showed significantly longer prothrombin time due to the effect of malnutrition itself or due to the effect of pills in this nutritional background.

Keywords: Low dose OCP, Coagulation status, Normal and low BMI women.

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Introduction:

OCP (combined) are very important component of family planning program. It is one of the effective methods of contraception and is well accepted by women ofvarious socioeconomic conditions. Millions of women use these drugs. So questions regarding the safety of these agents are important.

A number of side effects were encountered by the users. These included nausea, vomiting, dizziness, metabolic disorders such as hypertention, diabetes and thromboembolic manifestations in the form of pulmonary embolism, leg vein thrombosis, coronary thrombosis and thus the estrogen component of the OCP was initially implicatedin the pill-induced thromboembolic side effects[1,2]. But later it was shown that the gestagen componenttoo played a vital role in enhancing cardiovascular side effects[3,4]. The introduction of low dose OCP with 30µg estrogens was a step in the right direction but further reduction resulted in breakthrough bleeding[5].

The Dunlop committee for the safety of drugs in UK issued a declaration linking the estrogenic component

a. Dr.Setara Binte Kasem, Assistant Professor (Gynae& obstetrics), Sir Salimullah Medical College.

b. Prof. TA Chowdhury, Professor & Head of the Dept of Gynae and Obstetrics, Ibrahim Medical College, Dhaka.

c. Dr. Shaikh Abdur Razzaque, Associate Professor (Paediatric Cardiology), National Institute of Cardiovascular diseases.

d. Dr. Ferdousi Begum, Professor (Gynae&Obs), Ibrahim Medical College, Dhaka.

e. Dr. RaisaAdiba, Resident surgeon, Holly Family Red Crescent Medical College.

f. Dr. Selma Anika, Third year student, Bangladesh Medical College.

Address of Correspondence: Dr. Setara Binte Kasem, Assistant Professor (Gynae & Obstetrics), Sir Salimullah Medical College. Mob-01552314895, Email-dr.setaraa@gmail.com.

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of the pill with the risk of venous thrombosis. Consequently the doses of estrogen in the pill were reduced again and again until affecting contraceptive efficacy. As a result, the risks which were attributed to high estrogen content such as venous thrombosis, hypertension, diabetes etc were reduced. This was confirmed by the Royal College of general practitioners and the Walnat Creek Contraceptive drug study[6].

However, such low doses was possible primarily because highly effective and more specific progestogen such as levonorgestrel, desogestrel, gestadene, norgestimateetc were developed and introduced. The development of Levonorgestrel and third generation progestogens were potentially responsible for reducing severe cardiovascular side effects[7].

Several retrospective and prospective studies have suggested the existence of an increased risk of cardiovascular diseases, in particular venous thromboembolism, pulmonary embolism, myocardial infarction (MI) and hemorrhagic stroke in users of OCP a risk possibly related to the dose of estrogen[8,9,10]. It has been suggested that adhesiveness of blood platelets to a glass surface was greater in women than in man in the presence of a histone like substance derived from human brain, the adhesiveness of platelets were increased in woman because of OCP therapy[11].

A comparisonof Japanese and American women using OCP, concluded that the effect on the fibrinolytic system were considerably better among the Japanese women than among the Americans, indicating a decreased risk of cerebral thrombosis in Japanese women[12].

Antithrombin III (AT III) activity fell significantly during OCP useand the estrogen component was blamed for the fall[13,14]. Low serum ATIII activity was observed in patients with pulmonary embolism,MI and venous thrombosis. The use of low estrogen pill resulted in a significant reduction in the number of thromboembolic episodes and the reduction was found to be limited in venous thromboembolism[15].

Effect of OCP on Caucasian woman was studied and observed acceleration of the procoagulants in extrinsic and intrinsic clotting systems and reduction of the plasma AT III levels, indicating some imbalance of the hemostatic mechanism towards hypercoagulability. These changes increased with the duration of therapy and took some months to resolve when OCP were withdrawn. OCP should be avoided by woman with established cardiovascular disease or with cardiovascular risk factors, irrespective of age[16].They further suggested that OCP appear to unsuitable method of contraception even for healthy and nonsmoker women over 40 years of age.

A large number of Bangladeshi women of various socioeconomic status are using low dose OCP. There are different types of combined low dose OCP used by the Bangladeshi women eg: Shukhi$^{(R)}$, Femicon$^{(R)}$, Nordette-28$^{(R)}$ and Marvelon$^{(R)}$.All these OCPs contain 30µg of ethinyl estradiol, but their progestogen component varies.

Shukhi is mostly used by the women of low socio-economic status, because the family planning program of the government of Bangladesh has made it available to them free of cost. Studiesshows that newer combined low dose OCPs cause less upset in metabolic and coagulation parameters as it contains 30µg of ethinyl estradiol (EE)[17,18]. But these need to be confirmed in Bangladeshi population with low BMI as it is well known that diet and life style can affect pill induced changes in hepatic protein synthesis.Safety of OCP has not been studied in low BMI undernourished Bangladeshi women.Due to protein deficiencies in these low BMI groups there may be different biological response in these women resulting in different risk profile.

Materials and Method:

The study was conducted at the Department of Cell and Molecular Biology, Research Division, Bangladesh Institute of Research and Rehabilitation in Diabetes, endocrine and Metabolic disorders (BIRDEM) during the period of Jan2001 to Dec 2001.The patients were collected from family planning centre, Dhaka Medical college Hospital (DMCH). A total number of 40 women were included in this study having age range between 25-45 years. 29 were with normal BMI (>18.5) and 11 were with low BMI (<18.5) consuming Shukhi for six months to five years. Patients who were normotensive with no coexisting medical disorders were included. Patients who were hypertensive, diabetic, smoker, alcoholic and obese (BMI >30) were excluded.

Subjects: After taking consent of the patient blood samples were collected and plasma/serum were stored at -70C for biochemical analysis. The coagulation factorswere assessed as follows: Coagulation status–

(P Fibrinogen, Prothrombin time and Platlet aggregation) and anticoagulation status –Antithrombin III (ATIII).

Laboratory methods: Plasma fibrinogenwas estimatedby clotting method; Prothrombin time by using SimplastinExcel; Platelet aggregation by optical aggregometry and Antithrombin III was estimated by amidolytic method using a synthetic chromogenic substrate.

All statistical analysis were done by using SPSS. Results were expressed as median (range).The statistical comparison between the groups were done by Mann-Whitney test. Difference betweenBMI and other parameters were analysed by Pearson's correlation coefficient test. P value <0.05 was taken as level of significance.

Different groups discussed are as follows:

1. Clinical features (Age, BMI, Duration of pill use) of Normal BMI and low BMI study subjects.
2. Coagulation status (eg: Platelet aggregation, Plasma fibrinogen and Prothrombin time)of Normal BMI and low BMI study subjects.
3. Coagulation status among the Normal BMI andlow BMI study subjects with the same duration of OCP use (<24 months).
4. Antithrombin III activity of Normal BMI and low BMI study subjects.
5. Pearson correlation coefficient between BMI and coagulation status (Platelet aggregation, Fibrinogen, Prothrombin time) and Antithrombin III.
6. Pearson correlation coefficient between plasma fibrinogen and Antithrombin III in Normal and Low BMI Group.

Results:

1.Clinical features of different groups of the study subjects shown inTable I. No significant difference was observed in clinical features of different groups.

2.Coagulation status-Platelet aggregation, Plasma fibrinogen, Prothrombin time of study subjects. There was no statistically significant difference in platelet aggregation (p=0.387) and plasma fibrinogen level (p=0.332) between the Normal BMI and Low BMI groups studied .

3. There is significant difference in prothrombin time between the two groups (p=0.019), and significantly prolonged prothrombin time was noted among the Low BMI pill users (Table-III)

4.Antithrombin III activity of the study subjects.There was no statistically significant difference found in plasma antithrombin III activity between Normal and Low BMI groups (p=0.421), showed in table-IV.The AT III activity has found to gone up towards the upper limit in both groups of pill users (normal value 88-111%).

5.Pearson correlation coefficient between BMI and coagulationstatus and ATIII. A significantly towards positive correlation was found among AT III and Low BMI(r=0.591,p=0.072)No significant correlation was found among others with BMI

6. A positive correlation was found between fibrinogen and antithrombin III in normal BMI, which is not maintained in Low BMI

Table-I

Clinical features of different groups of study subjects

Groups	Normal BMI (n=29)	Low BMI (n=11)
Age (years)	28.00 (25-45)	26.00 (25-32)
BMI (kg/m2)	23.06 (19.40-30.08)	18.44 (15.04-18.50)
Duration (months)	24.00 (7-60)	12.00 (6-24)

Results are expressed as median (range)
Normal BMI=Subjects with normal BMI
Low BMI=Subjects with low BMI
n=Number of subjects
BMI=Body Mass Index
Duration= Duration of OCP use

Table-II

Coagulation status of Normal BMI and low BMI study subjects.

Groups	Normal BMI (n=29)	Low BMI (n=11)	U/p value
Platelet aggregation(%)	20 (6.25-71.25)	20 (6.25-47.50)	131/0.387
Plasma fibrinogen(mg/dl)	450(165-700)	318(142-788)	127.50/0.332
Prothrombin time(Second)	12.60 (10.50-16)	13.80 (12.00-16.30)	97.00/0.058

Table-III

Coagulation status among the Normal BMI and low BMI study subjects with the same duration of OCP use (<24 months).

Groups	Normal BMI (n=20) use OCP<24 months	Low BMI (n=11) use OCP<24 months	U/p value
Platelet aggregation(%)	21.88(6.25-71.25)	20 (6.25-47.50)	88.50/0.373
Plasma fibrinogen(mg/dl)	452 (165-700)	318 (142-788)	83.50/0.274
Prothrombin time(second)	12.20 (11.10-16.00)	13.80 (12.00-16.30)	53.50/0.019

Table-IV

Antithrombin III activity of Normal BMI and low BMI study subjects.

Groups	Normal BMI (n=29)	Low BMI(n=11)	U/p value
Antithrombin III (%)	108 (66-210)	105 (76-134)	120.00/0.421)

Table-V

Pearson correlation coefficient between BMI and coagulation status and Antithrombin III.

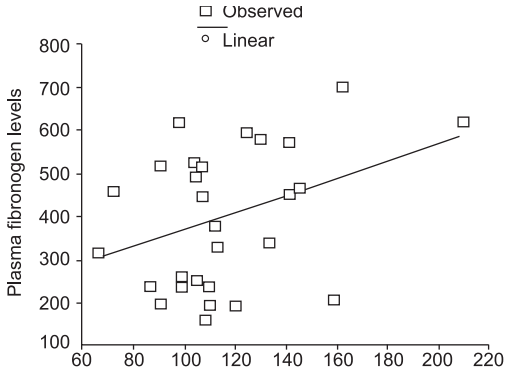
Group	Normal BMI		Low BMI	
	r	P	r	P
Pl.agg .	098.614		-.500.117	
Fibrinogen	-.033	.867	-.483	.132
PT	.036	.855	.189	577
AT III	-.033	.865	.591	072

Pl.agg= Platelet aggeregation, PT= Prothrombin time, ATIII=Antithrombin III.

Table-VI

Pearson correlation coefficient between plasma fibrinogen and Antithrombin III in Normal and Low BMI Group.

Groups	Normal BMI (n=11)		Low BMI (n=11)	
	r	P	r	P
Fibrinogen/AT III	.355	.o59	-.189	.602



Plasma anti-thrombin III of the subjects having normal BMI

Fig.-1: *Person correlation coefficient between plasma fibrinogen and plasma antithrombin III of normal BMI OCP users.*

Discussion:

Subtle but complex changes occur in coagulation mechanism in women on OCP. Oral contraceptives have been shown to induce more rapid platelet aggregation and adhesion and also to reduce the activity of the fibrinolytic system, which normally breaks down the blood clot. Thus, when clot forms, they may be less likely to dissolve and more likely to reach a size sufficient to block vessels and create a thromboembolic problem. The increased risk of venous thrombosis and pulmonary embolism is probably attributable in some women to the estrogencontent of their oral contraceptives.A positive correlation was found by Inman et al in United Kingdom between the risk of thromboembolic disease and the dosage of estrogen contained in OCP, when combined OCP containing high doses (75-100 ìg or more) of estrogen, were available at that time were used[19]. The availability of new generation monophagic and multiphagic formulations of OCP containing both low dose of estrogen and new progestogen has virtually changed the previous idea of thrombogenic effect of OCP [20,21].

The general belief is that OCP intake leads to a high index of suspicion of thromboembolic episodes of pill users.There is limited data available regarding thrombogenic potential of OCP among Bangladeshi users. In this study, the effects of OCP on certain parameters were measured.To see the coagulation status platelet aggregation, plasma fibrinogen, prothrombin time and antithrombin III activity were measured. There was no significant change in platelet aggregation, plasma fibrinogen and antithrombin III activity in the two groups of OCP users. The prothrombin time in low BMI users was slightly prolonged by 1.6 second in contrast to normal BMI (Table III), which was statistically significant.There may be deficiency in ionized calcium in low BMI OCP users as the study sample are from poor socioeconomic status.The plasma fibrinogen in normal BMI subject has gone up above the upper range as compared to low BMI subject (450mg/dl Vs 318 mg/dl in Normal BMI Vs Low BMI) but the difference is not significant (p=0.332) . In this study ATIII activity in both groups were gone at the upper limit eg: in normal BMI it is 108% and in low BMI 105% (normal range : 88-111%). It is well known that OCP increases the plasma fibrinogen level. Plasma fibrinogen and AT III activity in Normal BMI subjects has gone above the upper range (450mg/dl and 108% in Plasma fibrinogen and ATIII). A positive correlation found between plasma fibrinogen and AT III in the normal BMI OCP users (r=0.355,p=0.059).We can say from the above relationship between plasma fibrinogen and AT IIIthat the rise of plasma fibrinogen is due to pill use and rise in ATIII is a secondary response to plasma fibrinogen to counterbalance the coagulation activity. It may be assumed that after a certain level of BMI increment the plasma fibrinogen will be so high at which the ATIII will not be able to counterbalance with prolong use of OCP.There was no correlation exists between the plasma fibrinogen and AT III of Low BMI OCP users.There is no significant difference in platelet aggregation in normal BMI and low BMI groups. David et al revealed in their study that the platelet count, platelet aggregation ratio were not significantly altered and antithrombin III activity was not reduced among the users of low dose oral contraceptives[20].

Sinceprolonged prothrombin time was found within low BMI OCP users and a positive correlation existed between AT III and low BMI subjects. Reasons for such findings may be nutritional or OCP in this nutritional background. So a large extensive and indepth further study with prothrombin time, AT III, serum calcium, total plasma protein and serum albumin are also required to clarify this issue in nutritionally deprived low BMI OCP users.

Finally, the less number of low BMI subject is a limitation of this study. Initially it was thought that number of low

BMI women of child bearing age using OCP will be widely prevalent. During data collection it was found that low BMI women in this age group are not so common as compare to normal BMI. Cause may be gaining of weight and less linear height in this nutritional group. Reasons for gaining of weight of these women might be child bearing ,increasing age or OCP itself. On the otherhand, average height of Bangladeshi women are low in comparison to nutritionally privileged women possibly this is how the normal range of BMI is maintained in women with low socioeconomic background and also the BMI parameter in developing country is different from that of developed country.

Conclusion:

From the statistical analysis of the results obtained in present study and their comparison data suggested the following:

Low dose OCP do not seem to affect the coagulation status of Low BMI Subjects. The reported risks ofprocoagulant or thrombogenic changes in pill usersseem to be dependent on obesity, in the lower weight playing a protective role. Precautions, however, is necessary for possible bleeding disorders in low BMI users who showsignificantly longer prothrombin time due to the effect of malnutrition itself or due to the effect of pills in this nutritional background. Further studies are also required to clarify this issue of prothrombin time. AT III levels are not probably affected in underweight OCP users.It probably changes proportionately with serum fibrinogen in Normal BMISubjects. But this relationship can not be maintained in Low BMI Subjects.

References:

1. Royal College of General Practioners. Oral Contraceptives and health. An interim report for the oral contraception study of the Royal college of general practitioners. New York, Pitman Publishing Co. 1974; 98.
2. Prasad RNV, Ratnam SS. The cardiovascular and thromboembolic risks of oral contraception-A review. Sing J. ObstelGynecol 1980; 11:1, pp 7-19.
3. Ratnam SS,Prasad RNV. Oral contraceptives In: Practice of Fertility control (Chaudhuri,SK, Ed) Current Book Publishers, Calcutta 1983; p 103.
4. Ulysse JG Metabolic effects of Oral contraceptives. Am. J. ObstelGynecolpt II suppl, 1987;157:4, 1029-1014.
5. Ratnam SS,Prasad RNV. Recent developments in steroidal contraception. Sing J. Obstel Gynecol. 1980; 11:pp 7-13.
6. Hussain's current status of oral contraceptives. Bangladesh J.physiol. And Pharmacol. June 199; 7(1):40-41.
7. Skouby SO, Peterson KR and Jespersen J. The influence of new dose oral contraceptive on metabolic variables.Adv.Contra.Dec 1991; 7(suppl.2):77-88).
8. Start well PE, Masi AT, Arthes FG, Green GR and Smith HE. Thromboembolism and oral contraceptive. An epidemiologic Case Control Study. Am.J. Epidem. 1969;90:365-380.
9. Stadel BV. Oral contraceptive and cardiovascular disease. N. Engl. J. Med. 1981 a: 305(11): 612-618.
10. Anonymous. Oral contraceptives: mechanism in thromboembolism. Lancet. May 1980; 1118-1119.
11. Caspray EA and Peberdy M. Oral contraceptive and blood platelet adhesiveness Lancet, May 1965; 1142-1143.
12. Ogino M. Effect ofOral contraceptives on fibrinolytic system among Japanese and American women. Nippon SankaFujinkaGakkaiZasshi, ActaObstetrica EtGynocologica japonica. June 1986; 38(6): 817-826.
13. Vonkaulla E andVonkaulla KN. Oral contraceptives and low antithrombin III activity. Jan 1970; Lancet 1, 36.
14. Howei PW, Prentice CRM, Mallinson AC, Horne CHW and McNicol GP. Effect of combined estrogen-progesteron oral contraceptives, estrogen and progestogen on antiplasmin and antithrombin activity. Dec 1970; Lancet: 1329-1332.
15. Bottiger LE, Boman G, Eklund G and Westerholm B. Oral contraceptives and thromboembolic disease: Effects of lowering estrogen content. Lancet, May 1980; 1027-1101.
16. Poller L. Oral contraceptives, blood clotting and thrombosis. Br. Med. Bull. 1978; 34(2): 151-156.
17. Samsioe G. Comparative effects of Oral contraceptive combinations 0.15 mg desogestrel + 0.03 mg ethinyloestradiol and 0.15 mg levonorgestrel + 0.03 mg ethinyloestradiol on lipid and lipoprotein metabolism in healthy female volunteers. Contraception 1982; 25: 5, 487-503.
18. Lanchnit- Fixon. Triphasic pill "neutral"effects on lipid profile.XI world congress on fertility and sterility Newsletter. Schering AG.Publishers 1983;4.
19. Inman WHW, Vessey MP, Westerholm, Engeland A. Thromboembolic disease and the steroidal content of oral contraceptives. A report to the committee on safety of drugs. BMJ. April 1970; 2:203-209.
20. David JL. Gaspard UJ. Gillain D, Raskinet R, Leport MR. Haemostasis profile in woman taking low dose oral contraceptives. Am. J. Obstel. Gynecol.July 1990; 163 (1): 420-423.

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Comparative Study of Nutritional Status of Children (02-24 Months) with Acute Bronchiolitis and Pneumonia

NN SHAMPA[a], MAH MOLLAH[b], MM BILL[c], ARML KABIR[d], NC SAHA[e]

Summary:

Background: Acute Bronchiolitis and pneumonia pose significant morbidity and mortality of under five children. This outcome is further influenced by poor nutritional status of the affected child because of depressed immunity.

Objective: We sought to evaluate nutritional status of children suffering from acute bronchiolitis and pneumonia in Bangladesh.

Methods: This cross sectional study was conducted in the Department of Pediatrics of Dhaka Medical College Hospital and Dhaka Shishu Hospital from July, 2010 to June, 2011. A total of 50 patients of pneumonia aged 2-24 months and 50 patients of acute bronchiolitis of same age were enrolled in this study according to case definitions. After enrolment, the patients were thoroughly assessed with particular emphasis on the anthropometric measurements. Weight, length, MUAC and OFC were measured and recorded in a pretested semi structured questionnaire. For each group Z score of weight for age, weight for length, length for age, OFC and MUAC were calculated. Z score +2 to -1 was defined as normal, -1 to -2 z score as mild poor, -2 to -3 z score as moderate poor and <-3 z score was defined as severe poor status. Results were compared between pneumonia group and bronchiolitis group by using calculated Z value. A calculated Z value more than 1.96 was regarded significant (calculated z value > 1.96 is equivalent to p value< 0.05).

Results: Children with pneumonia more often had severe underweight (weight for age <-3 SD) (50% vs. 30%, p= 0.04), microcephaly (OFC <-3SD) (30% vs. 12%, p= 0.03), and low MUAC (<115 mm) (40% vs. 10%, p= 0.03) compared to those with bronchiolitis. Although, there was an increased trend of severe wasting (weight for length <-3 SD) and severe stunting (length for age <-3 SD) in children with pneumonia compared to those with bronchiolitis, the difference was not significant.

Conclusion: There thus, the overall nutritional status in children having pneumonia was poor compared to those with bronchiolitis. However, multicenter case control study with larger sample is imperative to consolidate our observation.

Key Words: Acute Bronchiolitis, pneumonia, Nutritional Status.

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Introduction:

Acute respiratory tract infection (ARI) accounts for nearly one third of all under five deaths in Bangladesh[1]. Among them, pneumonia is the single largest contributor and accounts for almost 28-34% of all under five deaths globally[2,3]. Acute bronchiolitis, another common respiratory problem, is responsible for hospital admission of 2-3% of all babies younger than one year of age[1,4]. Poor nutritional status leaves children susceptible to ARI and secondary infection because of impaired cellular immunity[5]. A recent systematic review revealed that death from pneumonia is as high as 15 folds with the co-morbidity of severe malnutrition compared to those without severe malnutrition[6]. Impact of severe malnutrition in children with bronchiolitis is also enormous[7]. However, in Bangladesh the studies evaluating the nutritional status of children suffering from pneumonia as well as bronchiolitis are limited. This study was designed to see the nutritional status of children suffering from pneumonia and bronchiolitis and to compare the results between the two groups. This understanding would encourage the improvement of nutritional status of children as a preventive measure against these two common respiratory problems.

Materials and Methods:

Study design , place and period: This observational cross sectional study was carried in Dhaka Medical

a. Dr. Nazmun Nahar Shampa, Assistant Professor, Harirampur Union Sub Center, Thana Health Complex, Tejgaon, Dhaka.
b. Prof. Md. Abid Hossain Mollah, Professor of Paediatrics & Neonatology, Dhaka Medical College Hospital, Dhaka.
c. Dr. Mallick Masum Billah, OSD, Directorate General of Health Services, Mohakhali, Dhaka.
d. Prof. ARM Luthful Kabir, Professor of Paediatrics, Sir Salimullah medical College & Mitford Hospital, Dhaka.\
e. Dr. Narayan Chandra Saha, Associate Professor of Paediatric Neurology, National Institute of Neuroscience and Hospital, Dhaka.

Address of Correspondence: Dr. Nazmun Nahar Shampa, Assistant Professor, Harirampur Union Sub Center, Thana Health Complex, Tejgaon, Dhaka. Mobile: 01715027955, E-mail: drnazmunnahar@yahoo.com

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College Hospital and Dhaka Shishu Hospital during July 2010 to June 2011.

Study population: The study was carried out among the 02-24 months old infants who were admitted in the selected hospitals with acute bronchiolitis and pneumonia.

Case definitions:

(A) Bronchiolitis: child below 2 years of age with fast breathing, wheeze, coryza and radiological evidence of bronchiolitis e.g hyperinflation of chest. (National ABC guideline, 2005, Asthma association, Bangladesh)

(B) Pneumonia: child below 2 years of age with cough, fast breathing, lower chest wall indrawing, fever, coarse crackles on auscultation and radiological evidence of pneumonia like consolidation or perihilar infiltrate (Pocket Book Of Hospital Care For Children: guideline for the management of common illness with limited resources: WHO 2005:71) .

In both of the pneumonia and bronchiolitis groups' features of hypoxia like nasal flaring, grunting, head nodding were noted.

Selection of cases:

Inclusion criteria: Any child from two months to two years of age with meeting the case definition of pneumonia or bronchiolitis irrespective of sex and nutritional status were enrolled in the study.

Exclusion criteria: Patients having congenital heart diseases or other congenital anomalies, suffering from chronic illness like TB, thalassemia, malabsorption syndrome were excluded from the study.

Sample size and sampling: The samples are selected purposively based on the inclusion and exclusion criteria form Dhaka Medical College Hospital and Dhaka Shishu Hospital during July 2010 to June 2011. A total of 100 cases were selected initially in the pneumonia group. 45 of them were excluded because of having no radiological evidence of pneumonia and five were excluded because of having associated congenital heart diseases. 85 cases were selected in bronchiolitis group but 35 of them were excluded because of having no radiological evidence. Finally 50 patients were enrolled in each group.

Data collection: After enrolment, thorough clinical assessment was done using a pretested semi structured questionnaire. As a part of anthropometric measures weight, length, Occipito Frontal Circumference (OFC) and Mid Upper Arm Circumference (MUAC) were noted. Naked weight was measured using an electronic scale that stands a maximum weight 15 Kg with 100gm precision. The measurement of length was done in infantometer from the top of the head to the heels with the child lying on a wood slab with a fixed piece on one side and a movable one on the other side (top of the head on the fixed part). MUAC and OFC were measured by a measuring tape with a precision of 1 mm. MUAC was measured among children of more than 6 months of age. We measured weight in Kilogram, Length and OFC in Centimeter and MUAC in Millimeter.

Classification of nutritional status: To assess the nutritional status z scores of weight for age, weight for length, length for age, MUAC and OFC were calculated. Normal range was defined as +2 to -1 z scores, mild poor status as -1 to -2 z scores, moderate poor status as -2 to -3 z scores and severe poor status as <-3 z score[8,9].

Statistical analysis: Calculated Z values were determined for each group for comparison between pneumonia and bronchiolitis cases. Z values > 1.96 were considered as significant (Z values > 1.96 equivalent to $p < 0.05$).

Ethical consideration: The ethics and research committee of Dhaka Medical College Hospital approved the study and was carried out.

Results:

In this study, among the data of 100 cases (50 in pneumonia and 50 in bronchiolitis group) male outnumbered female (58% in pneumonia and 68% in bronchiolitis groups). Children of 2-6 months age group were predominant (Table I). Fever, cough, respiratory distress and chest indrawing were present in 100% patients of pneumonia group. On the other hand, respiratory distress and wheeze were present in 100% patients of bronchiolitis group. Features of hypoxia like flaring of ala nasae, head nodding, grunting and cyanosis were more frequent among the children of pneumonia group than their bronchiolitis counterparts (Table II). Among the pneumonia cases, perihilar infiltrate on the chest x ray was the predominant finding (42%) followed by lobar consolidation (36%) and bilateral patchy opacity (22%). On the other hand hyperinflation (46%) was predominant among the bronchiolitis cases followed by both hyperlucency and hyperinflation (22%) (Table III). Children with microcephaly (OFC<-3SD), severe underweight (weight for age <-3 SD), and MUAC <115 were significantly more in pneumonia cases than their bronchiolitis counterparts (Table IV). Number of mild to severely wasted and stunted children were also more in pneumonia group than their bronchiolitis counterparts, though the differences were not statistically significant (Table IV).

Table-I

Age and sex distribution of pneumonia and bronchiolitis patients

Characteristics		Pneumonia n=50	Bronchiolitis n=50
Age (in months)			
	2-6	25 (50%)	31(62%)
	6-12	14 (28%)	14 (28%)
	12-24	11 (22%)	5 (10%)
Sex			
	Male	29 (58%)	34 (68%)
	Female	21 (42%)	16 (32%)

Table-II

Clinical features of pneumonia and bronchiolitis patients.

Clinical features	Pneumonian=50 (%)	Bronchiolitisn=50 (%)
Fever	50 (100)	32 (64)
Cough	50 (100)	42 (84)
Respiratory distress	50 (100)	50 (100)
Chest indrawing	50 (100)	35 (70)
Wheeze	10(20)	50 (100)
Flaring of ala nasae	20 (40)	12 (24)
Head nodding	13 (26)	03 (06)
Grunting	08 (16)	05 (10)
Cyanosis	06 (12)	02 (04)

Table-III

Radiological features of pneumonia and bronchiolitis patients

Group of patients	Radiological features	No. of patients (%)
Pneumonia	Perihilar infiltrate	21 (42%)
	Bilateral patchy opacity	11 (22%)
	Lobar consolidation	18 (36%)
Bronchiolitis	Hyperinflation	23 (46%)
	Hyperlucency	9 (18%)
	Both hyperlucency and hyperinflation	11(22%)
	Hyperinflation and streaky density	6 (12%)

Table-IV

Comparison of anthropometric measures of Pneumonia and Bronchiolitis patients

Anthropometry	Standard Deviation	Pneumonia n (%)	Bronchiolitis n (%)	Calculated Z value	p
Occipito Frontal Circumference	+2 to -1	06(12%)	06 (12%)	0	1.00
	-1 to -2	15 (30%)	23 (46%)	1.67	0.09
	-2 to -3	14 (28%)	15 (30%)	0.22	0.08
	<-3	15 (30%0)	06 (12%)	2.26	0.03
Weight/Age(under nutrition)	+2 to -1	06(12%)	09 (18%)	0.843	0.4
	-1 to -2	09(18%)	12 (24%)	0.73	0.4
	-2 to -3	10(20%)	14(28%)	0.94	0.3
	<-3	25(50%)	15 (30%)	2.08	0.04
Weight/Length (wasting)	+2 to -1	08 (16%	16 (32%)	1.9	0.06
	-1 to -2	12 (24%)	16(32%)	0.89	0.4
	-2 to -3	15 (30%)	10 (20%)	1.25	0.2
	<-3	15 (30%)	08 (16%)	1.68	0.09
Mid upper arm circumference	≥ 115	15 (60%)	17 (89.8%)	4.14	0.03
	<115	10 (40%)	02 (10.2%)	4.14	0.03
Length/Age(stunting)	+2 to -1	08(16%)	12 (24%)	1.005	0,3
	-1 to -2	20 (40%)	24 (48%)	0.8	0.4
	-2 to -3	12 (24%)	06 (12%)	1.5	0.1
	<-3	10 (20%)	08 (16%)	0.52	0.6

Discussion:

The most important observation of this study is the frequent association of microcephaly (OFC<-3SD), severe underweight (weight for age <-3 SD), and MUAC <115 with children having pneumonia compared to the children with bronchiolitis. Although, children with pneumonia proportionately more likely to be wasted and stunted compared to those with bronchiolitis, the difference was not significant and this might be due to small sample.

Common age group of pneumonia and bronchiolitis cases were 2-6 month of age. Several studies showed same findings that the younger age group is more vulnerable to lower respiratory tract infection[10,11]. There is a male predominance in both pneumonia (58%) and bronchiolitis (68%) groups. ARI as a whole affects males more frequently than females throughout the world[12,13]. This may be due to genetic factors or cultural practice of seeking medical care frequently for males than females, considering males more precious[14,15].

It is known that poor nutrition is one of the causes of microcephaly[16]. In this study under nutrition and wasting is more prevalent in pneumonia group and consistently microcephaly is also significantly more in pneumonia group in comparison to bronchiolitis group ($p<0.05$).

In a study conducted in Bangladesh to investigate the host risk factors in the outcome of severe pneumonia, the findings were consistent. Similar type of another study conducted on ARI in Bangladesh also had consistent observation[17]. On the other hand, one study on nutritional status of bronchiolitis patient showed that only 7.5% had severe under nutrition, 72% had good nutritional status[18]. And these are almost consistent with the observation of our study population with bronchiolitis.

A number of previous studies were conducted to evaluate the nutritional status of children with pneumonia and bronchiolitis. Most of those studies assessed only one or two components of nutritional

anthropometry. But our study is unique in the context of assessing most of the components of nutritional anthropometry (such as weight for age, weight for length, length for age, OFC and MUAC) of children having pneumonia and bronchiolitis patients of same demographic characteristics. Thus, on the basis of all the evaluated parameters our main observation was that the children with pneumonia more often had poor nutritional status compared to the children having bronchiolitis. The observation is understandable but very important. Children with poor nutritional status are immune-compromised due to depressed cell mediated and humoral immune responses and often more susceptible to severe bacterial infection[19]. Bacterial infection in children more likely to be associated with pneumonia compared to bronchiolitis[20]. Moreover, children with poor nutritional status more likely to be associated with bacterial pneumonia[21,22]. This explains our observation of association of pneumonia with poor nutritional status compared to bronchiolitis.

There were limitations in the study. The study was performed over small sample of children and selected the samples purposively. The selection bias could not be ruled out. But the study included all the children meeting the case definition and inclusion and exclusion criteria. As it was a cross sectional study, the findings did not determine the temporal relationship between the nutritional status and pneumonia and bronchiolitis.

Conclusion:

In conclusion, the results of our data suggest that children with low MUAC, severe under nutrition and microcephaly were more prone to have pneumonia compared to bronchiolitis. Overall nutritional status was poor in pneumonia cases in comparison to bronchiolitis cases.

Recommendation:

Multicenter case control study with large sample size may be conducted to determine more precise relationship between the nutritional status and pneumonia and bronchiolitis.

References:

1. Kabir ARML, Amin MR, Mollah MAH, Khanam S, Mridha AA, Ahmed S, Rokonuddin K, Chisti MJ. Respiratory disorders in under-five children attending different hospitals of Bangladesh: a cross sectional survey. Journal of Respiratory Medicine Research and Treatment 2015; [in press]
2. UNICEF. (2014). Committing to Child Survival: A Promise Renewed. Progress Report 2014.
3. Wardlaw T, Salama P, Johansson EW, et al. Pneumonia the leading killer of children. The Lancet 2006; 368: 1048-50.
4. Smyth RI, Peter JM. Bronchiolitis. The Lancet 2006;368:312-322.
5. Ahmed T, Ali M, Ullah MM, Choudhury IA, Haque ME, Salam MA, Rabbani GH, Suskind RM & Fuchs GJ. Mortality in severely malnourished children with diarrhoea and use of a standardised management protocol. The Lancet 1999;353:1919-22.
6. Chisti MJ, Tebruegge M, La Vincente S, Graham SM & Duke T. Pneumonia in severely malnourished children in developing countries - mortality risk, aetiology and validity of WHO clinical signs: a systematic review. Trop Med Int Health 2009;14:1173-89.
7. Bosa VL, Mello ED, Mocelin HT, Benedetti FJ, Fischer GB. Assessment of nutritional status in children and adolescents with post-infectious bronchiolitis obliterans. J Pediatr (Rio J) 2008;84(4):323-30.
8. WHO Expert Committee on Physical Status: the Use and Interpretation of Anthropometry: report of a WHO expert committee. WHO technical report series: 854, 1995.
9. World Health Organization. Management of Severe Malnutrition: a manual for physicians and other senior health workers. Geneva,1999.
10. Rijal P, Sharma A, Shrestha S and Upadhyay S. Profile of acute lower respiratory tract infection in children under fourteen years of age at Nepal Medical College Teaching Hospital (NMCTH). Nepal Med Coll Journal 2011; 13(1):58-61.
11. Simoes EA. Respiratory syncytial virus infection. Lancet 1999;354:847-52.
12. Kwon JM, Shim JW, Kim DS et al. Prevalence of respiratory viral infection in children hospitalized for acute lower respiratory tract diseases, and association of rhinovirus and influenza virus with asthma exacerbations. Korean J Pediatr 2014;57(1):29-34.
13. Victoria CG, Fuchs SC, Flores JAC, Fonseca W, Kirkwood B. Risk factors for pneumonia among children in a Brazilian metropolitan area. Pediatrics 1994; 93(6): 977-86.
14. Suwanjutha S, Ruangkanchanasetr S, Chantarojanosiri T, Hotrakitya S. Risk factors for pneumonia in Thai children under 5 years. Southeast Asian J Trop Public Health 1994;25(1):60-5.
15. Khanam R. Risk factors for acute respiratory infections (ARI) in children (dissertation). Dhaka. Bangladesh College of physicians and Surgeons, 1994.

16. Kabir ARML, Mollah AH, Anwar KS, Rahman AKMF, Amin R, Rahman ME. Management of bronchiolitis without antibiotics: a multi-center randomized control trial in Bangladesh. Acta Pediatrica 2009;98:1593-1599.

17. Paul SK, Sharma JD et al. Host risk factors in the outcome of severe pneumonia. D S (Child) H J. 2006;22(1):23-28.

18. Berman S. Epidemiology of acute respiratory infections in children of developing countries. Rev Infec Dis 1992;13(6):54-62.

19. Morgan G. What, if any, is the effect of malnutrition on immunological competence? The Lancet 1997;349: 1693-1695.

20. Adiku TK, Asmah RH, Rodrigues O, Goka B, Obodai E, Adjei AA, Donkor ES, Armah G. Aetiology of acute lower respiratory infections among children under five years in Accra, Ghana. Pathogens. 2015;4:22-33

21. Chisti MJ, Graham SM, Duke T, Ahmed T, Ashraf H, Faruque AS, La Vincente S, Banu S, Raqib R & Salam MA. A Prospective Study of the Prevalence of Tuberculosis and Bacteraemia in Bangladeshi Children with Severe Malnutrition and Pneumonia Including an Evaluation of Xpert MTB/RIF Assay. PLoS One, 2014 9, e93776.

22. Chisti MJ, Ahmed T, Faruque AS & Salam AM. Clinical and laboratory features of radiologic pneumonia in severely malnourished infants attending an urban diarrhea treatment center in Bangladesh. Pediatr Infect Dis J 2010;29:174-7.

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Impact of Seminal Plasma Zinc and Serum Zinc Level on Semen Parameter of Fertile and Infertile Males

P FATIMA[a], MM HOSSAIN[b], D RAHMAN[c], CR MUGNI[d], HB HOSSAIN[e], HN HOSSAIN[f], GM SUMON[g]

Summary:

Background: Despite Zinc (Zn) deficiency being prevalent in humans, less emphasis has been given on the understanding of its impact on male reproduction. Spermatogenesis has a strict requirement for zinc. The relationship of seminal plasma zinc level and semen parameter until now is controversial .

Objective : The study was done to find out the impact of seminal plasma zinc and serum zinc level on semen parameter of fertile and infertile males.

Subjects and methods: The study was done in Center for Assisted Reproduction, a tertiary Infertility center in Dhaka and in the Biochemistry Department of Bangabandhu Sheik Mujib Medical University (BSMMU), Dhaka. Sixteen fertile males were taken as control and sixty nine infertile males were taken as cases. Semen analysis was done according to WHO criteria (.2004). Serum zinc and seminal plasma zinc levels were measured in the Biochemistry Department of BSMMU by Graphite Furnace Atomic Absorption Spectrophotometer.

Result: Seminal parameters between fertile and infertile men showed significantly high sperm count, sperm motility, rapid linear motility, and morphology in fertile group. In fertile men, serum zinc level was lower than the infertile group, whereas the seminal plasma zinc level was higher in the fertile than the infertile group which was not statistically significant. In fertile men except for serum zinc, all parameters showed positive relationship; and in infertile men, except sperm morphology, all other parameters showed negative relationship. Seminal plasma zinc shows positive correlation with all semen parameters in fertile group and negative correlation in infertile group except for sperm morphology. There is negative correlation of serum zinc and seminal zinc-in both groups. Regarding other parameters, semen zinc shows positive correlation with all parameter except sperm morphology in fertile men and negative correlation with all parameter except sperm count in infertile men.

Conclusion: Seminal zinc levels in fertile men are higher than those in the infertile patients although the serum zinc level is lower. Zinc levels in seminal plasma has a direct relationship with semen parameters. Zinc deficiency may be an important risk factor for low semen parameters and idiopathic male infertility.

Key words: Seminal plasma zinc, Semen parameter, Male infertility.

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Introduction:

Zinc is essential for reproduction in human. World Health Organization (WHO) estimates that one-third of world population is deficient in zinc. The geographical regions most affected are believed to be in descending order of severity, South Asia (in particular, Bangladesh and India), Africa and the Western Pacific[1]. Although there is high prevalence of zinc deficiency in humans, the consequences of zinc deficiency on male reproduction is not well-understood. The Zinc concentration of semen is 87 times than that in the blood and has been reported to protect sperm from bacteria and chromosomes damage[2]. Male fertility is influenced by zinc and plays an important role in normal testicular development, spermatogenesis, and sperm motility[3,4]. The concentration of zinc in human seminal plasma is higher than in other tissues. There are conflicting reports on the role of human seminal plasma zinc on sperm quality. Some authors reported significantly different seminal zinc levels between fertile and subfertile groups, indicating low seminal zinc levels in the subfertile populations,[5,6] while some others have shown that there is no difference between the two groups[7,8]. Low zinc

a. Prof. Parveen Fatima, Professor (Infertility), BSMMU
b. Prof. Mohammad Moazzam Hossain, Professor & Chief Embryologist, Centre for Assisted Reproduction
c. Dr. Dilruba Rahman, Co-ordinator IVF, Centre for Assisted Reproduction
d. Dr.Chowdhury Rashedul Mugni, EMO, BIRDEM
e. Dr. Humayra Bushra Hossain, Medical Officer, Centre for Assisted Reproduction
f. Dr. Humayra Nawrin Hossain, Medical Officer, Centre for Assisted Reproduction,
g. Dr. G.M. Sumon, Asst. Director, Hospital, Centre for Assisted Reproduction

Address of Correspondence: Prof. Parveen Fatima, Professor of Infertility, Centre for Assisted Reproduction, 2/1-A, Iqbal Road, Mohammadpur, Dhaka-1207, Bangladesh. e-mail : drpfatima@gmail.com

levels have a negative effect on serum testosterone concentration and seminal volume[9]. Infertile males have lower levels of seminal plasma zinc, which is associated with reduced levels of zinc in the blood[9]. Zinc in seminal plasma stabilizes the cell membrane and nuclear chromatin of spermatozoa[10, 11]. It may also have an antibacterial function[12] and protect the testes against the degenerative changes[13]. It may play a regulatory role in the process of capacitation and acrosome reaction[14]. Despite the high prevalence of marginal Zn deficiency in humans, less emphasis has been placed on the understanding of its impact on male reproduction. Poor zinc nutrition may be an important risk factor for low quality of sperm and idiopathic male infertility[15]. The study was done to find the impact of seminal plasma zinc and serum zinc levels on semen parameters in fertile and infertile males.

Materials and methods:

The study was done in Center for Assisted Reproduction, a Tertiary infertility center in Dhaka, and in the Biochemistry Department of Bangabandhu Sheikh Mujib Medical University, Dhaka. Sixteen fertile males whose wives were pregnant at the time of the assessment were taken as control and sixty nine infertile males whose wives were facing difficulty in conceiving due to poor semen parameters, were taken as cases. Semen analysis was done according to as per World Health Organization guidelines (2004). Serum zinc and seminal plasma zinc levels were measured in the Biochemistry Department of BSMMU by Graphite Furnace Atomic Absorption Spectrophotometer.

Results:

In Table I semen parameters and zinc levels of the fertile and infertile males showed mean semen volume to be 2.46±1.27 ml and 2.47±1.07 ml respectively which was statistically not significant. Comparison of other seminal parameters between fertile and infertile group showed significantly positive parameters in fertile group. Total sperm count, total sperm motility, rapid linear motility of sperm and sperm morphology were 85.00±32.04 and 47.87±46.45 million/ml (P<0.01); 81.88±7.50 and 52.39±23.68% (P<0.001); 69.06±8.98 and 31.45±20.55% (P<0.001); and 52.50±4.47 and 25.00±11.97% (P<0.001) respectively among the fertile(control) and infertile(case) group. Comparison of serum zinc and semen zinc between control and case showed no significant difference in serum zinc 68.39±14.37 and 75.83±17.41 ìg/dl (P=0.116); and semen plasma zinc 6,175.44±2,569.52 and 5,851.46±2,076.11 ìg/dl (P=0.593) respectively.

Table II shows correlation coefficient (r) of seminal plasma zinc concentration with semen parameters. In fertile group, all parameters showed positive relationship; and in infertile, except sperm morphology, all other parameters showed negative relationship. In fertile group, only semen motility showed statistically significant relationship (r = +0.504, P<0.05); but none in infertile group.

Table III shows correlation coefficient (r) of serum zinc concentration with semen parameters. In control, except semen morphology and semen zinc, all parameters

Table-I

Semen parameters and Zinc levels in fertile and infertile males

Parameters (μg/dl) Mean±SD	Control (n=16) Mean±SD	Case (n=69)	P value
Semen volume (ml)	2.46±1.27	2.47±1.07	0.978^{ns}
Total sperm count (million/ml)	85.00±32.04	47.87±46.45	0.003**
Sperm motility (%)	81.88±7.50	52.39±23.68	0.0001***
Rapid linearity (%)	69.06±8.98	31.45±20.55	0.0001***
Morphology (%)	52.50±4.47	25.00±11.97	0.0001***
Serum zinc (ig/dl)	68.39±14.37	75.83±17.41	0.116^{ns}
Seminal P zinc (μg/dl)6175.44±2569.52	5851.46±2076.11	0.593^{ns}	

Unpaired Student's 't' test, ns = Not significant, ** = Significant (P<0.01), *** = Significant (P<0.001)

Table-II

Correlation coefficient (r) of seminal plasma zinc concentration with semen parameters

fertile (n=16)			infertile (n=69)	
Parameters	r value	P value	r value	P value
Volume (ml)	+0.384	0.142^{ns}	0.164	0.179^{ns}
Total sperm count (million/ml)	+0.080	0.768^{ns}	0.222	0.067^{ns}
Motility (%)	+0.504	0.047*	0.076	0.536^{ns}
Rapid linearity (%)	+0.426	0.100^{ns}	0.048	0.698^{ns}
Morphology (%)	+0.298	0.262^{ns}	+0.156	0.202^{ns}

Pearson correlation coefficient test, ns = Not significant, * = Significant (P<0.05)

Table-III

Correlation coefficient (r) of serum zinc concentration with semen parameters

Control (n=16)			Case (n=69)	
Parameters	r value	P value	r value	P value
Volume (ml)	+0.130	0.631^{ns}	0.086	0.481^{ns}
Total sperm count (million/ml)	+0.079	0.770^{ns}	+0.086	0.481^{ns}
Motility (%)	+0.337	0.201^{ns}	0.002	0.988^{ns}
Rapid linearity (%)	+0.508	0.045*	0.065	0.595^{ns}
Morphology (%)	0.368	0.161^{ns}	0.220	0.069^{ns}
Semen zinc (ìg/dl)	0.019	0.945^{ns}	0.112	0.360^{ns}

Pearson correlation coefficient test, ns = Not significant, * = Significant (P<0.05)

showed positive relationship; and in case, except semen total sperm count, all other parameters showed negative relationship. In control, only semen rapid linearity showed statistically significant relationship (r = +0.508, P<0.05); none of the parameters showed significant relationship in case group.

Discussion:

About 6 decades ago, zinc was recognized as an essential micronutrient for human health by Dr. Ananda Prasad, a nutrition chemist at Wayne State University in Detroit, Michigan [16]. The human body contains approximately 2 g zinc in total. Daily requirement of zinc is 10 mg Zn per day for adult women and 12 mg Zn per day for adult men. World Health Organization estimates that zinc deficiency affects one-third of the world's population (about two billion people) with the prevalence rates ranging from 4 to 73% in various regions[17]. In1990 lower levels of zinc were noticed in infertile patient by Kvist et al [18] which was similar in our study.

Some studies indicated that there is no significant difference between Zinc content in fertile and infertile men[19-22].Although in our study serum zinc and seminal zinc was low between fertile and infertile group also did not show any significant difference, serum zinc 68.39±14.37 and 75.83±17.41 ìg/dl (P=0.116); and semen zinc 6,175.44±2,569.52 and 5,851.46±2,076.11 ìg/dl (P=0.593), but some studies found a significant difference between them[23-26] . In our study,fertile subjects had higher levels of zinc in their seminal plasma than infertile group which was in concurrence with the study of Colagar[15].

Comparison of other seminal parameters between fertile and infertile group showed significantly positive parameters in fertile group with statistically significant

increase in total sperm count, total sperm motility, rapid linear motility of sperm and sperm morphology among the fertile(control) and infertile(case) group. Similar findings have reported in previous studies by different authors. High concentration of zinc to be associated with enhanced sperm parameters, including sperm count, motility[23-25,27] , and normal morphology[25, 28], Zhao et al[26] observed a positive relationship between poor production of sperm and poor sperm motility with a lower content of Zn in the seminal plasma of infertile subjects which is in concurrence with our study. In a study done in 1983 Stanwell found a significant positive relationship between sperm density and seminal plasma zinc concentration in the fertile, but not in the infertile men[29]. Wong *et al.*[19] reported increased proportion of spermatozoa with progressive motility after oral zinc supplementation. Steven *et al.*[30] *in his study* observed a negative correlation between seminal zinc content and sperm head defect. In the present study it was observed that there is positive but not significant correlations between zinc content of seminal plasma and motility, total count and sperm concentration. In contrast to our study Wong *et al.*[4], demonstrated that zinc content in fertile men were not different from those of infertile men. Abou-Shakra *et al.*[31], reported that zinc content in men grouped by sperm concentration was not different from each other.

Conclusion:

Zinc may contribute to fertility through its significant effects on various semen parameters. It seems that the estimation of seminal plasma zinc may help in investigation and treatment of infertile males. Seminal zinc may contribute to fertility through its effect on various semen parameters. Seminal zinc level in fertile men is higher than the infertile patients although the serum zinc level is lower. Zinc levels in seminal plasma has a direct relationship with semen parameters. Zinc deficiency may be an important risk factor for low quality of sperm and idiopathic male infertility.

Reference:

1. Holt C, Brown KH, eds. International Zinc Nutrition Consultative Group (IZiNCG) Technical Document #1. Assessment of the risk of zinc deficiency in populations and options for its control. *Food and Nutrition Bulletin*, 2004, 25 (Suppl 2):S94–S203.
2. Judith EB. Nutrition through life cycle. 3rd ed. St. Paul, Minnesota: Brooks/Cole publishing company; 2008.
3. Lin TH, Cheng SY. Determination of zinc fractions in human blood and seminal plasma by ultrafiltration and atomic absorption spectrophotometry. *Biol Trace Elem Res, 1996;* 51(3): 267-276.
4. Wong WY, Flik G, Groenen PM, Swinkels DW, Thomas CM, Copius-Peereboom JH, *et al.* The impact of calcium, magnesium, zinc, and copper in blood and seminal plasma on se-men parameters in men. *Reprod Toxicol 2001;* 15(2): 131-136.
5. Chia SE, Ong CN, Chua LH, et al. Comparison of zinc concentrations in blood and seminal plasma and the various sperm parameters between fertile and infertile men. J Androl. 2000;21:53-7.
6. Ebisch MW, Pierik FH, Jong FH, Thomas CM, Theunissen RP. Does folic acid and zinc sulphate intervention affect endocrine parameters and sperm characteristics in men. Int J Androl. 2006;29:339–45.
7. Umeyama T, Ishikawa H, Takeshima H, Yoshii S, Koiso K. A comparative study of seminal trace elements in fertile and infertile men. Fertil Steril. 1986;46:494–9. [PubMed]
8. Omu EA, Fernandes S. The relationship between zinc/ cadmium ratio in human semen: Effect on immune response. Kuwait Med J. 2001;33:38–43.
9. Hunt CD, Johnson PE, Herbel J, Mullen LK. Effects of dietary zinc depletion on seminal volume and zinc loss, serum testosterone concentrations, and sperm morphology in young men. Am J Clin Nutr. 1992;56: 148-57.
10. Chvapil M. New aspects in biological role of zinc. A stabilizer of macromolecules and biological membrane. Life Sci 1973;13:1041-9.
11. Kvist U. Sperm nuclear chromatin decondensation ability. An in vitro study on ejaculated human spermatozoa. Acta physiol scand suppl 1980;486:1-24
12. Langley J, Goldsmid J, Davies N. Venereal trichomoniasis role in men. Genitourin Med 1987;63:264-7.
13. Batra N, Nehru B, Bansal MP. Reproductive potential of male Portan rats exposed to various levels of lead with regard to zinc status. Br J Nutr 2004;91:387-91.
14. Riffo M, Leiva S, Astudillo J. Effect of zinc on human sperm motility and acrosome reaction. Int J Androl 1992;15:229-37.
15. Colagar AH, Marzony ET, Chaichi MJ. Zinc levels in seminal plasma are associated with sperm quality in fertile and infertile men. Nutrition Research, 2009; 29(2): 82-88.
16. Prasad AS. Clinical, endocrinological and biochemical effects of zinc deficiency. Clinics in Endocrinology and Metabolism 1085;14: 567–585
17. World Health Organization. The World Health Report 2002: reducing risks, promoting healthy life. Geneva: WHO, 2002.

18. Kvist, U, Kjellberg, S , Bjorndahl L, Soufir JC, Arver S. Seminal fluid from men with agenesis of the Wolffian ducts zinc binding properties and effects on sperm chromatin stability. InL J Androl 1990; 13: 245-252

19. Wong WY, Thomas CM, Merkus JM, Zielhuis GA, Steegers-Theunissen RP Male factor sub-fertility: possible causes and the impact of nutritional factors. *Fertil Steril 2000;* 73(3): 435-442.

20. Bakalczuk S, Robak-Cholubek D, Jakiel G, Krasucki W. Level of zincand magnesium in semen taken from male partners of married infertilecouples. Ginekol Pol 1994;65:67-70.

21. Colleen S, Mardh PA, Schytz A. Magnesium and zinc in seminal fluid of healthy males and patients with non-acute prostatitis with and without gonorrhoea. Scand J Urol Nephrol 1975;9:192-7.

22. Carpino A, Siciliano L, Petroni MF, De Stefano C, Aquila S, Ando S,et al. Low seminal zin bound to high molecular weight proteins in asthenozoospermic patients: evidence of increased sperm zinc content in oligoasthenozoospermic patients. Hum Reprod 1998;13:111-4.

23. Fuse H, Kazama T, Ohta S, Fujiuchi Y. Relationship between Zinc concentrations in seminal plasma and various sperm parameters. Int Urol Nephrol 199 9;31:401-8.

24. Mankad M, Sathawara NG, Doshi H, Saiyed HN, Kumar S. Seminal plasma zinc concentration and á-glucosidase activity with respect to semen quality. Biol Trace Elem Res 2006;110:97-106

25. Chia SE, Ong C, Chua L, Ho L, Tay S. Comparison of zinc concentration in blood and seminal plasma and various sperm parameters between fertile and infertile men. J Androl 2000;21:53-7.

26. Zhao RP, Xiong CL. Zinc content analysis in serum, seminal plasmaand spermatozoa of asthenozoospermic and oligoasthenozoospermic patients. Zhonghua Nan Ke Xue 2005;11:680-2

27. Caldamone AA, Freytag MK, Cockett AT. Seminal zinc and maleinfertility. Urology 1979;13:280-1

28. Edorh AP, Tachev K, HadouT, Gbeassor M, Sanni A, Creppy EE, et al.Magnesium content in seminal fluid as an indicator of chronic prostatitis. Cell Mol Biol 2003;49:419-23.

29. Stanwell-Smith R, Thompson SG, Haines AP, Ward RJ, Cashmore G, Stedronska J, *et al.* A comparative study of zinc, copper, cadmium, and lead levels in fertile and infertile men. *Fertil Steril 1983;* 40(5): 670-677.

30. Steven FS, Griffin MM, Chantler EN Inhibition of human and bovine sperm acrosin by divalent metal ions. Possible role of zinc as a regulator of acrosin activity. *Int J Androl 1982;* 5(4) : 401-412.

31. Abou-Shakra FR, Ward NI, Everard DM. The role of trace elements in male infertility. *Fertil Steril 1989;* 52(2): 307-310.

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Acute Kidney Injury in Sick Neonate: Incidence and Outcome

S HALDER[a], MM HOQUE[b], U RAHMAN[c], SF SONIA[d], SS BISWAS[e]

Summary:

Introduction: ***Acute kidney injury (AKI) is an important clinical problem in sick neonate. In most patients, AKI accompanies with a predisposing factor such as sepsis, asphyxia and surgery. The aims of this study were to determine the incidence, associated contributing factors and short term outcome of AKI in hospitalized newborn infants.***

Materials and Methods: ***This prospective cohort study was done in Dhaka Shishu Hospital from March 2011 to September 2011. This study included 300 sick neonates admitted during the study period. AKI was defined when serum creatinine level >1.5 mg/dl and BUN was >20 mg/dl on two separate occasions at 24 hours apart. Oliguria was defined as urine output <1ml/kg/ hr. Medical records of those patients were reviewed and data were analyzed using SPSS software.***

Results: ***Fourteen babies (4.66%) out of 300 sick neonates had AKI, of whom 64.2% were male and 35.7% female. The term and preterm neonates were 71% and 29% respectively. While a normal birth weight was observed in 57% cases, 35% had low birth weight and 7.14% had very low birth weight. Sepsis was the most common (71%) association of AKI, followed by perinatal asphyxia (52%). All patients had more than one predisposing factors. Frequency of oliguric kidney injury was 57% and non-oliguric was 43%. Mortality among the hospitalized neonate with AKI was 21%.***

Conclusion: ***This study showed that in a tertiary care hospital AKI is not uncommon (4.66%) in neonatal care unit. It is associated with some preventable conditions such as sepsis, perinatal asphyxia and shock. Outcome is poor in sick neonates with AKI (21% mortality) in comparison to sick neonates without AKI (10.3%).***

Key words: Acute Kidney Injury, Sick neonate.

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Introduction:

Acute kidney injury(AKI) is a common problem among sick newborns.[1,2] The sick newborns are those who are admitted in a hospital for any morbidities like perinatal asphyxia (PNA), septicemia, necrotizing enterocolitis (NEC), shock, heart failure, respiratory distress syndrome etc. Any critical illness in neonate leads to multiorgan dysfunction and the kidney is one of the organs frequently afflicted .[3,4] AKI previously called acute renal failure is characterized by a reversible increase in the blood concentration of creatinine and nitrogenous waste products and by the inability of the kidney to regulate fluid and electrolyte homeostasis appropriately.[5,6]. It is diagnosed on the basis of clinical history such as decreased urine production (Oliguria), and laboratory findings such as elevated blood urea nitrogen and creatinine. Although non-oliguric neonatal kidney injury is being detected with increasing frequency.[1,7]

Study done by Stapleton FB et al.[1], Gharehbaghi MM[8], Airede A et al.[9] and Andreoli SP[10] found that the incidence of acute kidney injury was 3% to 8% in sick neonate. A wide variety of predisposing factors such as asphyxia (40%), sepsis (22%), feeding problems (18%), heart failure, prematurity and urogenital anomalies are commonly reported causes of AKI in the developed countries.[2,11] Studies done in India showed that AKI was the common sequel of sepsis in neonatal care unit.[3,12]

Mortality among hospitalized neonate due to kidney injury was 20-50% and patient with sepsis had significantly higher rate.[8,13] In Bangladesh, neonatal mortality rate is still high which is more than two third

a. Dr. Soma Halder, Assistant Professor, Dept. of Paediatrics, Shahabuddin Medical College.

b. Prof. Dr. Md. Mahbubul Hoque, Professor of Neonatology, BICH& Dhaka Shishu Hospital.

c. Dr. Urmi Rahman, Registrar, Dept. of Paediatrics, Popular Medical college & Hospital.

d. Dr. Sheikh Farjana Sonia, Assistant Professor, Dept. of Paediatrics, MARKS Medical College &Hospital.

e. Dr. Sudhangshu Shekhar Biswas, Associate Professor, Dept of Otolaryngology & Head- Neck Surgery, BIRDEM.

Address of Correspondence: Dr. Soma Halder, Assistant Professor, Dept of Paediatrics, Shahabuddin Medical College & Hospital. Mail: Flat- 12D, Deen Monzil, 12 Paribagh, Dhaka 1000, Phone: 01718081288, Email: hsoma111@yahoo.com.

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of infant mortality rate.[14] The major causes of death in hospitalized neonates are preterm low birth weight and related consequences, asphyxia, infection, trauma etc.[15] To the best of our knowledge, a few studies have been conducted on assessment of renal function in perinatal asphyxia and preterm neonates in Bangladesh.[16] But it seems to be essential for early detection of AKI for planning appropriate fluid and electrolyte therapy and thereby for improved outcome. This study was conducted to see the incidence, predisposing factors of acute kidney injury in sick neonate and their outcome.

Materials and methods:

This prospective cohort study was conducted in Neonatology unit of Dhaka Shishu Hospital from March 2011 to august 2011. During the study period, admitted sick neonates were evaluated for presence of AKI. The sick neonates were those who were admitted for different morbidities like septicemia, perinatal asphyxia with hypoxic ischemic encephalopathy, shock, respiratory distress syndrome, necrotizing enterocolitis and undergone surgical procedure. Neonates of any congenital anomalies like skeletal, renal, urinary tract were excluded from this study. For each patient detailed history was taken and physical examination was done. First blood sample(2-3ml venous blood) was collected at admission and send to the Clinical Pathology and Biochemistry department in Dhaka Shishu Hospital for blood urea, serum creatinine and serum electrolytes values. For an abnormal value, repeat test was done after 24 hrs. Urine was collected by adhesive urine bag.

AKI was defined as serum creatinine concentration >1.5 mg/dl and blood urea nitrogen >20mg/dl on two separate tests 24 hours apart. Oliguria was defined as urine output less than 1ml/kg/h. Statistical analysis was performed using SPSS Version 17. Outcome was compared with the use of the Chi-square test. P value <0.05 was considered statistically significant.

Result:

Three hundred sick neonates were evaluated during the study period. Among them, 66.7% were male and 33.3% were female, 60% were term, 40% were preterm and 46% were normal birth weight and 38% were low birth weight. The newborns were admitted for different morbidities like sepsis (35.3%), perinatal asphyxia (34.6%) (Table-I).

Among 300 sick neonates 14(4.66%) babies developed AKI. Male to female ratio was 1.8:1. Most of the patients with AKI were term (n-10, 71%) and 4 (29%) cases were preterm (Table -2). Oliguric renal injury was found in 8 cases (57%) and non-oliguric was found in 6 cases. Sepsis was found to be the most common cause (71%) followed by perinatal asphyxia (52.8%) (Table II). There were more than one predisposing factors in all patients.

Mortality was significantly higher ($p<0.05$) in neonates with AKI (21%) than in neonates without AKI (10%). (Table-V)

Table-I

Disease pattern of the sick neonates (n=300)

Diagnosis	Frequency	Percentage (%)
Sepsis	106	35.33
Perinatal asphyxia	104	34.67
Neonatal jaundice	71	23.67
Respiratory distress syndrome	14	4.67
Pneumonia	13	4.33
Shock	13	4.33
Heart diseases	12	4
Surgical causes	10	3.33

Table-II

Demographic characteristics of neonates with AKI (n=14)

	Frequency	Percentage (%)
Sex Male	9	64.2
Female	5	35.7
Gestational age		
Term	10	71.4
Preterm	4	28.5
Birth weight		
Normal(2500-4000gm)	8	57
LBW(<2500gm)	6	43

Table-III

Predisposing factors for developing AKI in neonates (n=14)

Diagnosis	Frequency	Percentage (%)
Sepsis	10	71.43
Perinatal asphyxia HIE-III	6	52.86
Surgical causes	3	21.43
Shock	3	21.43
Intrauterine growth retardation	2	14.2
SIADH	3	21.3

Table-IV

Renal function and serum electrolytes values in repeat sample of AKI cases (n=14)

Investigations	1st sample Mean+_SD	2nd sample Mean+_SD
S. creatine (mg/dl)	2.8+_1.25	2.7+_1.15
BUN (mg/dl)	57+_27	47+_16.2
S. sodium (mmol/l)	134+_8.7	132.0+_6.5
S. Potasium (mmol/l)	5.6+_1.3	5.3+_1.2

Table-V

Short-term outcome of the sick neonates

Patients	Mortality (%)
Total sick neonates (300)	31(10.3%)
AKI (14)	3 (21.4%)

p value=<0.05

Discussion:

In this study, it was found that good number of sick neonates developed AKI. Stapleton et al.[1], Ghaebaghi MM et al.[8], Airede A et al.[9] and Andreoli SP[10] found that the incidence of AKI was 3-8% in sick neonates. In several studies[8,9,17] it was found that predominantly male and term babies developed renal impairment. In our study, similar findings were found. The high frequency of AKI in boys may be due to the susceptibility of boys to some perinatal disorders such as sepsis and respiratory distress syndrome.[17]

A wide variety of predisposing factors or prenatal, natal or postnatal events may cause AKI. In this study sepsis (71%) was the most common cause of AKI. Study done in India by Mathur NB[12] found that 26% septic babies developed AKI. The exact pathophysiology of sepsis-induced AKI is not known, however, it is generally accepted that it has a multi-pronged injury pathway. It may be due to ischemia-reperfusion injury, direct inflammatory injury, coagulation and endothelial cell dysfunction, and apoptosis.[3]

Perinatal asphyxia was high in this study. It was 53% in a study done by Airede A et al.[9] and Mortazavi F et al.[18] found 29.8% babies with perinatal asphyxia developed AKI. As kidneys are very sensitive to oxygen deprivation, renal insufficiency may occur within 24 hours of a hypoxic ischemic episode, which if prolonged, may lead to irreversible cortical necrosis.[18]

Other factors responsible for developing AKI were shock (hypovolumia and sepsis) (21%), surgical procedure (21%) and SIADH

(21%). Gharehbaghi MM[8] found that 43.5% neonates developed AKI following surgical procedure.

Serum creatinine and BUN were determined as an indicator of renal function following an initial insult. These laboratory tests are relatively inexpensive and widely available. Obstruction of tubular lumen and back leak mechanism (by damage to the intracellular junctions) contributed to increase in urea and creatinine levels in sick neonates[18,19]. In this study hyperkalemia was the main electrolyte abnormality. Hyperkalemia is a common complication of AKI as the kidney tightly regulates potassium balance and excretes 90% of dietary potassium intake.[20] It was observed that the babies with AKI had higher incidence of hyponatremia. The capacity of sodium reabsorption is limited and if the load of sodium reaching the distal convoluted tubule (DCT) increases significantly, reabsorption does not occur proportionately and sodium load excretes in the urine. Other contributing factors to develop hyponatremia may be occurrence of SIADH secondary to perinatal asphyxia and partial resistance to aldosteron.[21] Here, 7.14% babies with AKI were hypernatremic which might be due to association of poor feeding, VLBW etc.

Mortality rate was also high in sick neonates with AKI in comparison to sick neonates without AKI (10.3%). In

this study, renal function of 11 babies (out of 14) returned to normal and discharged. Gharehbaghi MM et al.[8] and Mortazavi F et al.[17] also reported the mortality rate of 20%, and 20.6% respectively. Mathur NB et al.[12] reported 70% mortality in septic neonates with AKI. The major risk factors for mortality were sepsis, perinatal asphyxia, IUGR, dehydration, electrolyte abnormality and delayed hospitalization.

Conclusion:

Renal function impairment is not uncommon in sick neonates. The predisposing factors for developing AKI are sepsis, perinatal asphyxia, IUGR, shock surgical procedures etc. Mortality of sick neonates with AKI is high in comparison to sick neonates without AKI.

References:

1. Stapleton FB, Jones DP, Green RS. Acute renal failure in neonates: incidence, etiology, outcome. Pediatric Nephrology 1987; 1(3): 314-320.
2. Durkan AM, Alexander RT. Acute kidney Injury in post neonatal asphyaxia. The Journal of Pediatric 2011; 158(2): e29-e33.
3. Majumdar A. Sepsis-induced acute kidney injury. Indian J Crit Care Med 2010; 14: 14-21.
4. Perlman J.M, Tack E.D, Martin T, Shackelford G, Amon E. Acute systemic organ injury in term infants after asphyxia. Am J Dis Child 1989; 143 (5): 617-620.
5. Webb S, Dobb G. ARF, ATN or AKI? It's now acute kidney injury. Anaesthesia and intensive care 2007 Dec; 35(6): 843-844.
6. Andreoli SP. Acute kidney injury in children. Pediatric Nephrology 2009; 24 (2): 253-263.
7. Karlowicz MG, Adelman RD. Nonoliguric and oliguric acute renal failure in asphyxiated term neonates. Pediatr Nephrol 1995; 9: 718-722.
8. Gharehbaghi MM, Peirovifar A. Evaluating causes of acute renal failure in newborn infants. Pak J Med Sci 2007; 23(6): 877-880.
9. Airede A, Bello M, Weerasinghe H D. Acute renal failure in the newborn: Incidence and outcome . J Paediatr Child Health 1997; 33: 246-249.
10. Andreoli SP. Acute renal failure in the newborn. Semin perinatol 2004; 28: 112-123.
11. Andreoli SP. Acute renal failure in the newborn. Curr Opin Pediatr 2002; 17: 713-717.
12. Mathur NB, Agarwal HS, Maria A. Acute renal failure in neonatal sepsis. Indian J Pediatr 2006; 76(6): 499-502.
13. Moghal NE, Brockolebank JT, Meadow SR. A review of acute renal failure in children: incidence, etiology and outcome. Clin Nephroph 1998; 49:91-95.
14. Bangladesh Demographic and Health Survey 2005.
15. Rashid AKMM, Rasul CHH, Hafiz SM. Neonatal mortality: a scenario in a tertiary level hospital of a developing country. Licensee PAGE Press, Italy Pediatric Reports 2010; 2: e9.
16. Moni SC. Serum electrolytes and kidney function status in perinatal asphyxia. FCPS Dissertation, BSMMU, Dhaka, 2007.
17. Mortazavi F, Sakha SH, Nejati N. Acute Kidney failure in Neonatal period. IJKD 2009; 3:136-140.
18. Myers BD, Chui F, Hilberman M, Michaels AS. Transtubular leakage of glomerular filtrate in human acute renal failure. Am J Physiol 1979; 273: F319-F325.
19. Gupta BD, Sharma P, Bagla J, Parakh M, Soni JP. Renal failure in asphyxiated neonates. Indian Pediatrics 2005; 42: 928-934.
20. Annabelle NC, Minnie MS. Acute renal failure management in the neonate. NeoReviews 2005; 6(8): e369-e376.
21. Greenbaum LA. Pathophysiology of Body Fluid. In: Behrman RE, Kliegman RM, Jension HB, Stanton BF. Eds. Nelson Text Book of Pediatrics 18th ed. Philadelphia: Saunders Co; 2007, 266-277.

REVIEW ARTICLE

Type 2 Diabetes Mellitus in Children and Adolescents: An update

UH BEGUM[a], MA RAHMAN[b]

Summary:

Childhood type 2 Diabetes Mellitus (DM) has increasingly been reported worldwide. It is commonly associated with childhood obesity.It may be presented with classical manifestation of DM such as polyuria, polydipsia, weight lossor acute complications like Diabetic ketoacidosis (DKA), Hyperglycemic Hyperosmolar State (HHS) or features of insulin resistance syndrome. Many a cases it may remain asymptomatic and hence undiagnosed.So,overweight children and adolescents who met screening criteria such as family history of type 2 DM, signs of insulin resistance, and high risk ethnics should undergo screening. Emphasis should be given on early diagnosis and optimum management plan to avoid grave consequences of it in early part of life. Diagnosis of type 2 Diabetes Mellitus in children should be done on the basis of standard diagnostic criteria such as American Diabetic Association (ADA) criteria. Both non-pharmacological and drug management are important equally. Multidisciplinary team approach including self-management plan is mandatory for obtaining optimal therapeutic goals of type 2 DM in children and adolescents. Lifestyle modification, dietary intervention, weight reduction, patient education, psychological support, and oral anti diabetic drugs and insulin therapy should be included in comprehensive diabetic management plan. Complications of type 2 DM should be minimized by all means with strict glycemic control and management of co-morbidity if any. Emphasis should also be given on prevention of type 2 DM by adopting a healthy lifestyle characterized by healthy eating behavior, regular physical activity and subsequent modest weight loss that can prevent the progression of impaired glucose tolerance to clinical diabetes mellitus.

Key words:American Diabetic Association (ADA), Diabetic Ketoacidosis (DKA), Hyperglycemic Hyperosmolar State (HHS), Overweight, Type 2 Diabetes Mellitus (DM).

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Introduction:

Type 2 diabetes mellitus(DM) happens when the body cannoteffectively use the insulin it produces. Formerly, it was called non-insulin dependent or adult onset diabetes mellitus as because, for many years it was seen only in adults.In type 1 diabetes mellitus, the body does not produce insulin and it is usually diagnosed in children and young adults. Recently,type 2 diabetes mellitushas increasingly been reported in children and adolescents, so much so that in some parts of the world type 2 diabetes has become the main type of diabetes in children. The global rise of childhood obesity and physical inactivity is widely believed to play a crucial role[1]. Currently, more than 200 children and adolescents develop the disease every day worldwide[2]. But healthy eating and lifestyle habits are a strong defense against the disease.

Risk factors and PathophysiologyofType 2 DM:

Type 2 DMis a complex metabolic disorder of heterogeneous etiology with social, behavioral, and environmental risk factors unmasking the effects of genetic susceptibility[3]. There is a strong hereditary component of the disease. The major risk factors of type 2 DM in children are: obesity and inactivity, family history of type 2 DM, age of 12-16 years, maternal gestational diabetes or type 2 diabetes, not breast feeding during infancy and ethnicity. Other factors that appear to increase risk include poor fetal growth, low birth weight and high birth weight[4]. Impaired glucose

a. Dr Most. Umme Habiba Begum, Associate Professor, Department of Pediatrics, Rangpur Community Medical College, Rangpur.

b. Dr Lt Col Md. Anisur Rahman, Specialist Medical Officer (Medicine), Combined Military Hospital (CMH), Rangpur.

Address of Correspondence: Dr Most. Umme Habiba Begum, Associate Professor, Department of Pediatrics, Rangpur Community Medical College, Rangpur. e-mail: uhabibarp27@gmail.com, arafanis@gmail.com Mobile: 01712546647, 01521248085.

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homeostasis is the key mechanism in type 2 DM and it depends on the balance between insulin secretion by the pancreatic â- cells and insulin action. The mean age range of onset of type 2 diabetes in youths coincides with the relative insulin resistance that occurs during pubertal development, resulting in hyper-insulinemia and play a major role in the development of type 2 DM in children and adolescents. The adverse effect of obesity on glucose metabolismis evident early in childhood. Obese children arehyper-insulinemicand have approximately 40% lower insulinstimulatedglucose metabolism compared with non-obesechildren[5].

Epidemiology of Type 2 DM in children and adolescents:

Type 2 DM in youth appears to be emerging as a seriousclinical issue. It's prevalence in the United States (USA) is approximately12:100000, while it is still rare in Europe[6](approx.,2.5:100000). In Bangladesh the exact prevalenceof Type 2 DM is not known. But in a studyamong 2152 students volunteers inBangladesh, Abu Sayeedet al[7]. observedthat the prevalence of type 2 DM and impaired fasting glucose (IFG)appears to be1.8% and 3.4% respectively. The majority of USA young peoplediagnosed with type 2 diabetes are found inspecific ethnic subgroups such as African-American,Hispanic, Asian/Pacific Islanders and American Indiansbeing highest in Pima Indians (22.3/1000 in 10-14 yearold children). Furthermore, the great majorityof the children are obese. Screening studies in obeseadolescents have reported a prevalence of 0.4% up to1% of type 2 diabetes in obese children e" 12years[8].

Clinical presentationof Type 2 DM:

The presentation of type 2 DMin children and adolescents varies according to the disease stage. Early in the disease, before diabetes diagnostic criteria are met, insulin resistance predominates with compensatory high insulin secretion, resulting in normoglycemiaand the patient likely to be asymptomatic[9]. At this stage, the disease may only be detected by abnormal blood glucoseconcentrations identified during screening. Obesity is the hallmark of type 2 diabetes in children and adolescents.Most children are obese orextremely obese at diagnosis and present with glycosuriawithout ketonuria, absent or mild polyuria and polydipsia,and little or no weight loss. In its severest form, the child presents with polyuria,polydipsia, and weight loss. Up to 33% in particularethnic groups have ketonuria at diagnosis and 5%-25%ketoacidosis at presentation[10]. Vary rarely, type2 diabetes mellitus manifest with a hyperglycemichyperosmolarstate (HHS). Acanthosis-nigricans and polycystic ovarian syndrome (PCOS), disorders associated with insulin resistance and obesity, are common in youth with type 2 DM[11]. Children with type 2 diabetes frequently have a positive family history, and 74%-100%first or second degree relative have type 2 DM. Some syndromes such as Klinefelter syndrome, BardetBiedl Syndrome, PraderWilli Syndrome and Alström Syndrome are also associated with type 2 DM. They all are associated with mental retardation and frequently to extreme obesity[12].

Differential Diagnosis:

Patients with type 2 DM may have clinicalpresentations indistinguishable from those of patientswith other types of diabetes mellitus[11]. It is important to classify diabetes mellitus in children and adolescents correctly, sothat appropriate therapy may be instituted. Typically, children with type 1 diabetes mellitus are not overweight and have recent weight loss, polydipsia, and polyuria. They have a short duration ofsymptoms and frequently have ketoacidosis at presentation[11].Type 2 diabetic children and adolescents may represent a form of early-onset latent autoimmune diabetes mellitus similar to that described in adults (LADA). These Patients with LADA share insulin resistance with that of type 2 diabetes mellitus patients but display a more severe defect in â-cell capacity[12]. Following the terminology 'latent autoimmune diabetes mellitus in adulthood, LADA', the non-insulin dependent diabetic children and adolescents with â-cell autoantibodies could be named 'latent autoimmune diabetes mellitus in youth' (LADY)[13]. Double diabetes mellitus or type 1.5 diabetes mellitus are other proposed names for this entity[13]. Maturity-onset of diabetes mellitus of the young(MODY) is another rare form of diabetes mellitus inchildren that includes several disorders caused by monogenicdefects in â-cell function[14]. MODY 2 and MODY 3 (defect in glucokinase and HNF1á respectively) are themost frequent types of MODY. Patients with MODYhave a dominant genetic traits, usually are non-obese andhave low fasting insulin levels. Recent studies suggestthat the clinical presentation of MODY is broad, rangingfrom asymptomatic hyperglycemia to a severe acutepresentation[13].

Diagnostic criteria for Type 2 Diabetes Mellitus:

Diagnosis of type 2 Diabetes Mellitus in children and adolescents can be made on the basis ofAmerican Diabetic Association(ADA)revised diagnostic criteria (Table1)[15] or any other diagnostic criteria. In the absence of unequivocal hyperglycemia, random, fasting or two-hoursblood sample should be confirmed by repeat testing.Other tests may be necessary in difficult cases for diagnosis of type of DM, such as fasting insulin or C-peptide determination and occasionally, β-cell autoantibodies measurements. C-peptide levels are elevated in individuals with type 2 diabetes mellitus in contrast to patients with type 1diabetes mellitus or MODY diabetes.

Table-I

Diagnostic criteria for type 2 DM[15]

- Symptoms of diabetes mellitus such as polydipsia, polyuria, and unexplained weight loss plus
- Random glucose concentration ≥ 200 mg/dL (11.1 mmol/L) in venous plasma,
- Fasting glucose ≥ 126 mg/dL (7.0 mmol/L) in venous or capillary plasma,
- Or two-hours glucose during oral glucose tolerance test (oGTT) ≥ 200 mg/dL (11.1 mmol/L) in venous plasma or capillary whole blood sample And
- Hemoglobin A1c (HbA1c) ≥ 6.5%

Screening for Type 2 Diabetes Mellitus:

Most of the children and adolescents with type 2 diabetes remain asymptomatic at diagnosis. So screening for it is necessary[16].It is found that unrecognized hyperglycemiacontributes to both microvascular and macrovascular risk in later life[17]. However, at the present time, a general screening for type 2 DM in youth is unlikely to be costeffective and so a targeted screening is necessary. The ADA recommends a screening in overweight children and adolescents at onset of puberty in high risk patients (Table 2). Screening test should be performed every 2 years starting at the age of 10 years or at onset of puberty. It should be done by testing fasting glucose or oGTT[18].

Table-II

Criteria for screening tests for type 2 DM in children and adolescents[18]

Overweight (BMI > 90 percentile) plus one of the following risk factors:

- Family history of type 2 DM in 1^0 or 2^0 relative;
- Race/ethnicity (Asian, American Indian, Africa-Americans, Hispanics);
- Signs of insulin resistance; or conditions associated with insulin resistancesuch as acanthosisnigricans, hypertension, dyslipidemia, polycystic ovarian syndrome (PCOS);
- Extreme obesity (BMI > 99.5 percentile).

Complications of Type 2 Diabetes Mellitus:

The chronic complications of type 2 DM in children and adolescents are macrovasculardiseases like accelerated developmentof cardiovascular disease leading to stroke andmyocardial infarction, and microvascular diseases likenephropathy, retinopathy and neuropathy leading toend-stage renal disease, loss of visual acuity, and limbamputations. Microvascular disease is the hallmark of hyperglycemia diagnosed at a younger age. As becausethe complications of DM are related to the duration of disease itself, risksof complications more common in children and adolescents as compared to adult diabetics[19].All of these complications contribute tothe excess morbidity and mortality in individuals withdiabetes mellitus.Youngpeople with type 2 DM appear to be at amuch higher risk of developing early diabetes associated complications than those with type 1 diabetesMellitus[20]. This higher level of risk does not appear to berelated to overall levels of glycemic control or durationof disease but to occurrence of hypertension and dyslipidemia.

Management of Type 2 Diabetes Mellitus:

The idealgoalof management(Table 3)[21]of type 2 diabetes inchildren and adolescents is normalization of blood glucose values, HbA1c and to decrease the risk of diabetes related acute and chronic complications. Successful control of the associatedcomorbidities, such as hypertension and dyslipidemia, isalso important[11]. The American Academy of Pediatrics has, very recently,

published the management guidelines for children and adolescents with type 2 diabetes mellitus[22].

Table-III

Therapeutic goal of type 2 DM in children and adolescents[21]

- Before breakfast sugar: 90–130 mg/dL (5.0–7.2 mmol/L);
- Before bed/ overnight sugar 90–150 mg/dL (5.0–8.3 mmol/L);
- Target HbA1C <7%;
- Target blood pressure consistently, <90th percentile for age, sex, and height;
- Target LDL cholesterol value, 100 mg/dL (2.6 mmol/L).

Insulin therapy should be initiated for children and adolescents with type 2DM who are ketotic or in diabetic ketoacidosis and in whom the distinction between type 1and type 2DM is unclear; and, in usual cases:who have random venous blood orplasma sugar concentrationse"250 mg/dL; orwhose HbA1c is >9%.In all other instances, lifestyle modification program, including nutrition and physical activity, and Metformin should be started as first-line therapy atthe time of diagnosis of type 2DM[22]. Despite of severe manifestation, initial management of obese children and adolescents with type 2 DM should consist of behavior modification strategies for lifestyle change such as decreasing high-caloric high-fat food choice and sedentary behavior, while increasing physical activity. Lifestyle changes should not be imposed and self-motivation is necessary[23].Treatmentoptions of type 2 DM include:

Diet: Balanced macronutrient diets at 900 to 1200 kcal per day are associated with both short and long-term (e"1 year) improvements in weight status and body composition in children 6 to 12 years of age[24].These calorie management are to be incorporated with lifestyle changes, including increased activity and medication. Restrictions of no less than 1200 kcal per day in adolescents 13 to 18years old result in improved weight status and body composition[25].

Physical activity:It is an integral part of weight management for prevention and treatment of type 2DM. Children and adolescents are encouraged to engage in 'moderate-to-vigorous' exercise for at least 60 minutes daily and to limit non-academic 'screen time' to less than 2 hours a day. Screen time contributes to a sedentary lifestyle, especially when the child or adolescent eats while watching television or playing computer games[26].

Patients education:All children with type 2 diabetes mellitus should receive comprehensive self-management education which include teaching self-monitoring of blood glucose,performed as needed and during periods of acute illness or when symptoms of hyper- or hypoglycemia occur[27].

Pharmacological treatment:If treatment goal with nutrition education and exercise is not met, pharmacological therapy is indicated. Metformin andinsulin are the only anti-diabetic agentscurrentlyrecommended for use inchildren. Thiazolidinediones andincretins are occasionally used inadolescents younger than 18 years[28].Metformin, a biguanide, is the most appropriatestarting point for pharmacological treatmentin children with type 2 diabetes mellitus if insulin therapy is not indicated. The effectivenesshas been proven for adolescents in clinical trials. Metformin decreases hepatic glucoseoutput and enhances primarily hepatic and also muscleinsulin sensitivity without a direct effect on â-cell function.It has the advantage of weight reduction,decrease in lipids without the risk of hypoglycemia.Because of concerns about lactic acidosis metformin iscontraindicated in patients with impaired renal function and should be discontinued with the administration ofradiocontrast material or hypocaloric diet. Metforminshould not be used in patients with known hypoxemicconditions, severe infection, hepatic disease, or alcoholabuse. The most common side effects of metformin aregastrointestinal disturbances. The dose of metforminshould be increased up to 2 gm in split doses, unless thereare gastrointestinal side effects. Metformin has a goodsafety record, but should not be given if there is anydoubt at all about the nature of diagnosis.Rosiglitazone, a thiazolidinedione hasbeen studied in some randomized trial in adolescents comparedto lifestyle intervention and metformin and found some effects. However,rosiglitazone has been withdrawn from the market due toits side effects and is not available any more[13].

If monotherapy with metformin is not successful over a reasonable period of time (3-6 months), insulin treatment will often be the only feasible way of controlling hyperglycemia. There is no specific contraindication to insulin in children. Any type of insulin and analogs can be used. Insulin regimes should be adopted that are carefully tailored to lifestyle such as bedtime insulin alone, twice-a-day insulin or multidose insulin regimes[13].Basal insulin is provided through either the use of long acting, relatively peak-free insulin by needle or via an insulin pump. Bolus insulin doses are given at meal-time, using one of the rapid-acting insulin analogs. The bolus dose is calculated by using a correction algorithm for the premeal blood sugar concentration as well as a "carb ratio," in which 1 unit of a rapid-acting insulin analog is given for "X" grams of carbohydrates ingested (For example, see Table 4)[15].

Table -IV

Calculation of Basal Bolus Insulin Regimen[15]

- If an adolescent has a blood glucose of 250 mg/dL, is to consume a meal containing 60 gm of carbohydrates, with a carbohydrate ratio of 1:10 and an assigned correction dose of 1:25>125 the mealtime bolus dose of insulin would be as follows: 60 gm/10 =6 units rapid-acting insulin for meal plus (250–125)/25 = 125/25 = 5 units rapid-acting insulin for correction; Thus, total bolus insulin coverage at mealtime is: 11 Units (6 + 5)
- Note: Insulin sensitivity-25; Target blood glucose level-125mg/dl,'carb ratio'-10.

Monitoring of Diabetes Mellitus and treatment of complications:

All children and adolescents with newly diagnosed type 2 DM, regardless of prescribed treatment plan, should perform finger-stick blood glucose monitoring before meals and at bedtime until reasonable metabolic control is achieved[29]. Once blood glucose concentrations are at target levels, the frequency of monitoring can be modified depending on the medication used, the regimen's intensity, and the patient's metabolic control.Monitoring of HbA1c concentrations every 3 months andintensification of treatment is required if treatment goals forblood sugar and HbA1c concentrations are not being met.Patients on insulin should also be monitored periodically for asymptomatichypoglycemia. To monitor retinopathy, dilated eye examinations should be performed regularly. Screening for microalbuminuria should be performed yearly[26]. Angiotensin converting enzyme(ACE) inhibitors are the agents of choice in children with microalbuminuria. Control of hypertension in children with type 2 diabetes mellitus is mandatory. If normotension is not achieved by ACE inhibitors, combination therapy with α-blockers, calcium antagonists or low-dose diuretics may be needed. It is unclear whether foot examinations are important in children. Testing for and treating lipid abnormalities are necessary to avoid macrovascularcomplications[30].

Psychological impacts of Type 2 DM in children and adolescents:

Adolescents with type 2 diabetes mellitus rate lower 'Quality of Life' scores than their peers with type1 DM and the burden ofneuropsychiatricdisorders in young people with type 2 DMis high, with as many as one in five experiencing eitherpsychiatric illness or neuro developmental/behavioral problems. It is found that psychosocial factors representa significant barrier to optimum self-management inadolescents with type DM, often leadingto a vicious circle of spiraling poor self-managementand increasing psychosocial problems.Poor psychosocial health may also be physiologically related to poorer glycemic control. Therefore psychologists should be the core component of care of children and adolescents with type 2 diabetes mellitus[13].

Prevention of Type 2 Diabetes Mellitus:

Prevention of Type 2 Diabetes Mellitus should startvery early in life, even before birth. Primary prevention has proven to be difficultor impossible in most societies. A multidisciplinaryteam approach is needed to develop and securepreventive strategies. Good nutrition and modest exercisefor pregnant women as well as monitoring of intrauterinegrowth of the fetus are mandatory. After birth,rapid weight gain should be avoided and the principlesof good nutrition and physical activity are to be taught at allages. Breastfeeding should be strongly recommended.Children's food choice can be influenced by early interventionand guidance[18].Teacher training, modificationof school meals and physical education are effectivein reducing

risk factors for obesity which is the hallmark of type 2 DM in children.Recent intervention studieshave convincingly demonstrated that adoption of ahealthy lifestyle characterized by healthy eating behavior, regularphysical activity and subsequent modest weight loss canprevent the progression of impaired glucose tolerance toclinical diabetes mellitus. The use of metforminis not effective to preventtype 2 DM inobese adolescents with impaired glucose tolerance[31].

Conclusion:

Type 2 diabetes mellitus is emerging as a new clinical problem within pediatric practice. Clinicians should be aware of the frequent mild or asymptomatic manifestation of type 2 diabetes mellitus in childhood. Therefore, a screening seems meaningful especially in high risk groups such as children and adolescents with obesity, relatives with type 2 diabetes mellitus, and clinical features of insulin resistance. Emphasis should be given on early diagnosis and comprehensive management plan to avoid grave consequences of it in early part of life. All efforts should be given on prevention of type 2 DM such as, healthy eating, physical activity, and modest weight reduction. Collaborative efforts from all corners of the modern society can efficiently combat against this emerging disease.

Reference:

1. World Health Organization (WHO). What are the risks of diabetes in children? Diabetes fact sheet 2016.available at: www.who.int/features/qa/65.
2. Suyanne FM, Márcio FM, Niciane Pessoa BM, Adman Câmara SL,Roberto WF, Marta Maria CD. Risk Factors for Type 2 diabetes mellitus in Children. Rev. Latino-Am. Enfermagem. 2010:18(5):936-42.
3. Kiess W, Böttner A, Raile K, Kapellen T, Müller G, Galler A. Type 2 diabetes mellitus in children and adolescents: a review from a European perspective. Horm Res 2003; 59 (l) :77-84.
4. JohnssonIW, Haglund B, Ahlsson F, Gustafsson J. A high birth weight is associated with increased risk of type 2 diabetes and obesity. PediatrObes. 2015;10(2): 77-83.
5. Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW et al. Obesity and the metabolic syndrome in children and adolescents. N Engl J Med 2004; 350: 2362-74.
6. Fagot-Campagna A, Pettitt DJ, Engelgau MM, Burrows NR, Geiss LS, Valdez R. Type 2 diabetes among North American children and adolescents: An epidemiologic review and a public health perspective. J Pediatr 2000; 136:664-72.
7. M. Abu Saeed, Mir Masudur Rahman, Nurrunnhar Fayzunnesa, ParvinAktar Khan, Tanjima Begum, HajeraMahtab et al. Childhood Diabetes in a Bangladeshi Population. J Diabetes Mellitus. 2013;3(1):33-37.
8. Wabitsch M, Hauner H, Hertrampf M, Muche R, Hay B, Mayer H. Type II diabetesmellitus and impaired glucose regulation in Caucasian children and adolescents with obesity living in Germany. Int J ObesRelatMetabDisord 2004; 28: 307-313.
9. Gungor N, Hannon T, Libman I, Bacha F, Arslanian S. Type 2 diabetes mellitus in youth: the complete picture to date. PediatrClin North Am. 2005;52(6):1579–1609.
10. Copeland KC, Zeitler P, Geffner M, Guandalini C, Higgins J, Hirst K. TODAY Study Group. Characteristics of adolescents and youth with recent-onset type 2diabetes: the TODAY cohort at baseline. J ClinEndocrinolMetab. 2011;96(1):159–67.
11. Rosenbloom AL, Silverstein JH, Amemiya S, Zeitler P, Klingensmith GJ. ISPAD Clinical Practice Consensus Guidelines2006-2007. Type 2 diabetes mellitus in the child and adolescent. Pediatr Diabetes 2008; 9: 512-26.
12. Carlsson A, Sundkvist G, Groop L, Tuomi T. Insulin and glucagon secretion in patients with slowly progressing autoimmune diabetes (LADA). J ClinEndocrinolMetab 2000;85: 76-80.
13. Thomas Reinehr. Type 2 diabetes mellitus in children and adolescents. World J Diabetes 2013; 15; 4(6): 270-81.
14. Schober E, Rami B, Grabert M, Thon A, Kapellen T, Reinehr T. Phenotypical aspects of maturity-onset diabetes ofthe young (MODY diabetes) in comparison with Type 2 diabetesmellitus (T2DM) in children and adolescents: experiencefrom a large multicentre database. Diabet Med J 2009; 26: 466-73.
15. American Diabetes Association (ADA). Diagnosis and classification of diabetes mellitus. Diabetes Care 2013; 36(1): s67-s74.
16. Lobstein T, Leach R. Diabetes may be undetected in many children in the UK. BMJ 2004; 328: 1261-62.
17. Arslanian SA. Type 2 diabetes mellitus in children: pathophysiology and risk factors. J Pediatr Endocrinol Metab 2000; 13(6): 1385-94.
18. American Diabetes Association. Type 2 diabetes in children and adolescents. Diabetes Care 2000; 23: 381-9.
19. Hillier TA, Pedula KL. Complications in young adults withearly-onset type 2 diabetes: losing the relative protection ofyouth. Diabetes Care 2003; 26: 2999-3005.

20. Hagman E, Reinehr T, Kowalski J, Ekbom A, Marcus C, Holl RW. Impaired fasting glucose prevalence in two nationwide cohorts of obese children and adolescents. Int J Obes (Lond) 2014;38(1):40-5.

21. William T. Cefalu; Standards of Medical Care in Diabetes-Children and Adolescents: Diabetes Care 2016;39(1): s86-s93.

22. Springer SC, Silverstein J, Copeland K, Moore KR, PrazarGE, Raymer T. Management of type 2 diabetes mellitusin children and adolescents. Pediatrics 2013; 131: e648-e664

23. Reinehr T. Lifestyle intervention in childhood obesity:changes and challenges. Nat Rev Endocrinol 2013; 9: 607-14.

24. American Dietetic Association. Recommendations summary: pediatric weight management (PWM) using protein sparing modified fast diets for pediatric weight loss. Available at:www.adaevidencelibrary.com:2012.

25. Knowler WC, Barrett-Connor E, Fowler SE,Hamman RF, Lachin JM, Walker EA. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393–403.

26. National Heart, Lung, and Blood Institute, US Department of Health and Human Services, National Institutes of Health. Reduce screen time. Availableat:www. nhlbi.nih.gov/health/public/heart/obesity/wecan/reduce-screen-time/index.htm. Accessed August 13, 2012.

27. Sabin M. Type 2 diabetes in children. Clinical Obesity 2013; 3:112-6.

28. Rapaport R, Silverstein JH, Garzarella L, Rosenbloom AL. Type 1 and type 2 diabetes mellitus in childhood in the United States: practice patterns by pediatric endocrinologists. J PediatrEndocrinolMetab. 2004; 17(6):871–7.

29. Naughton MJ, Ruggiero AM, Lawrence JM, Imperatore G,Klingensmith GJ, Waitzfelder B. Health-related quality of life of children and adolescents with type 1 or type 2 diabetes mellitus: SEARCH for Diabetes in Youth Study. PediatrAdolesc Med 2008; 162: 649-57.

30. American Diabetes Association. Type 2 diabetes in children and adolescents.Diabetes Care 2000; 23: 381-9.

31. Wiegand S, Allemand D, Hübel H, Krude H, Bürmann M, Martus P. Metformin and placebo therapy both improve weight management and fasting insulinin obese insulin-resistant adolescents: a prospective, placebo-controlled, randomized study. Eur J Endocrinol 2010; 163: 585-92.

Colouterine Fistula

LH BANU[a], A SIDDIQUA[b], S SIDDIQUE[c]

Summary:

Colouterine fistula is a extremely rare condition .It may be congenital,iatrogenic or secondary to malignancy.Here we report a congenital type of colouterine fistula with successful primary repair without hysterectomy in a nulliparous woman.Usually treatment of a parous women is hysterectomy followed by repair of rent in the colon.

Key words: Colouterine fistula, cause, diagnosis, treatment.

(J Bangladesh Coll Phys Surg 2017; 35: 31-33)

Introduction:

Colouterine fistula is an extremely rare condition because the uterus is a thick, muscular organ. It can be congenital or may be caused by foreign body, during surgery, following trauma or accidental or secondary to malignancy, diverticulitis & endometriosis. This condition can be deleterious for an infertile female because of introduction of infection via the colon. Treatment of colouterine fistula in parous women is hysterectomy followed by repair of rent in the colon. We present the case of a colouterine fistula in which repair of the uterus was done as primary procedure and colostomy done for sigmoid fistula. The uterus was conserved because the patient was a nulliparous woman.

Case Report:

A 18 years old married girl resident of Kamarpara, Shadullapur, Gaibandha, educated upto class ten, admitted in surgery ward of Prime Medical College & Hospital, Rangpur on 14.7.2013, presented as 5 months pregnancy with bouts of per rectal bleeding for 3 days & lower abdominal pain for 4 days. On admission, patient was moderately anaemic, pulse, blood pressure normal, abdomen tense and tender, fundal height of uterus was 24 weeks size. USG findings was 22 weeks pregnancy, placenta posterior away from the os with active fetal movement & cardiac activity, no sign of intestinal obstruction. Conservative treatment and boold transfusion started in the surgery ward as there was severe per rectal bleeding. One day after admission abortion process was started & on the next day early morning on 16.7.2013 she complained that something coming out per rectum. The attending doctors of surgery unit found that the placenta was outside through rectum & the umbilical cord was hanging from anus (fig-1). The patient was then transferred to gynae ward & on per vaginal examination a very premature infected dead foetus with foul smelling was found protruding through cervix with breech presentation (fig-2). Oxytocin drip was started for spontaneous expulsion of the foetus but still waiting up to mid noon there was no progress. So planned for examination under anesthesia and breech extraction. Under spinal anesthesia just a pull for extraction of the foetus the head was separated from the neck & retained inside the uterus.Then decision was taken for laparotomy & hysterotomy to remove the retained aftercoming head of breech. Abdomen was opened by right lower paramedian incision. The abdominal cavity was contaminated with fecal matter. The uterus was enlarge about 24 weeks size & part of the sigmoid colon was found adherent to anterior upper segment of uterus. So, the case was diagnosed as colouterine fistula, possibly congenital, which is extremely rare condition. The attachment was very dense & clean cut well defined, no omental or any other surrounding adhesion was found(fig-3). Surgery team dissected and separated the sigmoid colon from the uterus. A big hole in the anterior uterine wall near fundus admits two finger through which the retained head was searched but not found. Ultimately the head was found

a. Dr. Laila Husna Banu, Professor & Head of the Department of Obs. & Gynae, Prime Medical College & Hospital, Rangpur.

b. Dr. Afroja Siddiqua, Assistant Professor of Obs & Gynae, Northern (Pvt.) Medical College & Hospital, Rangpur.

c. Dr. Sohana Siddique, Assistant Professor of Obs & Gynae, Jahurul Islam Medical College & Hospital, Bhagolpur, Bajitpur, Kishoreganj.

Address of Correspondence: Dr. Afroja Siddiqua, Assistant Professor of Obs & Gynae, Northern (Pvt.) Medical College & Hospital, Rangpur, Mobile: 01712-552407

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in rectum which was driven down through the large fistula to the capacious colon to rectum & was brought out per rectum by an assistant. The big hole of the uterus was then closed with vicryl 1 in two layers. Colostomy was done at the level of sigmoid fistula by Hartman's procedure. Peritoneal toileting was done & a drain tube was placed in pelvic cavity. Abdomen was closed in layers. Patient was put on broad spectrum antibiotics & nothing per oral for seven days. Total six units blood was transfused. The post-operative period was uneventful except the abdominal wound got infected & secondary suture was given on 3.8.2013. The patient was discharged after ten days & adviced to come for follow up.

Fig.-1: *The umbilical cord was hanging per rectum & anus from where placenta was delivered first.*

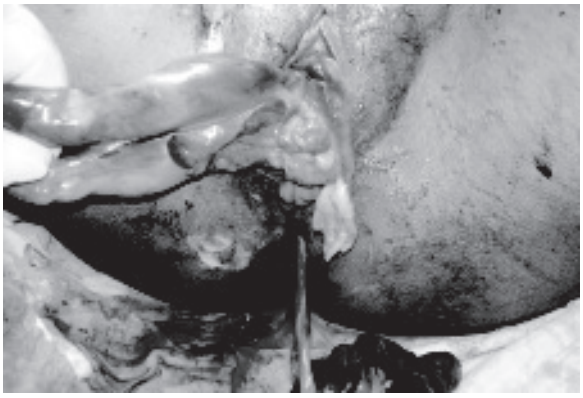

Fig.-2: *Aborted foetus delivered vaginally with breech presentation & the umbilical cord was hanging from anus.*

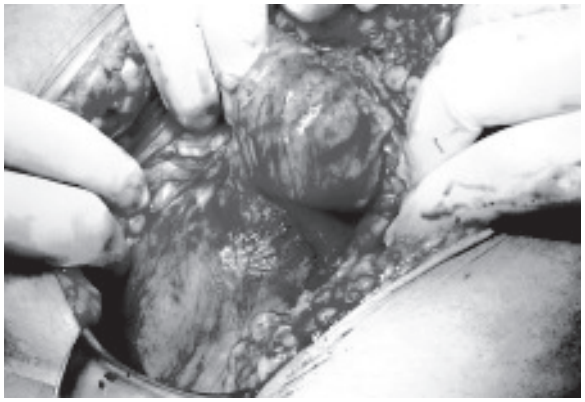

Fig.-3: *Laparotomy shows fistula in between the uterus & sigmoid colon.*

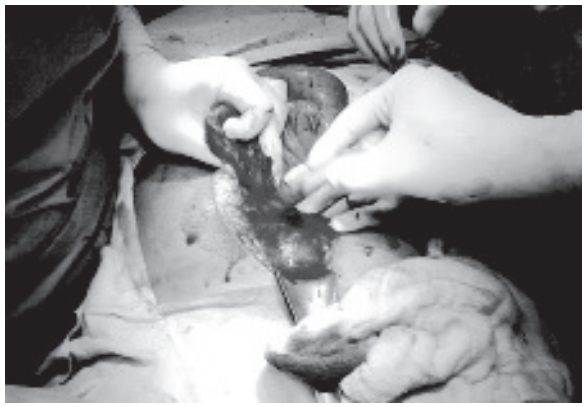

Fig.-4: *Separation & dissection of fistula was done.*

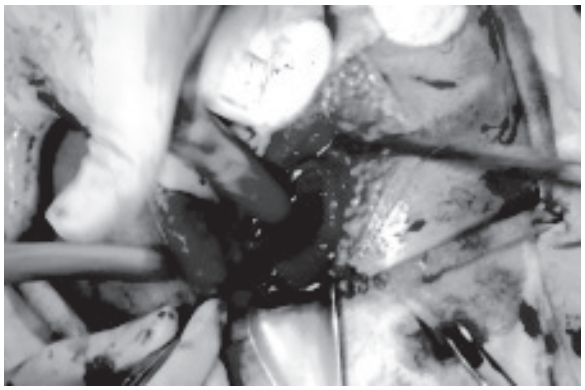

Fig.-5: *This figure shows fistula at the uterine site after dissection from sigmoid colon.*

Discussion:

Since long vaginal deliveries with obstetric & gynaecological interventions have been associated with vesicovaginal & rectovaginal fistulae[1]. Vesicouterine fistulae are relatively rare but world literature documents

only few case of colouterine fistula[2]. Usually these cases of colouterine fistulae were diagnosed by computerized tomography[3] or sonohysterography[4]. Just a conventional hysterosalpingography can also lead to the diagnosis[5]. Colouterine fistulae documented till now were secondary to malignancy[6], diverticulitis[6] & endometriosis. All these cases were treated by hysterectomy & resection of sigmoid colon[7] or colostomy with subsequent repair[8]. We report this case of colouterine fistula with successful primary repair of uterus without hysterectomy.

Initial evaluation comprises a detailed history. Important information includes associated symptoms such as pain, fever or changes in bowel or bladder function. Although clinical manifestations of a colouterine fistula vary according to causative pathology, typical symptoms include malodorous fecal or purulent vaginal discharge for days or months because the colonic lumen & the uterus are linked via a fistula tract[9, 10, 11]. In our case we suspect the fistula is congenital type, though there was no history of per rectal bleeding during menstruation nor any symptoms of malodourous fecal or purulent vaginal discharge. It is probably due to, the non-pregnant uterus is small and the fistular attachment with colon is partially closed and non-communicating. But when the patient became pregnant the uterus enlarged and the muscle wall comparatively thinner. The placenta implanted at or near the site of fistula. Subsequently the fistula opened up and due to separation of placenta there was severe per rectal bleeding and lower abdominal pain, the symptoms which appeared first. Later on the whole placenta separated and through the fistula it passed to the sigmoid colon, rectum, anal canal and ultimately come out through anus (Fig:1). So, the colouterine fistula was diagnosed as a congenital type and primary repair of uterus was done successfully. From patient detailed history, she got married just six month back and it was her first conception. There was no history of MR or induced abortion or any injury or trauma which may favour the diagnosis of acquired variety of fistula.

In conclusion a uterocloic fistula is a very very rare condition. Computed tomography (CT) is routinely performed for diagnosis is patients with a suspected colouterine fistula. However, confirming the diagnosis by using computed tomography (CT) might be difficult. Therefore other less-invasive modalities such as fistulography may be necessary & the utility of recently introduced modalities remains to be verified.

References:

1. Sotelo R, Mariano MB, Garcia-Segui A, Dubois R, Spaliviero M, Keklikian W, Novoa J, Yaime H, Finelli A. Laparoscopic repair of vesicovaginal fistula. J Urol 2005;173(5):1615–8.
2. Beattie GC, Nelson M, McMillen IM, McMurray AH. Colouterine fistula mimicking pyometrium–diagnosis established with multi-detector computed tomography. Ulster Med J 2005;74(1):51–3.
3. Andrew G, Harold VP, Richard AC. Colouterine fistula: computed tomography and vaginography findings, Can Assoc Radiol J 1996;47:186–8.
4. Takada T, Nakagawa S, Hashimoto K, Sone K. Preoperative diagnosis of colouterine fistula secondary to diverticulitis by sonohysterography with contrast medium. Ultrasound in Obstetrics and Gynecology 2004;24(6):682–3.
5. Dr.Aliya Islam, Associated professor Gynaecology, Military Hospital, Rawalpindi, Pakistan, present a case report on colouterine fistule with a foreign body. J Minim Invasive Gynecol. 2008 Sep-Oct;15(5):652-4. doi: 10.1016/j.jmig.2008.06.014.
6. Elliot LC, Richard PC, Andrew LW. Colouterine fistula secondary to diverticulitis. Diseases of the Colon & Rectum 1985;28(5):358–60.
7. Hoekstra AV, Doan T, Kosinski A, Dini M. Colouterine fistulas in elderly women: a report of 2 cases. J Reprod Med 2005;50(10):796–800.
8. Al-Azzam M, Cassidy L, Thomas M. Colouterine fistula as a complication of colonic diverticulitis: a conservative approach. Gynaecol Endoscop 2002;11(4):215–6.
9. Chaikof EL, Cambria RP, Warshaw AL. Colouterine fistula secondary to diverticulitis. Dis Colon Rectum 1985;28:358-60.
10. Sentilhes L, Foulatier O, Verspyck E, Roman H, Scotte M, Mar-peau L. Colouterine fistula complicating diverticulitis: a case re-port and review of the literature. Eur J Obstet Gynecol Reprod Biol 2003;110:107-10.
11. Vilallonga R, Baena JA, Fort JM, Gonzalez O, Gemar E, Armen-gol Carrasco M. Colouterine fistula complicating diverticulitis in elderly women. Int J Colorectal Dis 2009;24:599-600.

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Aortoesophageal Fistula Caused by Descending Aortic Pseudoaneurysm

S MAHMOOD[a], MM HOSSAIN[b], MA HOSSAIN[c]

Summary:

A 60 year old man presented in Square Hospitals LTD with hypovolaemic shock,and massive haematemesis.His BP was non-recordable with soft , non-tender abdomen and Hb was 8g/dl with normal prothrombin time and partial thromboplastin time and normal platelets .By endoscopy and CT scans aortoesophageal fistula with aortic pseudoaneurysm was identified and immediate surgery was done with complete occlusion of the pseudoaneurysm ,which was confirmed by repeat CT scan.

Key wards: Aortoesophageal fistula, Aortic pseudo aneurysm.

(J Bangladesh Coll Phys Surg 2017; 35: 34-35)

Introduction:

Aortoesophageal fistula (AOF) is a rare cause of gastrointestinal haemorrhage. Early diagnosis and surgical intervention are mandatory for survival. We report a case of an aorto-esophageal fistula due to a descending aortic pseudoaneurysm and review the causes, clinical manifestations, and diagnosis of this uncommon but often fatal case of upper gastrointestinal haemorrhage.

Computed tomography is the most valuable diagnostic method in the diagnosis of aortoesophageal fistula.CT may detect the aneurysm, its relation to the oesophagus and surrounding structures.It can also differentiate between true and false aneurysms. Once AOF is identified, immediate surgery is mandatory.

Case report:

The patient, a 60 year old man, presented with hypovolumic shock and massive haematemesis. The patient had repeated episodes of massive haematemesis & malaena without dysphagia, chest pain or loss of weight. The patient was detected HbsAg. positive incidentally. He was a smoker. On admission, his blood pressure was non-recordable and pulse rate was 125 beats/min, confirming haemorrhagic shock. Physical examination included a soft, non-tender abdomen with normal bowel sounds. Additional results were haemoglobin 8 g/dl, creatinine 0.9 mg/dl, normal prothrombin and partial thromboplastin times and normal platelets. Chest X-ray was normal.

After receiving and 5 units of blood , the patient was stabilized and after that endoscopy was performed. Under endoscopy, a large globular mass compressing the mid oesophagus was seen at 30 cm from the incisor teeth. A visible blood vessel was seen at the base of the ulcer at the tip of the mass. The vessel started spurting of the blood during the endoscopic process. Haemostasis was achieved instantly by injecting 10 ml of 5%. Ethanolaminoleate was injected in and around the bleeding vessels.

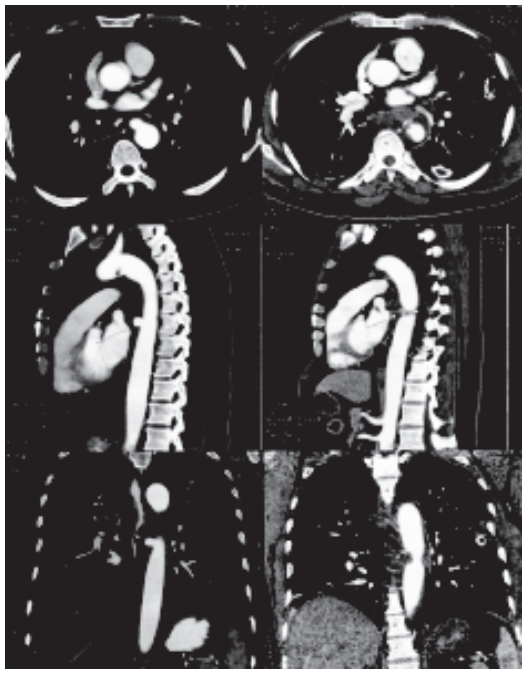

Fig.-1

a. Dr Shagufta Mahmood, Clinical Fellow (NUH , Singapore), Consultant, Radiology and Imaging, Square Hospitals Ltd.

b. Dr M. Motahar Hossain, Consultant, Hepatology & Gastroenterology, Square Hospitals Ltd.

c. Dr. M. Akhter Hossain, Consultant, Cardiac surgery, Square Hospitals Ltd.

Address of Correspondence : Dr Shagufta Mahmood, Apt : A-4 , House 72, Road 11/A, Dhanmondi R/A, Dhaka 1209, Email: sa.azhar@yahoo.com

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A subsequent contrast enhanced computed tomographic scan of the chest documented an outpouching at the antero-medial aspect of the mid part of descending aorta measuring approx. 2.5 cm x 1.3 cm in size suggesting oesophageal pseudoaneurysm (Fig.1). The aneurysm is situated approx. 6 cm distal to the isthmus, compressing and indenting the adjacent oesophageal lumen. Oesophageal wall at this site was mildly thickened. This may suggest aorto-esophageal fistula. Two small 9 mm right paraoesophageal lymphnodes are also detected.

Urgent surgery was planned to excise or occlude the pseudoaneurysm. Descending thoracic aorta was approached by left posterolateral thoracotomy through 4th intercostal space. Aneurysmal sac was identified and found badly adherent to the surrounding soft tissue. Decision was made to occlude the base of pseudoaneurysm and to avoid excessive difficult dissection. Control of aorta was taken both proximal and distal to the pseudoaneurysm. Purse string suture was given at the base of sac by 3-0 prolene. Blood pressure was lowered to 70 mm Hg and purse string suture tied. Two additional transfixation suture of 3-0 prolene through the aneurysmal sac were given and tied down. Haemostasis was achieved and chest was closed by keeping a drain tube.

A subsequent CT confirmed that the pseudoaneurysm was completely occluded (Fig. 2). The patient recovered well before discharge.

Discussion :

Development of a fistula between the aorta and oesophagus has an extremely poor prognosis. In 1991 Hollander and Quick (1) published a comprehensive review, including 500 cases of AEF gathered from the literature. The main aetiological factor involved aortic disease with 54.2% of cases being secondary to rupture of an aneurysm of the descending thoracic aorta into the esophagus. The next most frequent causes were foreign body (19.2 %) and advanced oesophageal cancer (17.0 %). Secondary AEF following operative treatment were rare (4.8 %) with 50% occurring after aortic surgery and 50% after oesophageal surgery. Diagnosis of AEF is rarely made before massive haematemesis. However most cases are associated with characteristic CHIARI's triad of aorto oesophageal syndrome, including chest pain and sentinel haematemesis of red blood followed at a variable interval of time by rapidly fatal massive exsanguinating haematemesis. Chracterestic triad features were present in 45% of patients included in the review series of Hallander' Quick (2), 80% of patients describe by Carter et al[2,3]. In a few cases AEF can be suspected on the basis of isolated sepsis or septic embolism in a lower extremity. Our suggestive findings include dysphagia and or chest pain, H/O surgical treatment of thoracic aorta.

Except in patients who require immediate emergency surgery, various investigative modalities can be used to confirm diagnosis, plan treatment.

Barium oesophagus may show compression by the aneurysm of the oesophagus[4].

Esophagoscopy can also show the presence of a variable amount of sub-mucosal haematoma indicating extravasation of blood into the oesophageal wall[5]. However even though some investigations advocate oesophagoscopy as the diagnostic modality of choice for evaluation of AEF, others have advised against its use because several cases of fatal haemorrhage precipitated by flexible endoscopy have been reported[6].

Although arteriogram rarely reveal the fistula site they can provide useful data for surgical planning.

Conclusion:

Pre operative contrast enhanced CT chest of the patient revealed the aorto-oesophageal fistula with pseudoaneurysm and post operative CT demonstrated complete occlusion of the tract (Fig1).So, CT scan is a valuable diagnostic method for both pre operative diagnosis and post operative follow-up in these patients.

Acknowledgement:

We remain indebted to Director, Square Hospitals Ltd. for his permission to publish this report.

References:

1. Hollander JE,Quick. G. Aorto esophageal fistula : A comprehensive review of the literature.Am J Med – 1991; 91 : 279-287
2. Yasuda F, Shimono T, Tonouchi H, et al : Successful repair of an aorto oesophageal fistula with aneurysm from oesophageal diverticulum. Ann Thorac.Surgery -2002;73 : 637-639.
3. Center R, Mulder GA, Snyder EN Jr, et al : Aorto oesophageal fistula. Am J surg. 1978;136: 26-30
4. Xia Min, GVO Ji-zhong , ZHAN Qiang,et al. Aortooesophageal fistula caused by descending aortic pseudoaneurysm : one case report . Chinese medical journal 2007;120 (23):2149-2150
5. Myers HS, Silber W. oesophageal bleeding form aorto-oesophageal fistula due to aortic aneurysm : case reports and review of literature , S Afr med. 1983;63 ; 124-127
6. Baron RL,KoehlerRE, Gutierrez FR, et al . clinical and radiological manifestation of aorto oesophageal fistulas . Radiology . 1981; 141: 599-605.

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Dissociative Disorders with Haemolacria: Series of Case Reports

MS RAHMAN[a], MR KARIM[b], MM ISLAM[c], MR KARIM[d]

Summary:

Bloody tears (Haemolacria) are a rare symptom that can be caused by local or systemic pathology. It is one of the most alarming symptom in ophthalmology. Besides those, idiopathic cases have been reported. A case of hyperthyroidism where haemolacria was secondary to the condition has also been reported. Haemolacria are also reported as secondary to epistaxis. Psychogenic causes are described including Munchausen Syndrome by proxy. Here we describe a series of four cases of haemolacria along with bleeding from other sites, found as associated features of dissociative disorders. In this series, patients with age ranging from 14-17 years, three of them are female and one male have been included. Examination excluded local ocular and nasal pathology, coagulopathy and hyperthyroidism. In course of their illness, two of these cases met the DSM 5 criteria for both dissociative disorders and conversion disorders, rest of them have been diagnosed as mixed dissociative disorders. After appropriate intervention, three patients recovered completely and in one patient symptoms (also bleeding) recurred on re-exposure to the previous stress factors.

We report three cases of Dissociative disorders and one with both dissociative and conversion disorder where bloody tears were one of the feature. To the best of our knowledge this is the first official report of its kind in Bangladesh.

(J Bangladesh Coll Phys Surg 2017; 35: 36-42)

Introduction

Hemolacria is a rare clinical condition, literally meaning "bloody tears". In the literature, it has been reported in cases with conjunctival capillary hemangioma, conjunctival telangiectasias, bacterial conjunctivitis, lacrimal sac tumors, lacrimal sac infections, nasal and paranasal sinus tumors[1]. There are cases of idiopathic haemolacria with no identified causes have been reported [2]. A case of bloody tears in a hyperthyroid female patient who displayed no evidence of localized ocular pathology has been reported[4]. Haemolacria has been described in Hereditary hemorrhagic telangiectasia[5], Henoch–Schönlein purpura and retrograde epistaxis and in women during menstrual period. Cases of 'bloody tears' in a hysterical young female[1], during episodes of cluster headache in a case of Gardner-Diamond syndrome[6] have been reported as well. Psychogenic purpura consists in the spontaneous appearance of recurrent bruising, is an unexplained reality which, in addition to cutaneous ecchymoses, may have bleeding from multiple sites, like, haemolacria along with haematuria, menometrorrhagia, GIT bleeding and epistaxis. There may be spontaneous psychogenic as well as self-inflicted iatrogenic bleeding. There is virtually no scientific information on the interaction between the nervous system and hemostasis or blood coagulation[5]. It is remarkable that blood coagulation and other hemostatic tests remain normal in all patients of psychogenic bleeding, including haemolacria. Other bleeding disorders with normal coagulation tests are an inherited failure of collagen biosynthesis or congenital or acquired vascular disorders, but no note of haemolacria as a sign in those disorders has been found[12]. Although in some literatures, haemolacria has been noted as a symptom of 'Hysteria' and other 'Psychological' illnesses[1,2,5,]. This sign has not been categorically included in any particular psychiatric disorder.

a. Dr. Md. Shafiqur Rahman, Associate Professor, Department of Psychiatry, Sylhet Women's Medical College

b. Professor Md. Rezaul Karim, Professor and Head, Department of Psychiatry and Principal, Sylhet Women's Medical College

c. Dr. Mohammed Misbahul Islam, Registrar, Department of Psychiatry, Sylhet Women's Medical College

d. Dr. Md. Redwanul Karim, Consultant Psychiatrist, Department of Psychiatry, Sylhet Women's Medical College Hospital

Address of correspondence: Dr. Md. Shafiqur Rahman, Associate Professor of Psychiatry, Sylhet Women's Medical College, Mirboxtula, Sylhet-3100, Bangladesh. E-mail: shafdoc@yahoo.com

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Case 1

A 16 years old male student of class X, from Sylhet City, admitted in Sylhet Women's Medical college Hospital

in the department of psychiatry on 1/6/2012 with the complaints of episodes of bloody tears from both eyes (haemolacria), bleeding from mouth, bleeding per urethra, chest pain and severe convulsion and inability to talk.

History revealed that the patient was alright about two years ago. Since then he had had multiple episodes of abnormalities characterized by unresponsiveness, convulsions, loss of power in the limbs, inability to hear and see and bleeding from the nose and eyes. According to the parents, first he developed difficulty in breathing and stiffness in both limbs followed by convulsion and paralysis of the lower limbs. Likely precipitating factor was the death of a cousin to whom he was very much attached. That was a single episode relieved after sometime with medical intervention. On another occasion, patient developed pricking sensation on the left side of his body followed by breathlessness, on receiving treatment from a nearby hospital he became symptom free after 24 hours. Since then episodes with different types of features have been continued off and on. About one and half months from the last episode, he started to bleed through mouth. Sometimes he cut his hands to bleed. His schooling hampered seriously and became irregular.

The patient had been evaluated by multiple doctors of different specialties. No physical abnormalities were detected. He was also seen by psychiatrist and clinical psychologist before admission in the hospital.

His father is a businessman, mother house wife; lives in an extended family with his parents, a brother and two sisters along with uncle, aunt and cousins. High expressed emotions within the family members noted from history. No consanguinity within the parents. The family is economically solvent. There is no history of psychiatric disorders among 1st degree relatives.

Patient's birth and early development was normal but in childhood, he used to show temper tantrums and increasingly became demanding, easily gets hurt. Patient complains of apparent lack of appreciation from his parents.

Relation with his siblings is mostly friendly, parents are over caring and classmates are cooperative. He lacks a sense of humor and unable to cope with the sarcastic remarks of his classmates and sometimes become irritated. He is polite, gets easily hurt, and very much sensitive; most of the time he remains depressed, and always tries to find a negative meaning of any remark made by his parents and peers. His performance was mediocre in the school. He has no hobby, passes the leisure time by walking around the house or sitting idle.

Past medical and psychiatric history is nothing contributory. No history suggestive of seizure disorder, mood disorder, anxiety symptoms or PTSD or Malingering. Factitious Disorder also excluded as per DSM 5 criteria.

General and systemic physical examination revealed normal findings. His mental state was otherwise normal except that he was found distracted most of the time during interview.

He complained of poor memory and thinks that he has no disease excepting sometimes his lower limbs become stiff and he lives with sorrow and pain.

All of his lab investigations on different occasions at different hospitals revealed normal findings which include: CBC, Calcium level, USG whole abdomen, CXR, Endoscopy of upper GIT, BT, CT, CT scan of the brain, MRI of the brain, S. bilirubin, AST, ALT, S. alkaline phosphatase, S. protein, urea, S. creatinine, phosphate, LDH, TFT, Urinalysis, APTT, S.C3, C4, ANA, CRP, Anti DS DNA, RF.

Patient is diagnosed as Mixed Dissociative Disorder.

Low dose antidepressants and anxiolytics have been used during his stay in the hospital and counselling continued. Improvement was minor and patient's parents wanted discharge for social reason.

As desired by his family, patient was referred to the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, for further evaluation and management, where he was treated as inpatient for three months. During his stay, the patient was started on individual therapy addressed intra-psychic conflicts, behavioral principles used to improve concentration and family therapy. Low dose antidepressant and anxiolytic used for a short period. Two other follow up visits every 6 months have been made.

Patient have been found stable without recurrences of features on a single follow up visit after 1 year in our hospital.

Case 2 (Fig.-1)

A 17 years old unmarried girl from a township of Sylhet, admitted in the department of psychiatry of Sylhet

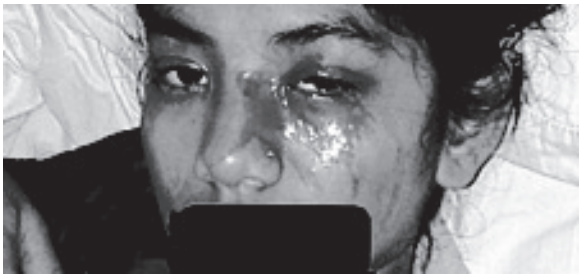

Fig.-1

Women's Medical College on 30/8/2012 with the complaints of episodes of flowing of tear (haemolacria) from both eyes, abnormal abdominal movement followed by blood vomiting after food and paroxysms of abdominal pain for about 2½ years; episodes of convulsions and loss of consciousness and could not remember anything after recovery. These features, episodic in nature, lasted for about 4½ years.

Patient stated that she was reasonably well about four years ago. At the outset, she started episodes of dizziness, headache and vomiting which lasted for about one and half months. After few days when she was a student of class VII (2007), one evening she had seen a small boy climbing in a bamboo in a nearby bush, on other occasion she saw a stranger milking a cow in their premises. As stated by the informant (maternal aunt), since then she used to have transient abnormal experiences, like hearing song or sudden single voice while nobody was around her, or as if somebody was coming to kill her. After About 2 months of marriage of her elder sister in mid-2008, changes in her behavior was noted by relatives; like loss of appetite, vomiting after meal, sometimes became increasingly demanding and aggressive. Whenever she wanted something, if not met with, she started screaming, talked non understandable languages, fell on the ground followed by loss of consciousness for a brief period.

She was very much shy since childhood but after development of above features, she became more extroverted and demonstrative, used to spend more time on grooming, (e.g. changing hair style frequently, putting on colors, plucking brow and manicure). She spent most of her time by watching TV or with her cell phone. She tries to act like TV Models, videos herself along with other family members. Her father works abroad, mother is a house wife, no consanguinity present. She has two sisters and no brother. She lived in a well to-do extended family along with her parents, grandparents, uncle, aunt and cousins and has very strong attachment with her mother. Born with low birth weight (?), achieved usual milestones, shy and reserved during childhood. Schooling was difficult as she has to walk alone about a kilometer to reach.

So when she was at class V, she left home to her maternal grandparents' house where school was nearer. Although her elder sister had been there since before, she missed her mother too much. When she was a student of class VIII, she started to see glimpses of things which nobody else can see.

She suffered from measles in her childhood. Infrequent migraine attacks on exposure to direct sunlight. No history of any other major medical illness is obtained.

Within her family, most of the time she remained happy and cheerful, passes leisure time watching TV. Her relationship was intense with her mother, aunt and maternal uncle. General examination revealed normal findings.

Among other examination, CBC, BT, CT, Endoscopy upper GIT, S. Electrolytes, S. Creatinine, ECG, CXR, and TSH, were within normal limits.

Patient was diagnosed as having mixed Dissociative Disorder and Migraine attacks. Factitious disorder, Malingering, Psychotic disorders and other differentials excluded.

Anxiolytics and low dose antidepressants used for short period. Interpersonal psychotherapy with explanation of her problems discussed targeting the patient and family.

Patient maintained irregular follow up at OPD up to 2 years without further sequel.

Case 3 (Fig.-2)

A 14 years old girl of 8th grade, presented at psychiatric OPD of Sylhet Women's Medical College Hospital 19/05/2014, with the complaints of episodes of burning sensation all over the body followed by bizarre behavior and unconsciousness, episodic bleeding through mouth, eyes and ears; self-mutilating behavior-particularly chewing of lower lip, and stiffness in the limbs; for about 2 months. All the symptoms started after a familial stress.

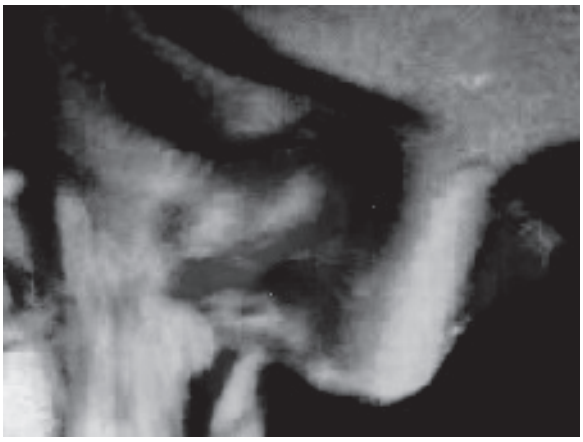

Fig.-2

As per statement of the patient and informants, she was reasonably well 7-8 years ago. When she was 6 years old, she suffered episodic respiratory distress, which was continued despite treatment. For about last 2 years, she has been suffering these episodes with increasing frequency. Moreover, for each episode new features were developed including bizarre behavior, like, tearing apart her clothes, breaking of household things, extreme agitation, running away from the house, biting herself and people around her, followed by brief unconsciousness when sometimes blood coming up through her mouth and both eyes. Each episode lasted for about 40 minutes and after regaining consciousness, patient could not remember anything regarding her behavioral abnormalities. With time she started bleed through her ear and eyes periodically without any other symptom. It was noted that her elder sister, used to have fits even with mild stress, when the patient also got the same by seeing her sister unconscious.

Her father is a businessman, step mother is a house wife. She has 2 sisters and 1 brother. No history of consanguinity between parents, neither any psychiatric illness among her 1st or 2nd degree relatives was obtained. Her birth was domiciliary. Mother died of cancer when she was 9 months old. Since then she has been living with her maternal aunt and brought up in an extended family along with her Grandparents, 2 sisters, uncle and aunt and cousins.

Early development was normal with no abnormal traits. Schooling was uneventful. Age of menarche was at 11. Family environment is otherwise favorable except overindulgence of superstitions. Social circumstances is also good. She had pneumonia in her childhood but no documents were obtained. Since her childhood she maintained a good relationship with her family members and other associates, always cheerful and fond of grooming beautifully. Leisure activity seems to be limited to watching TV. Currently she was asked by her father to shift from her grandparent's family to join her own family but she is unwilling to leave her aunt and live with her step mother.

General physical examination was revealed normal findings. Mental state exam was also normal, anxiety features are noted.

Routine laboratory examinations with BT, CT, were within normal limits.

Diagnosis- Mixed Dissociative Disorder

Patient has been treated with low dose antidepressants. Nature of her illness explained to the patient and family. She became symptom free within one month and remained so for about a year.

On re exposure to the foregoing family stressor, her symptoms recurred. She has been admitted on 31/05/2015 in the psychiatry department. Feigning or factitious disorder excluded by clinical assessment.

Patient received anxiolytics and inter personal psychotherapy therapy along with family therapy and discharged with improvement.

Case-4

A young 15 years old female student of class- IX from a semi urban area of Sylhet district was admitted 01/06/2014 in the psychiatry department of Sylhet Women's Medical College Hospital with the presenting complaints of episodic nose bleeding, bleeding through both ears and decreased sleep. All for about 8 months; episodes of fits for about 10 months; headache for 2 years.

History reveals that patient was in good health 2 year ago. When she was a student of class-VII, once she had an accident while travelling in tricycle (Rickshaw). Since then she had headaches off and on till now. She noticed unexplained change in her mind since then. When she was a student of class-VIII, her brother passed SSC examination and migrated to Sylhet city for higher study, she started to feel lonely as her brother was her

only playmate and friend within the house. Although her parents were willing to migrate to Sylhet city with all other members, she refused to leave her house mainly because her old friends. Gradually she became more demanding, easily gets angry and impulsive. The patient blamed her mother of not to be sympathetic enough to understand her. When she becomes sick her mother use to tell her of negative social impact of her illness which hurt her so much that sometimes she considered suicide. Due to strong religious conviction and considering her family status in the society, she refrained herself from committing so. Regarding fits she stated that whenever she gets hurt she used to cry which gets her a headache, when she read for a long time she gets headache, exposure to excessive heat also brings headache. Whenever she gets a headache irrespective of cause, she at first feels dizzy, then dimness and blurring of vision and loss of hearing, until she loses consciousness.

As her parent state, then she bleeds through nose and ears and recovers after a brief period. The patient's father is an established businessman, mother is a housewife. She has 3 sisters and 1 brother. No history of consanguinity between parents. Her family holds a middle class status. No history of mental illness in the family, but a cousin of her has been suffering from Bipolar Disorder. Her birth was domiciliary and early development was normal. Since childhood she was demanding and showed heightened reactivity to stress. Schooling and education was uneventful. Her age of menarche was at 11 years. She was born in an extended family but brought up in nuclear one.

Past medical and psychiatric history is normal. She used to maintain good and stable relationship with peer group as well as with her family members, especially with her brother and elder sister but somewhat reserved with her mother. She was always cheerful, with an up to the mark living standard. Her free time activities were limited to mobile gaming and occasionally reading books.

General physical examinations and neurological examinations are normal. ENT examination done previously was also normal. Routine laboratory tests including BT, CT, revealed normal findings.

Patient was diagnosed as Conversion Disorder and Migraine with anxiety features. Any other medical and ENT problems excluded after consulting respective specialties.

After discharge from the hospital the patient did not come back for scheduled follow up but her father responded over telephone. Patient remained symptom free for 1 year.

Discussion:

Bloody tears or haemolacria is an inexplicable and alarming condition to the physician, patient and guardian. Haemolacria literally means bloody tears, either frank blood and/or blood mixed discharge from one or both eyes. In the literature, this condition have been reported in the patients of different disciplines of medicine. Historically haemolacria could be traced back to the medieval 'stigmatists' of catholic faith, where bleeding from different wound sites (locations corresponding to the crucifixion wounds of Jesus Christ). Stigmata could take various forms including bloody tears [9,10]. In ophthalmology, sanguineous discharge is a relatively frequent finding in acute conjunctival hyperaemia and inflammation but occurrence of bleeding from eyes in isolated form is unusual and extremely rare. Many causes are outlined by different authors; like, conjunctivitis, capillary haemangioma, conjunctival telangiectasia, lacrimal sac tumours or traumma. Ahwalia et al reported case of haemolacria in a young female where episodes of blood tearing was only under stress, like house examinations. Presence of hysterical trait was confirmed by the consulting psychiatrist. We found mutiple stressors working in our cases at the outset of symptoms. M F Wiese reported a 56 years old woman presented with the history of bleeding from the right nostril. When she had tried to stop it by pinching her nose, she then experienced bleeding from her right eye and ear. Bleeding was ultimately found to be due to haemorrhagic telangiectasia inside nasal cavity [7]. Cases of haemolacria secondary to other ENT causes has also been found in literature which include nasal and paranasal tumours. Ozcan KM reported an 11 years old paediatric patient with the complaints of bilateral haemolacria along with recurrent epistaxis where examination revealed a right side deviated nasal septum and increased hyperemic vascularity in the nasal mucosa, other ENT examinations were normal [3]. A case of haemolacria and epistaxis secondary to hyperthyroidism has been reported by Jason et al where local pathology and coagulopathy have been excluded by examination. Symptoms resolved after appropriate treatment [4]. Ho et al reported a series

of four cases, one boy and three girls ranging 6-14 years where workup finding were normal. In all cases haemolacria resolved without any sequelae over a follow up period of 9-11 months; those cases were reported as idiopathic [2]. Oyenusi and Ananti reported two cases of bloody tears, first one, a boy, presented with cough and bloody tears, the bleeding stopped after routine treatment. The second case was a girl, presented with redness and yellowish mucoid discharge from both eyes with low grade fever for three days followed by bloody tears; this patient was finally diagnosed as orbital cellulitis and managed with antibiotics[8]. M Versetrate wrote in his paper regarding psychogenic bleeding. Psychogenic purpura (Auto-erythrocyte sensitisation) consists in the spontaneous appearance of recurrent bruising, which is still unexplained. Most often woman with an underlying emotional disorder are affected. In addition to cutaneous ecchymoses and hematomas, there may be many other complaints encompassing multiple organ systems along with menorrhagia, metrorrhagia, haematuria, epistaxis and gastrointestinal bleeding and haemolacria. Spontaneous psychogenic cutaneous bruising is very difficult to distinguish from self-inflicted iatrogenic bleeding. The only therapeutic approach in patients with psychogenic bleeding is psychiatric, with particular attention to the sociocultural background of the patient and his family [5, 12]. In our report, four cases of haemolacria along with bleeding from multiple sites associated with psychiatric disorders are described. After meticulous history, direct observation, mental state examinations, examinations to exclude local pathology in collaboration with other departments and work-up for all relevant laboratory investigations, three patients were diagnosed as Mixed Dissociative Disorder and one case with conversion disorder. Dissociative disorders are characterized by a disruption and/or discontinuity in the normal integration of consciousness, memory, identity emotion, perception, body representation motor control, and behavior. Dissociative symptom can potentially disrupt every area of psychological functioning. Dissociative disorders have a high percentage of comorbidities like depression, PTSD, anxiety, self-mutilation, non-epileptic seizure and other psychiatric disorders.[13] Bozkurt et al found high comorbid depression and PTSD in adolescents diagnosed with Dissociative disorder.[14] In our case no.1, conversion symptoms witnessed might be an associated feature, but history revealed that in a previous occasion at least once the patient was diagnosed as conversion disorder. No associated physical illnesses were found in any of them. In case no. 4, concomitant migraine was present. All cases were given the diagnoses as per DSM 5 criteria. Dissociative Identity Disorder (300.14), Dissociative amnesia (300.12), Depersonalization/ Derealization (300.6), along with found.

All of our cases possess hysterical trait, all are adolescents, and there is a female preponderance, which is a common occurrence in Dissociative Disorders. It was noted that, most of the time, severity and intensity of the condition either aggravated or precipitated by detachment (actual or perceived) from the attachment figures. In all of our reported cases, we witnessed the events during their hospital stay.

Limitations: All of our reported cases did not present to us at the beginning of their symptoms. Physicians of different discipline were consulted for physical symptoms. Parents also sought for treatment from traditional and Spiritual healers. As it is not within the scope of this reporting, we did not provide the detailed psychiatric history and diagnostic issues which could be helpful for better understanding. We excluded malingering and factitious disorder through psychiatric assessment as it is known that those who feign dissociative symptoms remain undisturbed with their symptoms and they only report symptoms those are well known to other members of the society, yet definite absence of feigning could not be reliably determined, as no test or procedure is available to date. Could it be a self-injurious behaviour prior to hospital presentation, were not known.

Conclusion: Bloody tearing or haemolacria is an unusual complaint which concerns patients and guardians and many times may baffle physicians. In most of the cases reported so far, haemolacria accompanied bleeding from other body sites as well. This unusual condition has been described in patients with underlying pathology and more importantly sometimes without any known pathology. In the literature, haemolacria has been described as a 'rare' phenomenon, but we are in the opinion that this condition is not that uncommon, as similar cases are increasingly being reported than before. Many cases have been described as idiopathic from different countries. We suggest a multidisciplinary

approach including psychiatric consultation for evaluation of the haemolacria patients when there is no known pathology. Although it is not recorded as an associated feature of Dissociative Disorders in any literature so far, we found bleeding through eyes in our cases of Dissociative disorders and conversion disorder, where no physical pathology were present,. However, it needs more case reports by psychiatrists. We reported physical symptom of bleeding through eyes in our cases of dissociative disorders and conversion disorder which cannot be explained by any standard criteria practiced at present.

References:

1. Ahluwalia, B.K., Khurana, A.K., and Sood, S., Bloody tears (haemolacria). Indian J. Ophthalmol. 1987; 35: 41–43
2. Ho VH, Wilson MW, Linder JS, Fleming JC, Haik BG., "Bloody tears of unknown cause: case series and review of the literature." Ophthal Plast Reconstr Surg. 2004 Nov; 20(6):442-7.
3. Özcan KM, Özdaº T, Baran H, Ozdogan F, Dere H., "Haemolacria: Case report." International Journal of Pediatric Otorhinolaryngology. 2013 Jan; 77(1): 137-138.
4. Jason Z. S. Ho, Julian de Silva, and Jane Olver, "A Very Rare Case of Bloody Tears with Enigmatic Epistaxis and Haematuria." *Orbit*, 2011; 30(2), 116–117.
5. Verstraete M, "Psychogenic Haemorrhages.," Verh K Acad Geneeskd Belg. 1991; 53(1):5-28.
6. Gisele S. Silva, Patricia Nemoto, Paulo H. Monzillo, "Headache Bloody Tears, Gardner–Diamond Syndrome, and Trigemino-Autonomic Headache" Headache, 2014 Jan; 153-54 Available at www.researchgate. net/ publication/ 257750231_Bloody_Tears. *(Accessed on 01/ 01/2015)*.
7. Wiese M F., "Bloody tears, and more! An unusual case of epistaxis." *Br J Ophthalmol* 2003;87:1051
8. Oyenusi EE, Ananti CH," Haemolacria (bloody tears): A perplexing symptom: A report of two cases" Niger J Paed 2015; 42 (1): 68 –70
9. Fessler D, (2002). "Starvation, serotonin, and symbolism. A psychobiocultural perspective on stigmata" Mind and Society: Cognitive Studies in Economics and Social Sciences 3 (2): 81–96. Retrieved on 30/05/2015
10. Wikipedia 2015. Available at http://en.wikipedia.org/wiki/ stigmata, accessed on 30/05/2015.
11. Wikipedia 2015. Available at http://en.wikipedia.org/wiki/ haemolacria, accessed on 18/04/2015
12. Renu Saxena et al. de Gruchy's Clinical Haematology in Medical Practice, 6th adapted ed., India: The Magic International Pvt. Ltd. 2013.
13. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth edition. Arlington, VA, American Psychiatric Association, 2013.
14. Bozucart, H.,Duzman Mutluer, T., Kose, C. and Zoroglu, S. (2015), High psychiatric comorbidity in adolescents with dissociative disorders. Psychiatry and Clinical Neuroscieces,69:369-374 doi:10.1111/pcn.12256

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Posterior Reversible Encephalopathy Syndrome (PRES)

A BEGUM[a], K KHANAM[b]

Summary::

Posterior Reversible Encephalopathy Syndrome is a rare and acute neuro-radiological entity, characterized by several symptoms of different aetiologies. The main etiologies of PRES are HTN, Pre-eclampsia, Eclampsia, Immunosuppressive therapy etc, but there are many unexplained causes too. Here we report a case of post-partum woman who developed PRES in post-operative period, who was complicated by the postdural puncture headache following spinal anesthesia- a rare and uncommon etiology.

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Introduction:

Posterior Reversible Encephalopathy Syndrome (PRES) is a proposed cliniconeuroradiological entity, characterized by several symptoms of different etiology. It predominantly affects the posterior circulation territory and clinical hallmarks are headache, confusion, altered mental status, seizures, visual disturbance and rarely other neurological signs[1]. PRES is seen, not only in relation to pre-eclamsia, but in a variety of disease or condition[3]. Postdural puncture headache is a well described complication of spinal anesthesia in caesarian delivery. Although PRES has not been associated with postdural puncture headache after spinal anesthesia in post partum women[4].

This is a case report of post partum women of an uneventful pregnancy who developed PRES after spinal anaesthesia which was complicated by the postdural puncture headache.

Case Report:

A 20 years old primipara underwent caesarean delivery under spinal anesthesia at her 40th week of gestation because of failure to progress. Her medical history and laboratory examination were unremarkable and pregnancy was uneventful throughout the antenatal period.

After an initial I/V preload of Lactate Ringer's solution (1000 ml), Spinal block was performed, using a midline approach. On the first attempt, clear cerebrospinal fluid was obtained. The patient delivered a healthy baby. The mother's vital signs were normal in per- operative and post operative period.

a. Lt Col Amena Begum, Gynae & Obs, Border Guard Hospital

b. Prof. (Col) Khaleda Khanam (Rtd.), Gynaecologist, Army Medical Corps.

Address of Correspondence: Lt Col Amena Begum, Gynae & Obs, Border Guard Hospital.

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The patient was well until two days of post surgery. On the third day she developed severe postdural headache over bi frontal area, particularly in erect posture, which was relieved by recumbent position. The diagnosis of post dural puncture headache was made. The headache improved after two days of supportive therapy which includes aggressive intravenous hydration, bed rest without pillow and oral analgesics. On 5th postoperative day the patient developed a severe throbbing headache over the occipital area which was no longer postural. On the same day, she developed convulsion which was tonic-clonic in nature with aura. There were 2-3 episodes of convulsion at an interval of 1-2 minute within 25-30 minutes. During this seizure she was unconscious, B/P was 120/80mmHg, pulse 100/m, and urine albumin was nil. Her hematological and biochemical marker were within normal limit. She was nursed in ICU with Anticonvulsive (Mgso4) for 24 hrs, parenteral antibiotic and sedative. Routine hematological, biochemical test as well as chest X- ray, ECG were done and found normal. Diagnostic lumbar puncture revealed clear CSF fluid without any inflammatory cell. The patient's condition was stabilized after 48 hours of ICU nursing. Afterward CT scan and MRI of brain were performed and revealed edema of the bilateral Parieto occipital lobes with density changes and signal alteration respectively, impression was PRES.

During the period of post convulsion hospitalization, there was no episode of marked hypertension, urine albumin was nil and biochemical marker were absolutely normal. After diagnosis patient was treated by multidisciplinary approach by medical specialists and obstetricians. Treatment regimen was initial intravenous nalepsin followed by Injection Mannitol, parentral steroid and later on oral phenytoin were added.

Considering the stability and general condition of the patient gradually medications were withdrawn. She was

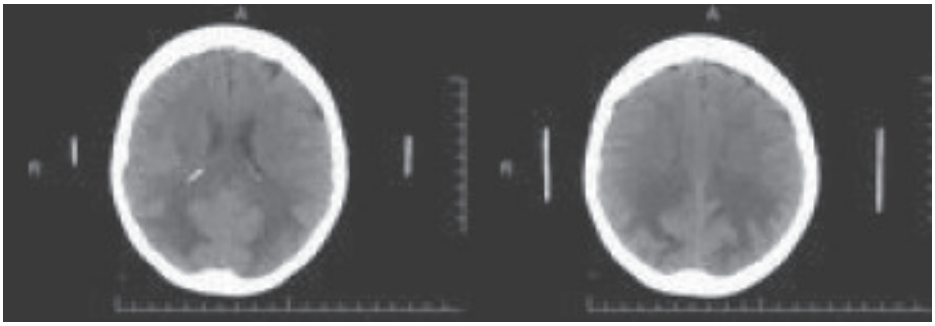

Fig.-1: *CT Scan- Diffuce hypodensity in both parieto occipital region.*

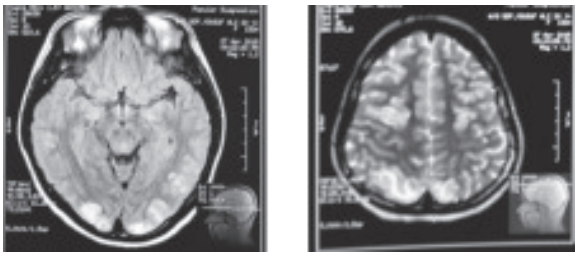

Fig.-2: *MRI- Hyper intense signal in both parieto occipital region in T2 and flare image.*

discharged from hospital at 12th post operative day with the advice for follow -up after 02 weeks. After 02 weeks MRI of brain was done which showed an almost complete resolution of the previous lesion.

Discussion.

PRES was first introduced into clinical practice in 1996[2]. Pathogenesis of PRES is thought to be multi-factorial, yet two different theories are dominating and still being debated[3]. The hyper perfusion theory also called the "vasogenic theory" and the hypo perfusion/ ischaemic theory also called the "cytotoxic theory"[3]. However, the pathogenesis is attributed to a failure of cerebral auto regulation that is probably facilitated in posterior brain region due to sparse sympathetic innervations of the vertebrobasilar vascular system[2].

Clinical symptoms, as well as neuroimaging finding in this patient are compatible with PRES. The patient presented with severe headache over the frontal followed by occipital area, decreased awareness and confusion followed by convulsion. These occurred 2 days after an episode of typical postdural puncture headache following spinal anesthesia for cesarean delivery. CT scan finding was bi lateral patchy hypodensities involving the cortex and subcortical white matter in parieto-occipital lobe. The MR imaging revealed cytotoxic edema of the cerebrum involving bilateral parieto-occipital lobes; MR angiography was unremarkable. These finding indicate that the lesion of PRES of this patient was associated with ischemia-induced cytotoxic edema.

Although the exact mechanism for PRES remains unknown, the temporal association of encephalopathy with diffuse cerebral vasospasm after an episode of postdural puncture headache may have been causative in this patient[4] .Persistent leakage of CSF through the dural opening left by the lumbar puncture needle can result in sagging of the brain and traction on nerves and meningeal vessels. Presumably, the diminished volume of CSF in the cerebral ventricle may collapse the ventricle. This traction might cause mechanical stimulation on the arterial wall and in theory, could induce vasospasm. Clearly, more clinical data are needed to prove this putative mechanism of collapsed ventricle-induced vasospasm[4]. In the current patient, diffuse cerebral artery vasospasm possibly was due to the traction of this vessel by anatomic brain displacement, could It provides an explanation for the development of PRES after spinal anesthesia .Furthermore, lack of evidence for systemic vasculopathy argues against an immune-mediated vacuities in our patient. In addition due error in the CNS, blood pressure auto regulation, and lack of sympathetic innervations of vessels emanating from basilar and vertebral arteries , blood flow in the CNS will increase. this cause elevated capillary filtration pressure and damage the capillary wall, eventually leading to increase blood brain barrier permeability and the consequence of cerebral oedema. All these observations suggest that diffuse cerebral vasospasm after an episode of post dural puncture

headache following spinal anesthesia could have caused PRES in this patient.

PRES has been reported to be reversible; although, irreversible brain damage can sometimes occur due to late recognition or incorrect treatment [2, 4]. Importantly, institution of early treatment, leads to symptom resolution without neurologic deficit, as was seen in this patient. Therefore, aggressive treatment for cerebral vasospasm is essential.

Several clinical studies have also shown that intravascular magnesium sulfate safely relieved maternal cerebral vasospasm[4]. In this case, all syndromes subsided after treatment with magnesium sulphate, Manitol, steroid, with sedative and other supportive treatment. The abnormal findings on neuro imaging had almost reversed after 15 days.

We describe the successful management of a postpartum woman with cerebral vasospasm-induced PRES associated with postdural puncture headache following spinal anesthesia as another condition underlying PRES. This management could be successful only with good intensive care support, proper monitoring and a team work combined with obstetrician and medical specialist.

Conclusion:

The cause of PRES is certainly multifactorial. The syndrome should be promptly recognized since it is reversible. The key to diagnosis is certainly the image, but clinicians must raise suspicion when there is a case with atypical features.

Referencs:

1 A case of Posterior Reversible Encephalopathy Syndrome. G Merra, A Dal Lago, L Natale, E Gaetani, A Caricato, A Clanfoni, P Pola, G Gasbarrini, G Ghirianda. The internal Journal of Neurology, 2008 Volume 11 Number 2

2 Case Report: Posterior Reversible Encephalooathy Syndrome in an eclamtic patient after delivery of a baby. Shaheen Bano 1, Shashi Prakash 2 and Yashpal Singh 3. Asian Journal of Modern and Ayurvedic Medical Science. Issu 2279-0772 volume 01 number July 1 2012.

3 Posterior reversible Encephalopathy Syndrome Postpartum. Lise Hald Nielsen, Brian Stausbol Gron and Per Glud Ovesen.07 December 2014. Dept of OBGYN, Aarhus University hospital. Denmark. 3(4):266-270 2015

4 Posterior reversible Encephalopathy Syndrome with Vasospasm in a Postpartum Woman after Postdural Puncture Headache following Spinal Anesthesia. Ho, Chiu-Ming MD; PhD; Chan, Kwok-Hon MD. Dept of anaesthesia, Taipei Veterans General Hospital and National yang –Ming University. Taipei, Taiwan. 01 June 2007.

Atypical Presentation of Pretibial Myxoedema in Graves' Disease

QT ISLAM[a], ABI MOMEN[b], AK KHONDOKAR[c], HAMN AHASAN[d], H TAHSEEN[e]

(J Bangladesh Coll Phys Surg 2017; 35: 46)

A 26-year-old man presented with gradual swelling of both legs for the last 5 years (Figure 1). The skin over the legs are thickened, with irregular nodular swelling. He also complained of significant weight loss in past few months, together with frequent passage of loose stool, sweating and palpitation. Patient was previously treated by Diethylcarbamazine as a case of Filariasis.

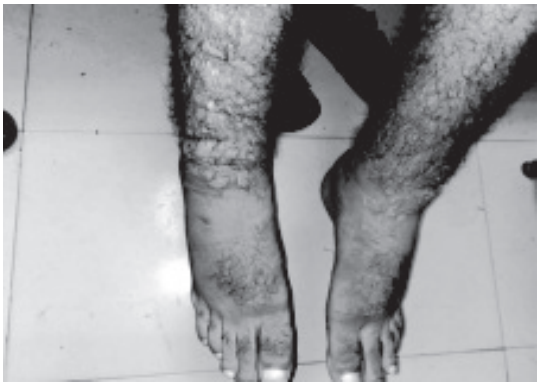

Fig .-1:

On examination the patient was anxious with a staring look and mildly anaemic. There was clubbing (Figure: 2) in digits of hands and feet, tachycardia, irregular nodular non tender and firm goitre with no bruit or retrosternal extension, warm and moist palm, fine tremor.

There was bilateral non pitting oedema of the legs (Figure: 3) and overlying skin is thick, irregular, nodular. There is no organomegaly, ascites or lymphadenopathy. There was exopthalmus, but no diplopia, opthalmoplegia, lid lag or lid retraction.

His thyroid profile revealed TSH - 0.00 mIU/L, F-T4 - 30.27 pmol/L, F-T3 - 16.51pmol/L, Anti-Thyroglobulin Ab - 1.66 IU/ml

The patient was diagnosed with Thyrotoxicosis due to Graves disease with Thyroid acropachy with Dermopathy. This atypical nodular dermopathy is a rare presentation in Graves diseases.

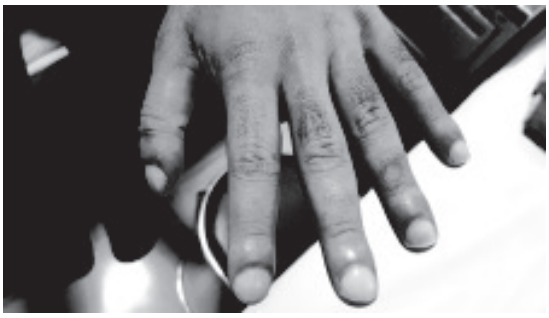

Fig .-2:

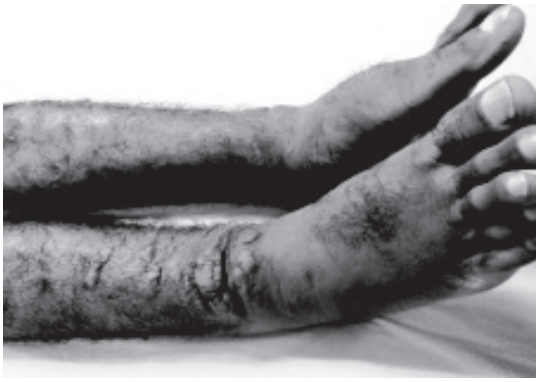

Fig .-3:

a. Quazi Tarikul Islam, Professor of Medicine, Popular Medical College, Dhanmondi, Dhaka
b. Abdul Basit Ibne Momen, Assistant Registrar of Medicine, Popular Medical College, Dhanmondi, Dhaka
c. Abul Kashem Khondokar, Professor and head of Medicine, Popular Medical College, Dhanmondi, Dhaka
d. HAM Nazmul Ahasan, Professor of Medicine, Popular Medical College, Dhanmondi, Dhaka
e. Homayra Tahseen, Associate Professor of Medicine, Popular Medical College, Dhanmondi, Dhaka
Address of Correspondence: Quazi Tarikul Islam, Professor of Medicine, Popular Medical College, Dhanmondi, Dhaka, E-mail: prof.tarik@gmail.com

FROM THE DESK OF EDITOR in CHIEF

(J Bangladesh Coll Phys Surg 2017; 35: 47)

Dear Fellows,

Seasons Greetings and Happy New Year.

I take he opportunity to thank all my Authors, Reviewers, Editors and Office Bearers for their fabulous support throughout 2016. You have made the last year a very successful year for JBCPS. We have been able to publish numerous wonderful articles that has been well appreciated hoe and abroad. New we look forward to take our beloved journal to a higher level in 2017.

Your all out support is my strength.

Thank you

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