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Journal of Bangladesh College of Physicians and Surgeons (JBCPS)

INFORMATION FOR AUTHORS

MANUSCRIPT PREPARATION AND SUBMISSION

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

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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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FIve types of manuscripts may be submitted:

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

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

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

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

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

Review Process:

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

rapidly as possible, and the journal strives to return reviewers' comments to authors within 3 weeks. The editorial board will re-review manuscripts that are accepted pending revision. The JBCPS editorial board will try to publish the manuscript as early as possible fulfilling all the rigorous standard journal needs.

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

Conditions for submission of manuscript:

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

- Ethical aspect of the study will be very carefully considered at the time of assessment of the manuscript.
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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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- Authors need to work closely with editors in developing or using such new publication formats and should submit supplementary electronic material for peer review.
- Double-spacing all portions of the manuscript—including the title page, abstract, text, acknowledgments, references, individual tables, and

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

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

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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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The title page should have the following information:

1. Article title. Concise titles are easier to read than long, convoluted ones. Titles that are too short may, however, lack important information, such as study design (which is particularly important in identifying type of trials). Authors should include all information in the title that will make electronic retrieval of the article both sensitive and specific.
2. Authors' names and institutional affiliations.
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To prevent potential conflicts of interest from being overlooked or misplaced, this information needs to be part of the manuscript. The ICMJE has developed a uniform disclosure form for use by ICMJE member journals (http://www.icmje.org/coi_disclosure.pdf) and JBCPS has accepted that.

I. A. 4. Abstract

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

I. A. 5. Introduction

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

I. A. 6. Methods

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

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

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

I. A. 6. b. Technical Information

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

I. A. 6. c. Statistics

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

I. A. 7. Results

- Present results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Please keep the result the sequence of specific objective selected earlier.
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I. A. 8. Discussion

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

I. A. 9. References

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

- Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible.
- On the other hand, extensive lists of references to original work of a topic can use excessive space on the printed page. Small numbers of references to key original papers often serve as well as more exhaustive lists, particularly since references can now be added to the electronic version of published papers, and since electronic literature searching allows readers to retrieve published literature efficiently.
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- References should be numbered consecutively in the order in which they are first mentioned in the text.
- Identify references in text, tables, and legends by Arabic numerals in superscript.
- References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure.

I. A. 10. Tables

- Tables capture information concisely and display it efficiently.

- Use tables /fig that are relevant to study
- Try to limit the number of tables/figure
- Type or print each table with double-spacing on a separate sheet of paper. Number tables consecutively in the order of their first citation in the text and supply a brief title for each.
- Do not use internal horizontal or vertical lines. Give each column a short or an abbreviated heading. Authors should place explanatory matter in footnotes, not in the heading. Explain all nonstandard abbreviations in footnotes, and use the following symbols, in sequence:

  *, †, ‡, §, _, ¶, **, ††, ‡‡, §§, _ _, ¶¶, etc.
- Identify statistical measures of variations, such as standard deviation and standard error of the mean.
- Be sure that each table is cited in the text. If you use data from another published or unpublished source, obtain permission and acknowledge that source fully.

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- Figures should be either professionally drawn and photographed, or submitted as photographic-quality digital prints. In addition to requiring a version of the figures suitable for printing,

  (for example, JPEG / GIF)
- Authors should review the images of such files on a computer screen before submitting them to be sure they meet their own quality standards. For x-ray films, scans, and other diagnostic images, as well as pictures of pathology specimens or photomicrographs, send sharp, glossy, black-and-white or color photographic prints, usually 127 _ 173 mm (5 _ 7 inches)
- Letters, numbers, and symbols on figures should therefore be clear and consistent throughout, and large enough to remain legible when the figure is reduced for publication.
- Photographs of potentially identifiable people must be accompanied by written permission to use the photograph. Figures should be numbered consecutively according to the order in which they have been cited in the text.
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- Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples.
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- Drug concentrations may be reported in either SI or mass units, but the alternative should be provided in parentheses where appropriate.

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

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

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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:

1. Forwarding/Cover letter and declaration form
2. Authorship and conflicts of interest form
3. Manuscript
    - o Sample of the above documents is available in the following links: http://www.bcpsbd.org (registration required for download)
    - o If you have submitted mention document (1, 2, 3) above, when you first submitted your article then you don't need to re-submit but if there is change in the authorship or related then you have to re-submit it.

- General outline for article presentation and format
    - ❑ Double spacing
    - ❑ Font size should be 12 in arial
    - ❑ Margins 5 cm from above and 2.5 cm from rest sides.
    - ❑ Title page contains all the desired information (vide supra)
    - ❑ Running title provided (not more than 40 characters)
    - ❑ Headings in title case (not ALL CAPITALS, not underlined)
    - ❑ References cited in superscript in the text without brackets after with/without comma (,) or full stop (.)
    - ❑ References according to the journal's instructions – abide by the rules of Vancouver system. Use this link to get into the detail of Vancouver system.
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    - ❑ Uniformity in the language
    - ❑ Abbreviations spelt out in full for the first time
    - ❑ Numerals from 1 to 10 spelt out
    - ❑ Numerals at the beginning of the sentence spelt out
- **Tables and figures**
    - ❑ No repetition of data in tables/graphs and in text
    - ❑ Actual numbers from which graphs drawn, provided
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    - ❑ Labels pasted on back of the photographs (no names written)
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- **Title**
    - ❑ Complete title of your article
    - ❑ Complete author information
    - ❑ Mention conflict of interest if any

- **Abstract**
  - Do not use subheadings in the abstract
  - Give full title of the manuscript in the Abstract page
  - Not more than 200 words for case reports and 250 words for original articles
  - Structured abstract (Including introduction, methods, results and discussion, conclusion) provided for an original article and (Introduction, results and discussion , conclusion) for case reports.
  - Key words provided – arrange them in alphabetical order (three – five)
- **Introduction**
  - Word limit 150 -200 words
  - Pertinent information only
- **Material and Methods**
  - Study Design
  - Duration and place of study
  - Ethical approval
  - Patient consent
  - Statistical analysis and software used.
- **Result**
  - Clearly present the data
  - Avoid data redundancy
  - Use table information at the end of the sentence before full stop between the small bracket
- **Discussion**
  - Avoid unnecessary explanation of someone else work unless it is very relevant to the study
  - Provide and discuss with the literatures to support the study
  - Mention about limitation of your study
- **Conclusion**
  - Give your conclusion
  - Any recommendation
- **Acknowledgement**
  - Acknowledge any person or institute who have helped for the study
- **Reference**
  - Abide by the Vancouver style
  - Use reference at the end of the sentence after the full stop with superscript
- **Legends**
  - Table
  - Figures

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CONTENTS

EDITORIAL

Management of Diabetes Mellitus: Shifting Paradigm

Though Diabetes Mellitus was known to mankind since dawn of civilization, until 1500 AD, medical science was mixture of clinical observation and philosophy. After 1500 AD experimental science started. Scientist observed sweet taste of diabetic urine, presence of sugar in urine, sweet taste of diabetic blood serum, charges in pancreas in diabetic subject, calcification of pancreas etc.

Paul Langerhans (1848-88) demonstrated the special tissue in pancreas i.e. Islets of Langerhans. E.L. Opie (1873-1921) observed reduced number of Islet in Diabetes. Landmark experimental study was done by Oscar Minkowski (1859-1931) and Joseph Von Mering (1849-1908) of Germany. They did pancreatectomy of a dog and that caused it diabetic, presence of ketone in urine. Then they injected the pancreatic tissue extract in the body of pancreatectomised dog and that proved to prevent diabetic symptoms. Though in 1907, William Lane distinguished A and B islet cells, beta cell first drew the attention.

Discovery of Insulin

Working at a University of Toronto Laboratory in 1921 Fred Banting and Charles Best were able to make a pancreatic extract which had antidiabetic characteristics. They were successful in testing their extract on diabetic dogs. Within months professor J.J.R MacLeod, who provided the lab space and general scientific direction to Banting and Best, put his entire research team to work on the production and purification of insulin. J.B. Collip joined the team and with his technical expertise the four discovers were able to purify insulin for use on diabetic patients. The first tests were conducted on Leonard Thompson early in 1922. These were a spectacular success. Word of this success spread quickly around the giving immediate hope to many diabetic persons who were near to death. A frenzied quest for insulin followed. Some patients in a diabetic coma made miraculous recoveries.

Evolution of Insulins

Animal Insulin

Beginning in 1922, and in the face of great demand for the new medicine, several companies were granted licenses by the University of Toronto to manufacture insulin. Initially patient needed several injections daily to maintain blood sugar level which was painful. In 1936, protamine, a low-weight protein, was used to develop a slow-release insulin.

In 1950 yet another approach led to the presently available isophane NPH (Neutral Protamine Hagedorn) insulin, which is also bound to protamine. It has a maximal effect of 24 h and can be mixed with any proportion of fast-acting regular insulin, which reduced injection number.

Despite the discovery of insulin scientist were in the quest of development oral medicine. In 1956, the first antidiabetic oral drugs – sulfonamide (tolbutamide, carbutamide) and biguanide derivatives (metormin, phenformin) – came to the market. But till today scientist are yet to develop ideal oral drug.

In 1974, chromatographic purification techniques allowed the production of highly purified animal insulin (less than 1 pmol/l of protein impurities). This product was called 'monocomponent MC'. Before this development, porcine and bovine insulin at times caused antibody allergies and lipoatrophy.

Human Insulin and Analogues

After several years of laboratory work, during the years 1963-1966 human insulin was chemically synthesized in Germany by Meienhofer et al. and in the United States by Katsoyannis et al. In 1978, scientists in San Francisco using a genetically manipulated plasmid of *E. coli* bacteria, succeeded in producing insulin with the same amino sequence as seen in humans.

Problems with conventional insulins: The need for analogues

Until some time back there are only human soluble short-acting (regular) insulin, intermediate-acting insulins

(NPH and lente insulin) and mixtures of regular plus NPH insulin in various proportions (30/70 mixture being used more widely). The pharmacokinetics of these conventional insulin preparations fail to match the physiological insulin secretion profile, and due to this in most patients it has been virtually impossible to obtain HbA_1c values around or <7.0%[1,2]. Attempts to reach the target of HbA_1c <7%, patients are facing hyperglycemia as well as hypoglycemia in post-meal state. Another drawback with these insulins are that a considerable number of patients have been characterized by a degree of control with a huge day-to-day variation in glycaemic level[2]. This variation is a result of several factors including variability in insulin action, insulin absorption, etc. and is observed both within an individual (intra individual) and between different individuals (inter individuals). Even though insulin therapy has evolved over the years with advances in purity, species, retarding agents, and other excipients, scientists were unable to overcome these inherent limitations of conventional insulins.

Search for newer insulins: meeting the unmet needs

Efforts were focused at searching for better insulin formulations that can mimic endogenous insulin secretion more closely, so that optimal glycaemic control becomes a reality. It was the advent of biotechnology in the 1980s, which facilitated the efforts and helped scientists modify the native insulin molecule and design insulins with more desirable properties. The pioneering work on rapid-acting insulin analogues were performed by Brange and colleagues in the mid-80s[3,4]. A later work on long-acting designer insuins was initiated. Several strategies were studied and a few of them were applied to bring out *designer insulins*, commonly called *insulin analogues*.

The concept of designer insulins has raised great expectations. The arrival of the rapid-acting analogues contributes to improved patients' convenience and reduced postprandial glucose excursions[5] with a lower risk of hypoglycaemia. On the other hand the basal insulin analogues have fulfilled to a great extent the need for a more physiological basal insulin.

The availability of better monitoring tools along with the evidence to show that near-normal glycaemic control reduces the risk of diabetic complications has increased the need for insulin preparation that offer greater effectiveness, safety and versatility[6]. Insulin analogues have met this need to a great extend as these newer insulins have made possible the near-physiological replacement of prandial as well as basal insulin. The proper use of insulin analogues allows people with diabetes greater flexibility in the timing of meals, snacks, and exercise, which in turn enhances their ability to lead normal lives[7]. Their availability will help treatment strategies to be tailored to the needs of individual patients thereby helping them to achieve the best possible metabolic control. Insulin analogues will also provide physicians with the appropriate tools to overcome the obstacles to improve metabolic control and subsequently improve diabetes outcomes[8,9].

Glucagon Factor and Peptide Analogues

If we consider pathophysiology of DM, we know it is not only insulin factor which is decreased and insulin resistance which prevent insulin to work efficiently are responsible, but there is also glucagons factor. In response to a carbohydrate meal, in nondiabetic subject not only there is increase is increase in insulin secretion but also simultaneously decrease in glucagon secretion. In contrast glucagons secretion in type 2 diabetics is not decreased, and may paradoxically increase. These produce an excessive postprandial glucose excursion by increased hepatic output.

Increatin hormones which are secreted in various parts of the gut e.g. glucagons-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), regulate glucose homeostasis by increasing insulin synthesis, decreasing glucagons secretion from pancreatic alpha-cells resulting in decreased hepatic out put it also works by slowing gastric empting and thus suppressing food intake. Both GLP-1 and GIP are rapidly inactivated by the enzyme dipeptidyl peptidase-4).

Glucagon-like peptide (GLP) and analogs and agonists

GLP agonists bind to a membrane GLP receptor. As a consequence of this, insulin release from the pancreatic beta-cells is increased. Endogenous GLP has a half life of only a few minutes; thus an analogue of GLP was produced.

- Exenatide is the first GLP-1 agonist approved for the treatment of type 2 diabetes. It is not an analogue of GLP, but rather a GLP agonist and has only 53% homology with GLP, which increases its resistance

to degradation by DPP-4 and extends its half-life. Typical reductions in A1C values are 0.5-1.0%[10].

- Liraglutide, a once daily human analogue (97% homology), is rather better GLP-1 analogue. Animal model shows that GLP-1 analogue preserve even regenerate B-cell mass.

These agents may also cause a decrease in gastric motility, responsible for the common side effect of nausea, and is probably the mechanism by which weight loss occurs.

DPP-4 inhibitors:

Dipeptidyl peptidase-4 (DPP-4) inhibitors increase blood concentration of the incretin GLP-1 (Glucagon-like peptide-1) by inhibiting its degradation by dipeptidyl peptidase-4 (DPP-4). They are vildagliptin, sitagliptin, saxagliptin etc. But there are also limitations in their action.

Conclusion:

Management of diabetes actually started after the discovery of insulin. From insulin scientist tried to shift to oral drug. But observing the limitations of oral drugs both secretogogues and senstizer, attention focused again of insulin with various modification of its formulation. Simultaneously, keeping pathophysiology of diabetes, role of alpha cell secreting glucagons and various gut hormones are also now strongly focused. Another hormone secreted by B-cell i.e. Amylin is perhaps going to be another tool in managing diabetes mellitus.

Despite of development of newer molecules having capability of good glycemic status with less adverse effect, along with preservation and regeneration of B-cell mass, a good number of patients are going to have diabetes related complications. Modern treatment prolonging life expectancy of good number of patients with all deadly complications causing them a handicapped.

So, can we prevent development of DM? The answer is 'yes'. Prevention of DM does not cost any money rather it saves money. Many studies proved beyond doubt that simple life style modification by changing eating habits and increase in physical activity, DM can be prevented in 60-65% of subjects. So, there remains a great hope.

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Haemoglobin Level in Children of a Northern District of Bangladesh

MN ABSAR

Summary:

Objective: To find out the reference level of haemoglobin and other haematological parameters(PCV, MCV, MCH, MCHC, S. Iron and S. Ferritin) of the children of Northern area of Bangladesh and to see the relation of socio demographic features and other haematological parameters with haemoglobin level.

Methodology: Observational cross sectional study.

Setting: Outpatient department of Rangpur Medical College and outpatient department of eight Upozilla Health Complexes of northern Bangladesh.

Patients:300 clinically healthy 1yr. to 14yr. age children.

Outcome measures: Mean Hb. level in age groups and influence of sex, age, economic status, parental education, nutrition and serum iron on level of Hb. PCV, MCV, MCH, MCHC, S. Iron and S. Ferritin was estimated to see the confounders and if they are affecting Hb. level significantly.

Results: Mean haemoglobin among study population was 11.4gm/dl(SD;1.07). Haemoglobin was normally distributed among the study population. Mean haemoglobin among age groups differed significantly. No significant difference in mean haemoglobin was observed among two sex groups.

Mean haemoglibin level corresponded well with WHO defined haemoglobin level in the same age group of children.

Conclusion: Reference level of mean Hb. in the studied population is 11.4gm/dl(SD;1.07). Age affects the Hb. level but sex does't. Hb. level in this population is comparable with WHO reference value for this age.

Key ward: Reference level of haemoglobin, haemoglobin level in children, mean haemoglobin, racial difference in haemoglobin.

(J Bangladesh Coll Phys Surg 2012; 30: 127-131)

Introduction:

In preschool age 47.4% are suffering from iron deficiency anaemia. Prevalence in Asia is 65.5%[1]. In Bangladesh prevalence in preschool age is 47% according to 2001 survey[2]. To define anaemia WHO cut off value of haemoglobin is being used. But it is well known that normal level of haemoglobin in a population varies with age,gender, altitude, race and ethnicity. Lower level of haemoglobin has been observed in children of Asian and African origin in comparison with American and European origin[3,4,5]. Weihang et al concluded in their study that blood values differ by age ,sex and race. It was obvious that there was significant difference of Hb, PCV, MCV, MCH, MCHC values between white and blacks in all ages[(6)]. Normal haemoglobin level should be defined for each particular group of population in order to see the prevalence of anaemia in the particular population group. We have to know the haematological parameters in our children for better understanding of their normal growth and nutrition status.

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Methodology:

Study was conducted in Rangpur district of Bangladesh. Children of 1 yr. to 14 yr. attending the out patient departments of Rangpur Medical College and eight upazilla health complexes were included in this study. Systematic random sampling was done. Chronic and recurrent illness and any inflammatory condition was excluded by history and clinical examination. Anaemia was screened out clinically. Nutrition status was determined by anthropometry and Z score of height for age and weight for age. Venous blood sample was collected and Hb., PCV, MCV, MCH, MCHC, S.Iron and S.Ferritin were estimated. Haemoglobin was done by cyanmethaemoglobin method and other haematological parameters were estimated by fully automated haematology analyzer; Sysmex XT – 1800i, Japan and Immulite – 1000 analyzer USA. Peripheral blood film

was scaned by qualified haematologist to exclude the possibility of congenital haemolytic anaemia. Study was done during the period of January'08 to December'08. Sample size was 250 to give 95% confidence interval of 0.04 with standard error of 1.96. It was rounded upward to 300 to reduce sample error.

Result:

Age of the study population ranges from 1.4 yr. to 14 yr. Mean age was 7 yr. with SD;±3.12yr. Demography of the study population is as follows.

Table-I

Demography of study population

Parameters	No(%)
Age group:	
1 – 4 yrs.	58(19.3)
4 – 9 yrs.	156(52)
9 – 14 yrs.	86(28.7)
Sex:	
Male	165(55)
Female	135(45)
Maternal education:	
Illiterate	112(37.3)
Primary	106(35.3)
Secondary	64(21.3)
Higher secondary	18(6)
Occupation of the parents:	
Labourer	133(44.3)
Service	70(23.3)
Business	82(27.3)
Other	15(5)
Total monthly family income(Taka):	
Range	1500 – 30000
Mean(SD)	5357.33(±3675.797)
Per capita monthly income(Taka*):	
< 1000	136(45.3)
1000 – 2000	120(40)
2000 – 3000	31(10.3)
>3000	13(4.3)

*1$=70Tk.

Z score(Weight for age): Mean Z score was -2.3457, SD=+5.45.

Hb. was distributed normally with no skew ness. Hb. level and other haematological parameters are given bellow(Table II). Haematological parameters were normal in comparison to their reference value, which indicates that the studied population was not anaemic.

Table-II

Haematological parameters

Parameters	Mean value(SD)
Hb(gm/dl)	11.4±1.07
PCV(%)	36.324±3.31
MCV(fl)	79.134±.29
MCH (pg)	24.82±2.59
MCHC(gm)	31.29±1.85
S.Iron (µ/dl)	59.72±32.94
S.Ferritin(ng/dl)	59.4±52.79

In this population haemoglobin is distributed normally(Fig:1). There was no skewness. There was no significant difference in haemoglobin level between the male and female groups(P = 0.65). Mean haemoglobin distribution in different age group differed significantly(P = .000). Factors those affected mean Hb. level were father's education(P = 0.01), Parental occupation(P = 0.002), total monthly family income(P= 0.014). Z score for weight for age was found to have no significant correlation with haemoglobin level of the study group(r = 0.005, P = 0.927).

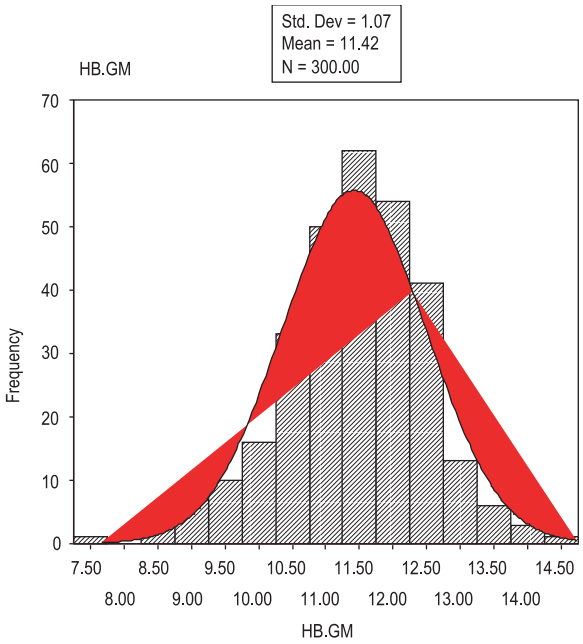

Fig-1: *Distribution of haemoglobin in studied population*

There are high correlations of haemoglobin in the studied population with PCV, MCV, MCH, MCHC, S.Iron, but no correlation was found with S.Frritin. These are shown in Table-III.

Table-III

Correlation of Hb with other Haematological Parameters

Parameters	Pearson Correlation(r)	2-tailed significance(P)
PCV	0.884	0.000
MCV	0.476	0.000
MCH	0.591	0.000
MCHC	0.198	0.001
S.Iron	0.242	0.000
S.Ferritin	0.017	0.776

Discussion:

WHO defined Hb. cut off level is being used for our children. This cut off is based on the studies, mostly done in western children[1,2]. There is lack of adequate representative information regarding the haemoglobin level in south east asian region and socio demographic and nutritional factors influencing the haemoglobin level in children of our country and South East Asia. There is a unique study done by Faruk et al. in different socio demographic group of adolescent school boys in Dhaka city which estimated haemoglobin level in these groups and compared the influence of education of parents, occupation of parents, percapita income, nature of food consumed, nutrition status etc[7]. Present study was done in a section of children in the northern part of Bangladesh in Rangpur district. The mean age was 6.9±3.12 yrs. This study doesn't provide haematological values bellow 1 yr of age. Children of bellow 1 yr. was not included in the study because haemoglobin stabilizes to normal value at about 1 yr age[8]and normal haemoglobin also appears by this age[9].

It was found that the mean haemoglobin among the study population was 11.417gm/dl(SD;±1.07). The rang was 7.5gm/dl to 14. 7gm/dl. Percntile values are; 5th percentile= 9.5gm/dl, 25th percentile=10.8gm/dl, 50th percentile=11.5gm/dl, 75th percentile=12.1gm/dl and 95th percentile was 13.1gm/dl. Haemoglobin was found to be normally distributed in the study population. Median and mode was same(11.5gm). There was no skewness. WHO recommended lowest cutoff value for haemoglobin in children at sea level are: 11gm/dl for 6month to 59 month., 11.5gm/dl for 5yrs. to 11yrs. and 12gm/dl for 12 to 14yrs[1,2]. in comparison to that, the mean Hb. in this study in different age group are; 10.73gm/dl(±0.99) for 1 to 4 yrs., 11.33gm/dl(±0.98)

For 4 to 9 yrs. and 12.03gm/dl(±0.94) for 9 to 14 yrs. age. It indicates that mean haemoglobin is almost same as compared with WHO cut off value except for 1 to 4 yr age group which is lower in this study. In another study Frag et al. observed lower value in younger age group of children[7]. This difference is probably physiological. Nutrition seems doesn't have anything to do with this difference. Because in all age group mean Z-score for wt. for age was -2SD. More over it was found that there was no significant correlation between mean haemoglobin and mean Z-score for wt. for age(r=0.005, P=0.927). There was no observed significant difference in Hb. distribution in different sex groups in the study population. There was also no significant difference in mean haemoglobin among male and female children in different age groups. In this study mean haemoglobin for male children was, 11.4gm/dl(±1.13) and that for female children was, 11.43(±0.99). Mann and WhitneyU test shows no significant difference of mean haemoglobin between two sexes(P=0.836). Hawkins et al. has shown in their study that sex difference in mean haemoglobin becomes apparent after 20 yrs of age[10].WHO also has not recommended any different value for male and female children[1]. However there is significant age specific variation in mean haemoglobin.Significant difference was observed in mean haemoglobin among different age groups(P=0.01). This was noted in other studies also[11,12,13,14].Age difference and age group variation is well documented by WHO and other studies[1,15]. Other factors influencing mean haemoglobin were family income, occupation of the parent, education of the parents and nutrition status. There was significant correlation between haemoglobin level and age(r=0.478, P=0.01). Iron status and nutritional status could be low in young children group. Mayer et al. observed that young children are vulnerable to anaemia, and nutritional anaemia is the most common cause[16]. Ahmed et al. in their study in Dhaka city in Bangladesh implicated pattern of foods as a significant factor for low hemoglobin in adolescent school boys[7]. How ever

Duggan et al. found no correlation between biochemical iron status and protein energy nutritional status[14]. However other studies support the view that deficient iron intake is important contributor for low haemoglobin in infancy and early childhood[17,18]. In the studied population haemoglobin was normally distributed and there was no skewness. This indicates that haemoglobin values found in this study are normal for the studied population.

The WHO cut off value for haematocrit below which anaemia is considered to be present in children are as follows[1];

Age group	Haematocrit
6mo. to 59mo.	0.33
5yr. to 11 yr.	0.34
12yr. to 14yr.	0.36

In the present study mean PCV was 36.24%(SD;±3.31). In age groups in comparison to WHO cut off the mean PCV were: 1 to 4yr.; 34.35%(±3), 4 to 9 yr.; 36.03(±3.04), and 9 to 14 yr.;38(±3.05). This indicates that the children studied were not anaemic even as per WHO standard. More over there was a positive correlation found between Hb. level and PCV(r= .884, P= .000). So,the haemoglobin value found in this group can be taken as normal. Mean value for MCV was 79.13fl(SD;±8.2fl), which is much above the lowest value (72fl) bellow which haemoglobin falls bellow the lowest cut for anaemia[18]. Domellof et al. has suggested – 2SD cut off value for MCV as 73 – 71 fl. in infants who are fed with iron fortified formula and ferritin > 10ng/L[19]. In the present study MCV is much higher than these values. It can be presumed that the population studied is having normal MCV, so haemoglobin level found was the normal value of that population. Mean corpuscular haemoglobin (MCH) remains higher bellow 6mo. of age. It falls progressively to reach it's nadir at 21 to 24 month of age. Duggan et al. found mean MCH in Asian healthy children at different age groups as follows[14]; at 3 – <6mo = 25.7, 6 - <9mo. = 24.1, 9 - <12 mo. = 23.7and at about 21 - <24 mo. = 21.9pg. The authors implicated it to the deficient iron intake. In the present study mean MCH was 24.82pg(SD; ±2.59) which is quiet higher than the Dggan's study and comparable to the value at 3 - <mo. age group. This fact also support the assumption that the children of this study are not iron deficient. Age wise distribution of normal mean corpuscular haemoglobin concentration(MCHC) is[9]; 3mo. to yr. = 30 – 36 gm/dl.RBC, 2yr. to 18 yr. = 31 – 37 gm/dl.RBC. Mean MCHC in this study was 31.29gm±1.84gm/dl.RBC. So, it is obvious that distribution of MCHC in this study is within normal limit. Mean MCHC was positively correlated with haemoglobin level(r = 0.198, P = 0.001). Serum iron was found to be positively correlated with level of haemoglobin in this study(r = 0.242, P = 0.000) The mean value was 59.72±32.94µgm/dl which was also within normal limit(22 – 184 µgm/dl)[11]. However iron depletion state is better reflected by serum ferritin level. WHO cut off value for serum ferritin is 15ngm/dl. Bellow this level iron store is considered to be depleted[1]. In the present study mean serum ferritin level in apparently non infectious children was 59.4ngm/dl. So, it can be assumed that the studied population was not iron depleted.

Conclusion: With all these observations and analysis it can be concluded that the normal mean haemoglobin of the study group of children (1yr to 14 yr. age) is 11.41gm/dl with SD=±1.07. Median value is 11.5gm/dl. Percentile values are; 5^{th} percentile= 9.5gm/dl,50^{th} percentile=11.5gm/dl, 75^{th} percentile=12.1gm/dl and 95^{th} percentile=13.1gm/dl. Haemoglobin is distributed normally in the studied population. No significant difference in mean haemoglobin between two sexes was observed. There was significant difference in mean haemoglobin between different age groups. Socio demographic factors that affect haemoglobin in a positive way are; total monthly income of the family, parental literacy and occupation of the parents. Important factor that was found to have no significant correlation with haemoglobin level was weight for age Z score. Haemoglobin distribution among 1yr. to 14 yr. age group of children was almost same as WHO set level.

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Clinicopathological Profile of Rhabdomyosarcoma in Children

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Summary:

Objectives*: To describe the clinical profile as well as histopathological sub-types of Rhabdomyosarcoma in children.*

Methods*: A hospital base prospective observational study was conducted among 20 diagnosed cases of Rhabdomyosarcoma in children, those attending in Hemato-Oncology department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka in the period between January to December 2009.*

Results*: The peak incidence of Rhabdomyosarcoma was in 1-5 years of age group (n=9, 45%) with mean age 6.83 years with male to female ratio 5.66:1. The common sites of primary tumor was in head and neck region (40%, n=08), followed by genito-urinary tract, 30% (n=06), extremities 20% (n=04), trunk 10% (n=02). The most common clinical presentation was mass lesion 100% (n=20), followed by local pain 25% (n=05), urinary obstructions 15% (n=03) dysphagia, chronic otorrhea, dysuria, haematuria, and proptoses were 10% each (n=02, each); The histological sub-types were Embryonal 60% (n=12), alveolar 30% (n=6), and Botryoid 10% (n=02); Of Embryonal variety in head and neck region 58.33% (n=7), and Genito-urinary sites 41.67% (n=5); of Alveolar variety in trunk 66.67% (n=4), and in extremities33.33% (n=2), of Botryoid sub-type frequency was equal in head - neck region and genitourinary site 50% each (n=1).*

Conclusion*: Children with Rhabdomyosarcoma presented mostly in 1 to 5 years of age, with mass lesion (100%), predominantly in head and neck region (40%) and the commonest histological sub-type was Embryonal variety (60%).*

Key words*: Rhabdomyosarcoma, clinicopathological profile, histological sub-types.*

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Introduction:

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children.[1] Although Weber first described Rhabdomyosarcoma in 1854, a clear histologic definition was not available until 1946, when Stout recognized the distinct morphology of Rhabdomyoblast. Stout described Rhabdomyoblasts as appearing in round, strap, racquet, and spider forms. As its name suggests, the tumor arise from a primitive muscle cells[2].Although the tumor is believed to arise from primitive muscle cells, it can occur anywhere in the body except bone. The most common sites of Rhabdomyosarcoma in children are the head and neck region (35%), the genitourinary tract (35%) and the extremities (17%). The orbit is the primary site in about 10% of these tumors; the most common localization in the head and neck area is parameningeal, including the nasopharynx, the paranasal sinuses, the middle ear and mastoid and the infratemporal fossa or pterygopalatine space. Most children are younger than 10 years of age (72%).[3]

Rhabdomyosarcoma may be presented as a wide range of clinical features depending on the site of primary tumor. The most common presenting feature is a mass that may or may not be painful. Tumor arising from extremities may be presented with asymptomatic mass. But symptoms from other site involvement are caused by displacement or obstruction of normal structures. Tumors originating in the nasopharynx may be associated with nasal congestion, mouth breathing,

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epistaxis, and difficulty with swallowing and chewing. Rhabdomyosarcoma extended into the cranium can produce cranial nerve palsies, blindness and signs of increased intracranial pressure with headache and vomiting and that in the face or cheek may present with swelling, pain, and trismus. Tumor in the neck can produce progressive swelling with neurological symptoms after regional extension. Orbital primary tumor usually diagnosed with periorbital edema, proptosis, change in visual acuity, and local pain. When the tumor arises in middle ear, the most common early signs are pain, hearing loss, chronic otorrhea, or external ear mass. Rhabdomyosarcoma arising from urogenital tract may present with recurrent urinary tract infection or hematuria.[4]

Rhabdomyosarcoma is defined as demonstrating at least minimal evidence of Rhabdomyogenesis, or skeletal muscle differentiation. However, in a large proportion of cases, morphological evidence of myogenesis is limited to a small percentage of tumor cells or may be extremely difficult to detect. The use of antibodies for immunohistochemical detection of myogenesis-associated proteins such as desmin, myogenin (MYOG), and MyoD (MYOD1) have aided the diagnostic workup of such cases, and when combined myogenin and MyoD have 97% sensitivity to detect Rhabdomyosarcoma. The identification of muscle related differentiation is key and clinically relevant because some Rhabdomyosarcoma cases can be virtually indistinguishable from the group of so-called undifferentiated or non-Rhabdo-myosarcoma soft-tissue sarcomas. [5]

Two major forms of the disease are described, conventionally termed Embryonal Rhabdomyosarcoma (ERMS) and Alveolar Rhabdomyosarcoma (ARMS), reflecting morphological similarities to fetal muscle or pulmonary alveoli, respectively. These distinctions are clinically relevant because the embryonal form typically shows less aggressive clinical behavior and a better prognosis. There is an embryonal variant known as spindle or botryoid tumors which are highly curable. When clinical stages and other variables are taken into account, survival rates range from 90% in localized form of embryonal Rhabdomyosarcoma to as low as 20% for patients with metastatic alveolar histologic tumors.

Though Rhabdomyosarcoma is a very common soft tissue sarcoma in children, there is no published literature of clinicopathological profile of this tumor in our country. The findings of this study could help the health professionals of our country in early diagnosis of Rhabdomyosarcoma and initiating treatment with a view of rewarding outcome.

Materials and methods:

The study was a hospital based prospective observational study, carried out in the department, of paediatric Hemato- Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka in between January to December 2009. Total 20 diagnosed cases of Rhabdomyosarcoma in children aged 1 to 15 years, those attending in and out patient department of the hospital were enrolled in this study. Children aged over 15 years and soft tissue sarcomas other than Rhabdomyosarcomas were excluded from the study.

There were no ethical problems, as before study procedure conducted, verbal consent of patients' attendants and also from the patients was taken. Disagreed cases were not included in this study.

Data was collected from in and outpatient departments of Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka. Cases were selected according to inclusion and exclusion criteria. Face to face interviews were taken. Relevant informations (according to questionnaire) were taken from attendants preferably from parents and patients (10 years and older). In the history of illness, clinical presentation of the tumor particularly related to primary sites, and presenting physical problems were analyzed. Physical examinations were done in detail. During examination, emphasis was given on identifying primary tumor site. In all cases available documents were examined to see investigation reports particularly imaging and histopathological reports to correlate clinical presentations with histological sub-types.

After data collection all data was entered in master sheet and analyzed manually in view of the objective of the study. Frequency, distribution and proportions were calculated for the values. Results were published in graph and tabulated form.

Results:

Total 20 cases were included in this study and following results were found.

Table-1 shows *Age distribution.* Mean age was 6.83 years, and standard deviation was 4.41. Minimum age was 5 months and maximum age was 13 years. Maximum number of patients were in 1-5 years age group (n=9, 45%).

Table-I

Age distribution (n=20)

Age in years	Number of patients	Percentage (%)
0-1	03	15%
1-5	09	45%
5-10	04	25%
10-15	06	40%
Total	=20	100%

Figure-1shows *sex distribution.* Among all the patients male was 85% (n=17) and female was 15% (n=03) with male to female ratio 5.66:1.

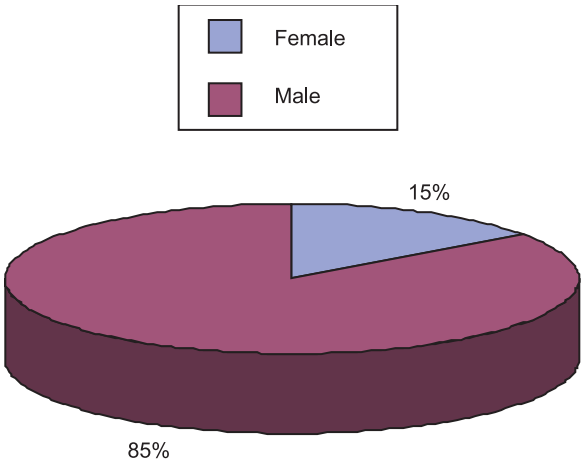

Fig.-l: *Pie chart showing sex distribution*

Table-ll summarizes *Anatomical Location of primary tumor.* Most common anatomical location of primary tumor was in head and neck region 40% (n=08). The next common sites were genito-urinary 30% (n=06), extremity 20% (n=04), and trunk 10% (n=02). In the head and neck region, orbit 15% (n=03), ear 10% (n=02), nasopharynx 05% (n=01), paranasal sinuses 05 % (n=01), tongue 05% (n=01).

Table ll

Anatomical Location of primary tumor

Anatomical location	Frequency	Percent (%)
Head and neck	08	40%
Orbit	03	15%
Nasopharyx	01	05%
Ear	02	10%
Paranasal sinuses	01	05%
Tongue	01	05%
Genito- urinary	06	30%
Urinary bladder	03	15%
Testes	03	15%
Extremity	04	20%
Lower limb	04	20%
Trunk	02	10%
Total	=20	= 100%

Table-lll summarizes *Clinical presentations.* The most common presenting feature was primary tumor mass 100% (n=20) irrespective of sites. Other presenting features were local pain 25% (n=05), urinary obstruction 15% (n=03), and dysphagia, otorrhea, proptosis, haematuria, dysuria 10% each (n=02); epistaxis, ocular palsy, and nasal obstruction 5% (n=01).

Figure ll- shows distribution of histopathological sub-types of Rhabdomyosarcoma. The Embryonal Rhabdomyosarcoma was the most common histological sub-type 60 % (n=12,). Other types were Alveolar sub-type 30% (n=06), and Botryoid sub- type of embryonal variety10% (n=02); No pleomorphic or anaplastic variety was found.

Table-lV summarizes *Clinical presentations in relation to pathological –subtype.* Among 12 cases of Embryonal variety 7 was found in head and neck region (58.33%), 5 was found in genito-urinary tumors (41.66%), among total 6 cases of Alveolar variety 4 was found in trunk (66.66%) and 2 in extremities (33.33%), total 2 cases were of Botryoid sub-type, among them 1 was from head and neck region, other one from genitourinary site.

Table-lll

Clinical presentations

Anatomical location		Clinical presentation	Frequency	Percentage
Head and neck	Orbit	Tumor mass	03	15%
		Proptosis	02	10%
		Ocular palsy	01	05%
		Local Pain	01	05%
	Nasopharyx	Tumor mass	01	05%
		Dysphagia	01	05%
		Epistaxis	01	05%
	Ear	External ear mass	02	10%
		Local pain	02	10%
		Otorrhoea	02	10%
	Paranasal sinuses	Tumor massNasal obstruction	0101	05%05%
	Tongue	Tumor mass	01	05%
		Dysphagia	01	05%
Genito-urinary	Urinary bladder	Tumor mass	03	15%
		Haematuria	02	10%
		Dysuria	02	10%
		Urinary obstruction	03	15%
	Testes	Tumor mass	03	15%
		Local pain	02	10%
Extremities	Lower limb	Tumor mass	04	20%
Trunk		Tumor mass	02	10%

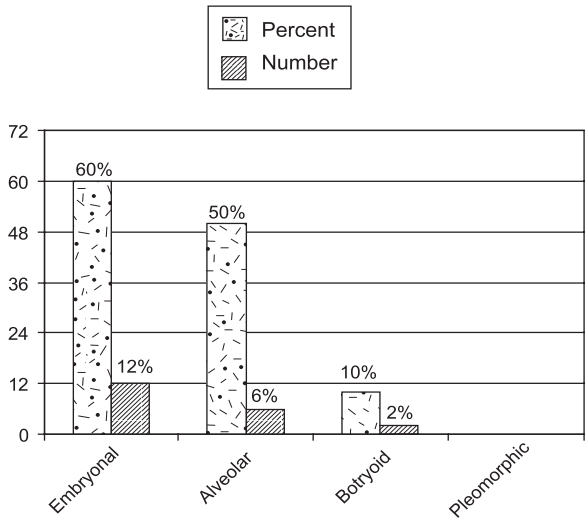

Fig.-2: *Bar diagram showing histopathological sub-types of Rhabdomyosarcoma (n=20)*

Table-lV

Clinical presentations in relation to pathological –subtypes

Primary sites	Embryonal (Number)	Alveolar (Number)	Botryoid (Number)	Pleomorphic (Number)
Head and neck RMS	7	0	1	0
Genito-urinary RMS	5	0	1	0
Trunk RMS	0	4	0	0
Extremity RMS	0	2	0	0
Total	12	6	2	0

Discussion:

This hospital based prospective observational study showed that the peak incidence of Rhabdomyosarcoma was in 1-5 years of age group (n=9, 45%) with mean age 6.83 years, though the age range was 5 months to 13 years and male to female ratio was 5.66: 1(17:3). In a study by Brown BJ et al. at the University College Hospital Ibadan, Nigeria (between 1984 and 2003)

showed mean age of presentation of Rhabdomyosarcoma was found 6.2(4.1) years.[6] The highest incidence of tumors was found in head and neck region (40%, n=08), among them orbit 15% (n=03), nasopharynx 05% (n=01), ear 10% (n=02), paranasal sinuses 05% (n=01), and tongue 05% (n=01). The next common incidence of Rhabdomyosarcoma was found in genito-urinary tract, 30% (n=06) among them urinary bladder 15% (n=03), testes15% (n=03).Tumor incidence in extremities was 20% (n=04).The least incidence of the tumor was in trunk 10% (n=02). Brown BJ et al. observed the majority (50.6%) of tumors was in the head and neck region and the common primary sites were soft tissue of the head, face (24.2%) and orbit (14.3%). Other sites included soft tissue of the pelvis (11.0%), genito-urinary tract (9.9%) and abdomen (9.9%).[6]The variation of incidence the tumor with other international studies regarding primary tumor site may be due to small sample size.

In the current study tumor mass was found in 100% (n=20) cases, most lesions of limbs and trunks were painless; only in 25% (n=05) cases located in ear and orbit lesions were associated with local pain. Urinary retention was the next common presenting feature (n=03, 15%) in our study. Urinary retention was due to involvement of urinary bladder leading to bladder outflow obstruction. Proptosis was observed in 10% (n=02) cases. It was due to tumor growth in retro orbital space and associated with ocular palsy (n=01, 05%).Chronic otorrhea was found in 10%(n=02) cases whose were due to middle ear involvement of Rhabdomyosarcoma leading to chronic otitis media. Dysuria and haematuria was found in 10% (n=02) cases whose were associated with urinary bladder involvement and urinary obstruction. Dysphagia was observed in some tumors 10% (n=02) involving tongue and nasopharynx. The least manifestation was nasal obstruction, observed in 05% (n=1) cases. Epistaxis was another uncommon presentation. Rhabdomyosarcoma involving nasopharynx was presented with the same. There was no feature of raised intracranial pressure in any case.

In our study, we got almost all histological sub-types of Rhabdomyosarcoma except pleomorphic one. The embryonal sub-type was found 60% (n=12), and alveolar sub-type 30% (n=06) cases. Botryoid sub-type was found in 10% (n=02) cases of whose mostly found in genitourinary tract tumor. This finding is almost consistent with the finding observed by Pappo AS et al. who observed the incidence of Embryonal Rhabdomyosarcoma in 55% of patients; the Botryoid variant in 5% of patients and Alveolar Rhabdomyosarcoma in 20% of patients.[7] In current study, of Embryonal variety more was found in head and neck region (n=7, 58.33%), and also in Genito-urinary sites (n=5, 41.67%); on the other hand, of Alveolar variety more was found in trunk (n=4, 66.67%) and also in extremities (n=2, 33.33%); of Botryoid sub-type frequency was equal in head and neck region and genitourinary sites (n=1 each, 50%). Parham et al. has shown that Embryonal subtype is the most frequently observed Rhabdomyosarcoma in children (60% to 70%) and typically arise in the head and neck region or in the genitourinary tract; Botryoid tumors represent about 10% of all Rhabdomyosarcoma cases that arise under the mucosal surface of body orifices such as the vagina, bladder, nasopharynx, and biliary tract; approximately 20% is alveolar subtype with primary sites involving the extremities, trunk, and perineum or perianal region; Pleomorphic one occurs rarely in children.[8]

Conclusion:

In this study, children with Rhabdomyosarcoma presented mostly in 1 to 5 years of age with male to female ratio 5.66: 1(17:3); predominant lesions were in head and neck region (40%) followed by genitourinary sites (30%) and extremity (20%). Common presentations were mass lesion (100%), local Pain (25%), urinary obstructions (15%), proptosis, dysphagia, otorrhea, and haematuria (10% each). The most common histological sub-type was Embryonal (60 %), followed by Alveolar (30%) and Botryoid (10%).

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The Role of FNAC in Diagnosis of Breast Disease at Different Ages - 208 Cases

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Summary:

All breast lesions are not malignant, and all the benign lesions do not progress to cancer; however the accuracy of diagnosis can be increased by a combination of preoperative tests. About 30% of women suffer from breast disease in their lifetime. The main objectives are to explore the role of FNAC in diagnosis of breast disease at different ages. Fine needle aspiration cytology (FNAC) has become a critical component in the investigation of palpable breast masses.

Total 208 cases included in this study at Comilla. The data was formulated and analyzed by SPSS-12. 79(37.98%) cases were at the age of 21-30 years and next one was 11-20 years which was 48(23.07%). Among them 40(19.23%) cases were malignant and 168(80.77%) cases were benign in nature. The incidence of malignancy was increased with relation to age. As the age is more chance of malignancy is more. In benign types fibroadenoma was the common disease then the duct cell carcinoma, fibrocystic change, suppurative inflammation respectively. The findings were 43.75%, 19.23%, 18.27% and 8.65%.

In conclusion, fine needle aspiration cytology, for diagnosis of breast lump can reduce the number of open biopsy and surgery.

(J Bangladesh Coll Phys Surg 2012; 30: 137-140)

Introduction:

Breast, a sign of womenhood and fertility has been a subject for clinicians from the time medicine is being practiced. Breast diseases are the most common ailment from which women suffer throughout the world. About 30% of women suffer from breast disease in their lifetime[1].

The palpable breast lesion is a common problem at the surgical outpatient clinics. The aim in management is to exclude malignant disease and in this aspect, fine needle aspiration cytology (FNAC) plays an important role [2].

Fine needle aspiration cytology is an excellent safe and cost effective diagnostic procedure. One can get on site immediate report with minimal cost using inexpensive equipment and a simple technique. The most significant advantage of FNAC is the high degree of accuracy, rapid results, and a less invasive procedure than a tissue biopsy. FNAC of the breast can reduce the number of open breast biopsies.[3-6]

The triple diagnostic method (consisting of clinical evaluation, mammography and fine needle aspiration cytology) gives a precise diagnosis and reduces the risk of a missed diagnosis of breast cancer to <1%[7].The aim of this study is to find out the common causes of breast lump at different ages and offer treatment.

Materials and Methods:

This study was carried out at Comilla in different clinics and hospitals. It was undertaken from 01.01.2010 to 31.12.2010.All breast lump of female patient were included in this study. Data was collected randomly as per inclusion and exclusion criteria. The age of the patient and FNAC report were recorded for analysis of data. Data was analyzed by manually and by SPSS-12(SPSS= Statistical Programmed for Scientific Study). The results were plotted in tables, charts and graphs.

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Inclusion criteria:

1. All patients presented with breast lump.
2. All female patients of at any age.

Exclusion criteria:

1. Male patient with breast disease.
2. Lump negative patients.
3. Patient with histopathological diagnosis of malignancy.

Results:

Table-I

Age distribution

Age of the patient	Number of cases	Percentages
11-20	48	23.07%
21-30	79	37.98%
31-40	39	18.75%
41-50	27	12.98%
51-60	11	5.29%
61-70	03	1.44%
71-80	00	00
81-90	01	0.48%
Total	208	100%

The total number of cases was 208. Most of the patients were in the age group 11-50 years. Among them 79 cases were present in 20-30 years age group. This data consists of both benign and malignant disease. Only one case was at 81-90 years.

Table-II

Disease type

	Number of cases	Percentages
Benign	168	80.77%
Malignant	40	19.23%
Total	208	100%

In Table II shows the benign and malignant diseases of the breast. Most of the cases were benign, which was 168 cases. But malignant disease was 40 cases only.

Table-III

Comparison of benign and malignant disease of different age (cross table test).

Age	Benign	Malignant	Total
11-20	47(97.92%)	01(2.08%)	48
21-30	75(94.94%)	04(5.06%)	79
31-40	29(74.36%)	10(25.64%)	39
41-50	14(51.85%)	13(48.15%)	27
51-60	03(27.27%)	08(72.73%)	11
61-70	0	03(100%)	03
81-90	0	01(100%)	01
Total	168	40	208

In correlation of benign and malignant disease with age showed that the number of malignant disease was increased with increasing age. Benign disease of breast was more in younger ones. Maximum benign disease were in the age of 21-30 years which was about 75. Older at the age of 81-90 years single malignant disease was present.

Table-IV

Types of disease

Disease	Number of cases	Percentages
Fibroadenoma	91	43.75%
Fibrocystic change	38	18.27%
Duct cell carcinoma	40	19.23%
Suppurative Inflammation	18	8.65%
Granulomatous mastitis	09	4.32%
Galactocele	09	4.32%
Lipoma	02	0.96%
Accessory breast tissue	01	0.48%
Total	208	100%

The commonest disease of breast was fibroadenoma which was about 91 cases. Duct cell carcinoma was the malignant disease, it was about 40 cases and 38cases had fibrocystic change.

Table-V

Test statistics

	Age	Disease type	Disease
Chi-square	159.702	78.769	299.894
df	06	01	8
Asymp. Significance	.000	.000	.000

Discussion:

Total 208 patients were included in this study. All patients were female and FNAC done in all cases and reports were interpretated in a tabulated form.

Age distribution of the disease was 48, 79, 39, 27, 11, 03 and 01 cases at different age distribution. The breast disease was more common between the age of 21-30 years and was commoner among 11-20 years age group. Another study showed that the distribution was 23, 76, 166, 86, 53, 16 and 5 cases respectively. This disparity due to more number of cases in this study.[8]

Among the 208 cases 168(80.77%) cases were benign and 40(19.23%) cases were malignant. The benign cases were more than the malignant cases.Tiwari M. found only 6.6% cases were malignant and others were benign in out of 91 cases.[9]Usually the percentage of benign is 80% and that of malignant was 20%[13].

In comparison of malignancy at different age showed that the number of malignancy with advancement of age of the patients. Here 01(one) case was found at the age of 11-20 years but at 41-50 years 13 cases were malignant out of 27 cases. At the age of 61-70 years almost 100% cases were malignant. Carcinoma of the breast is extremely rare below the age of 20 years about, thereafter; the incidence steadily rises so that by the age of 90 years nearly 20% of women are affected [10].

In type of disease, maximum disease was benign in nature. Among them fibroadenoma was the most common which was 91(43.75%) and it correlates with other studies [8.9].Malignant breast lump present in 40(19.23%) of cases. In different studies it was 6.6% [9] and a recent study in Pakistan showed breast cancer only in 6.9% [11]. A recent study by Yousuf [12] in Rawalpindi also observed 21% cancer in their study. Next suppurative inflammation and galactocele present in 18(8.65%) and 09(4.32%). Tiwari M. found breast abscess in 6.6% and galactocele in 5.5% of cases [9]. Tuberculous mastitis was present in 4.32% of cases and showed in breast tuberculosis in 2.3% of cases [8].

Conclusion:

This prospective study was done at Comilla district with sample size was 208. FNAC was done in all female patients having breast lump and male patients were excluded from the study.

The commonest age of breast disease was 21-30 years which was 79(39.98%) of cases. The next commoner age group was 11-20 years, it was about 48(23.07%) and 31-40 years 39 (18.75%). 80% cases were suffering from benign disease and rest of the patient were malignant in nature.

The comparison of disease at different ages showed that the percentages of malignancy increases with the increasing of age. At the age of 11-20 years most of the cases were benign and only one case was malignant but at the age of 51-60 years 100% of cases become malignant.

The type of diseases was variable. Most common was fibroadenoma 43.75 %(91) and the next one was fibrocystic change which was 38(18.27%) cases. Duct cell carcinoma was found in 40(19.23%) cases and tuberculosis in breast disease was 09 (4.32%) of cases.

Small sample size does not depict the picture of whole nation. A large scale study in required for further evaluation of disease.

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Validation of the Modified Friedewald's Formula to Calculate Low-density Lipoprotein Cholesterol in Bangladeshi Population

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Summary:

Objective: A modification of Friedewald's formula was proposed to calculate LDL cholesterol in Bangladeshi population up to serum triglyceride concentration of 1000 mg/dL. The aim of this study was to validate the modification of Friedewald's formula in Bangladeshi population.

Methods: Serum total cholesterol, triglyceride, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol concentrations were measured in specimens obtained form 314 adult Bangladeshi subjects selected conveniently. LDL cholesterol concentrations were also calculated by modified Friedewald's formula and original Friedewald's formula. Results were expressed as mean ± SD and calculated LDL cholesterol was compared with measured LDL cholesterol by two-tailed paired t test and Pearson's correlation coefficient (r).

Results: The mean ± SD of measured LDL cholesterol was 138.3 ± 54.58 mg/dL. LDL cholesterol calculated by modified Friedewald's formula and original Friedewald's formula were 135.9 ± 59.26 mg/dL (P>0.05) and 123.5 ± 65.75 mg/dL (P<0.001) respectively. Compared to measured LDL cholesterol, calculated LDL cholesterol were 2.47 mg/dL and 17.20 mg/dL lower for modified formula and original formula respectively. The correlation coefficient (r) with measured LDL cholesterol was 0.8601 (P<0.0001) for LDL cholesterol calculated by the modified Friedewald's formula and 0.8565 (P<0.0001) for the LDL cholesterol calculated by the original Friedewald's formula.

Conclusion: The study validates the modified Friedewald's formula to calculate LDL cholesterol in Bangladeshi population.

Key words: Friedewald's formula, LDL cholesterol, Calculated LDL cholesterol

(J Bangladesh Coll Phys Surg 2012; 30: 141-144)

Introduction:

The reference method for the measurement of serum low-density lipoprotein (LDL) cholesterol is the ß-quantification.[1] It is not readily available and also impractical in the routine laboratory. Direct methods have been developed and are recommended to measure LDL cholesterol alternatively. The direct methods are costly and require expensive automation. So the most convenient method of LDL cholesterol estimation is the Friedewald's formula that allows the calculation of LDL cholesterol from serum total cholesterol (TC), serum triglycerides (TG) and high-density lipoprotein (HDL) cholesterol [LDL cholesterol = TC – TG/5 – HDL cholesterol].[2] This formula is applicable up to serum TG concentration of 400 mg/dL and it is the most commonly used procedure in clinical practice worldwide as well as in Bangladesh. But this formula underestimates LDL cholesterol in different populations studied as well as in Bangladesh.[3,4,5,6] A recent study in our population proposed a modification of Friedewald's formula to calculate LDL cholesterol up to serum TG concentration of 1000 mg/dL.[7] The modification of Friedewald's formula was based on the absolute differences between direct LDL cholesterol and LDL cholesterol calculated by Friedewald's formula (ÄLDL

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cholesterol) and the linear regression equation of the absolute difference with serum triglyceride to total cholesterol ratio. The linear regression equation, ÄLDL cholesterol = (15.3×TG:TC – 12.4) mg/dL was added to the original Friedewald's formula to get the modified equation, LDL cholesterol = TC – TG/5 – HDL cholesterol + (15.3 ×TG:TC – 12.4) (when all concentrations are expressed in mg/dL). The aim of this study was to validate the modified formula for the calculation of LDL cholesterol.

Methods and materials:

The study was conducted in Armed Forces Institute of Pathology (AFIP), Bangladesh during the period of January to March, 2011. Serum total cholesterol (TC), serum triglyceride (TG), serum high-density lipoprotein (HDL) cholesterol and serum low-density lipoprotein (LDL) cholesterol were measured on 314 sera obtained from adult subjects of both sexes after 12 hours fast. Serum TG and TC were measured by enzymatic end-point method. HDL cholesterol and LDL cholesterol were measured by direct automated method using ABX Pentra 400 clinical chemistry analyzer (France). All kits, calibrators and quality controls were purchased from Horiba, France through local distributor.

Subjects with serum TG concentration > 1000 mg/dL and TG/TC > 4 were excluded. Subjects with serum TG d" 400 mg/dL were considered as group A and subjects with serum TG > 400 mg/dL were considered as group B.

Results were expressed as mean±SD and compared by two-tailed paired t test and Pearson's correlation coefficients of calculated LDL cholesterol with measured LDL cholesterol (using GraphPad Prism 5.04 for Windows and STATISTICA 8.0 for Windows).

Results:

Mean ± SD of age of the total study subjects was 48.28 ± 11.08 years, in which 65% subjects were males and 35% subjects were females. The mean ± SD of lipid parameters in group A, group B and in the total study subjects are presented in table I and comparison of calculated LDL cholesterol and measured LDL cholesterol is shown in table II. In the total study subjects, the mean ± SD of measured LDL cholesterol, LDL cholesterol calculated by modified Friedewald's formula and LDL cholesterol calculated by original Friedewald's formula were 138.3 ± 54.58 mg/dL, 135.9 ± 59.26 mg/dL and 123.5 ± 65.75 mg/dL respectively. The difference between measured LDL cholesterol and LDL cholesterol calculated by modified Friedewald's formula was not statistically significant (P>0.05, table II); but the difference between measured LDL cholesterol and LDL cholesterol calculated by original Friedewald's formula was statistically significant (P<0.0001, table II). Pearson's correlation coefficients of measured LDL cholesterol with LDL cholesterol calculated by modified Friedewald's formula and original Friedewald's formula were 0.8601 (P<0.0001) and 0.8565 (P<0.0001) respectively.

In group A, mean ± SD of age was 48.67 ± 11.59 years in which 67% subjects were males and 33% subjects were females. The mean±SD of measured LDL cholesterol, LDL cholesterol calculated by modified Friedewald's formula and LDL cholesterol calculated by original Friedewald's formula were 141.4 ± 54.78 mg/dL, 139.4 ± 58.11 mg/dL and 130.5 ± 63.02 mg/dL respectively. The difference between measured LDL cholesterol and LDL cholesterol calculated by modified

Table-I

Mean ± SD of lipid parameters

Parameters	Group A (n=233)	Group B (n=76)	Total subjects (n=309)
Total cholesterol (mg/dL)	222.1±65.2	237.9±71.8	226.0±67.1
Serum triglyceride (mg/dL)	289.2±51.3	518.6±103.1	345.6±119.8
Serum HDL cholesterol (mg/dL)	33.7±8.0	32.2±7.0	33.3±7.7
Measured LDL cholesterol (mg/dL)	141.4±54.8	128.8±53.2	138.3±54.6

Table II

Comparison of LDL cholesterol calculated by modified Friedewald's formula and original Friedewald's formula with measured LDL cholesterol

	Mean ± SD		
	TG: up to 1000 mg/dL (n=309)	Group A TGd"400mg/dL (n=233)	Group B TG>400 mg/dL (n=76)
Measured LDL cholesterol	138.3±54.58	141.4±54.78	128.8±53.20
LDL cholesterol by modified FF	135.9±59.26^{NS}	139.4±58.11^{NS}	125.0±61.79^{NS}
LDL cholesterol by original FF	123.5±65.75***	130.5±63.02***	102.0±69.71***
Correlation coefficient of mLDLC with measured LDL cholesterol	0.8601***	0.9044***	0.7242***
Correlation coefficient of fLDLC with measured LDL cholesterol	0.8565***	0.9014***	0.7348***
Difference between mLDLC and measured LDLC	-2.47±20.93^{NS}	-1.83±18.98^{NS}	-4.43±26.08^{NS}
Difference between fLDLC and measured LDLC	-17.20±31.71***	-11.21±23.54***	-35.58±44.29***

TG, Serum Triglyceride; FF, Friedewald's formula; mLDLC, LDL cholesterol calculated by modified Friedewald's formula; fLDLC, LDL cholesterol calculated by original Friedewald's formula; ***, P<0.0001; NS, Not statistically significant

Friedewald's formula was not statistically significant (P>0.05, table II); but LDL cholesterol calculated by original Friedewald's formula was significantly different from measured LDL cholesterol (P<0.0001, table II). Pearson's correlation coefficient (r) of measured LDL cholesterol with LDL cholesterol calculated by modified Friedewald's formula was 0.9044 (P<0.0001) and that of measured LDL cholesterol with LDL cholesterol calculated by original Friedewald's formula was 0.9014 (P<0.0001).

In group B, mean ± SD of age was 47.09 ± 12.47 years in which 62% subjects were males and 38% subjects were females. The mean ± SD of measured LDL cholesterol, LDL cholesterol calculated by modified Friedewald's formula and LDL cholesterol calculated by original Friedewald's formula were 128.8 ± 53.20 mg/dL, 125.0 ± 61.79 mg/dL and 102.0 ± 69.71 mg/dL respectively. The difference between measured LDL cholesterol and LDL cholesterol calculated by modified Friedewald's formula was not statistically significant (P>0.05, table II); but LDL cholesterol calculated by original Friedewald's formula was significantly different from measured LDL cholesterol (P<0.0001, table II). Pearson's correlation coefficient of measured LDL cholesterol with LDL cholesterol calculated by modified Friedewald's formula was 0.7242 (P<0.0001) and that of measured LDL cholesterol with LDL cholesterol calculated by original Friedewald's formula was 0.7348 (P<0.0001).

Discussion:

In this study, LDL cholesterol calculated by modified Friedewald's formula and original Friedewald's formula correlated strongly and significantly with the measured LDL cholesterol within and above the valid TG range of Friedewald's formula. LDL cholesterol calculated by original Friedewald's formula was significantly lower than measured LDL cholesterol in both groups (P<0.0001); but no significant difference was observed between measured LDL cholesterol and LDL cholesterol calculated by modified Friedewald's formula (P>0.05).

Our study findings conform to the findings of the recent study[7] done in our population, based on which modified Friedewald's formula to calculate LDL cholesterol up to serum TG concentration of 1000 mg/dL has been proposed.

Friedewald's formula was validated and modified in different populations. Study with large number of samples indicated that original Friedewald's formula can be used up to serum TG concentration of 800 mg/dL.[8] But in case of specimens with high serum TG, Friedewald's formula frequently underestimates LDL cholesterol and sometimes produces negative results. In these cases the results are not reportable. Since the correlation coefficient of LDL cholesterol calculated by original Friedewald's formula with measured LDL cholesterol is high and statistically significant, underestimation of LDL cholesterol can be subsided using the modified Friedewald's formula and can be used to calculate LDL cholesterol approximately when original Friedewald's formula is invalid. However, this calculation formula should be used with caution in case of high risk individuals.

Conclusion:

The present study is consistent with the previous study done in our population. So we also conclude that the modified Friedewald's formula can be used to calculate LDL cholesterol in Bangladeshi population.

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Choriocarcinoma - Varied Presentations

SN BEGUM

Summary:

Choriocarcinoma is a highly malignant tumour that originates in developing trophoblast of pregnancy. It is a potentially fatal disease but current management protocol has turned the prognosis highly favourable.

Gestational choriocarcinoma is not a rare disease in our country. Various mode of presentation sometimes makes it difficult to diagnose.

Eleven cases of choriocarcinoma were presented here along with treatment modalities and prognosis. Two patients expired during treatment while other respond well with chemotherapy. Early diagnosis and appropriate treatment have better prognosis.

(J Bangladesh Coll Phys Surg 2012; 30: 145-150)

Introduction:

Choriocarcinoma is a highly malignant epithelial tumour arising from the trophoblastic tissue of any gestational event.[1] It is a potentially fatal disease, but availability of different diagnostic aid (ultrasonogram, serum β-hCG) and its unique sensitivity to chemotherapy has turned the prognosis highly favourable.

It is one of the rare human malignancy which is completely curable even with wide spread metastasis[2].

It has an incidence of 0.05 to 0.23 per thousand live births. The frequency of the disease is estimated as 1 in 30,000 pregnancies in the West and 1 in 11,000 pregnancies in Oriental communities.[3]

Preceding gestational events are hydatidiform mole (50%), term pregnancy (20%) , non molar abortion (5%) and ectopic pregnancy (5%). [4]

Patients may present with irregular vaginal bleeding, amenorrhoea , abdominal or vaginal swelling or symptoms of metastasis like haemoptysis.[4] It can virtually spread anywhere in the body through haematogenous or lymphatic route. Most commonly it spreads to lungs (80%), lower genital tract (cervix, vagina, vulva), brain and liver. [5] It can spread to small bowel producing intestinal obstruction, renal mass with hematuria, splenic metastasis with intraperitoneal bleeding with severe anaemia.[3.6.7,8]

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Gestational trophoblastic tumour always contain only paternal genes as such they are considered to an allograft in the maternal host.[9] A few postmolar choriocarcinomas are biparental, and are considered to represent 'new pregnancies' or 'carcinoma *ab initio*'.[10,11] Most of the choriocarcinoma patients of belong to poor socioeconomic class and that may directly related to poor nutritional status .

The clinical presentation, treatment modalities and outcome of 11 cases of choriocarcinoma are discussed here.

Methods:

This prospective study on 11 cases of choriocarcinoma with varied clinical features was undertaken in Sylhet MAG Osmani Medical college.

All data regarding clinical presentation, investigation and treatment with outcome was recorded meticulously for analysis.

Result:

Sociodemographic characteristic of the patients were presented in Table I. Mean age of the patient were 33.39 yrs (range18-46yrs), among them six were > 40 years of age. 73.75% were multipara (n-8) out of which four were grandmulti. All but one belongs to poor social class. Blood group was O in seven cases while rest have A or AB group.

Time interval between antecedent pregnancy and diagnosis of disease varies from 3months to 13 yrs. Antecedent pregnancy events were term pregnancy (n-5), abortion (n-5) and molar pregnancy (n-1) in this study.

Clinical presentation was depicted in Table II. Irregular per vaginal bleeding was the common presentation in all case. Other clinical features were lower abdominal pain (case2,3,4,5,6), bleeding from vaginal growth (case1,8) and Shock (case1,4). Two patients (case 4,6) present with acute abdomen for internal haemorrhage needed emergency laparotomy. Uterus was enlarged (about 10-20cm. size) in seven cases due to myometrial involvement and misdiagnosed as fibroid uterus by ultrasonogram. Case 7 was diagnosed as cervical fibroid by USG. Serum β-hCG level varies from 412-15,00,000 miu/ml. Pulmonary metastasis was present in 7cases. Case 1 had metastasis in vagina, lungs and brain. Histopathology showing features of choriocarcinoma in 8 cases.

Regarding treatment 63.63% (n-7) patients had total abdominal hysterectomy (TAH) due to severe bleeding with extensive involvement of myometrium. Four patient had internal haemorrhage as the growth invade the uterine wall. Chemotherapy was given in 81.80% of cases. EMA-CO regime was given in six patient while three received MTX. Both surgery (TAH) and chemotherapy was needed in seven cases.

Regarding treatment outcome, seven had good recovery while two patient expired . Two patient lost to follow-up. Case no.6 expired suddenly on 2nd POD following TAH due to respiratory problem (? pul.embolism). Case no.8 having vaginal and pulmonary metastasis with high βhCG level, treated with surgery (TAH) and chemotherapy but the patient succumb suddenly on 7th POD.

Autopsy examination was needed to confirm the cause of death in such cases.

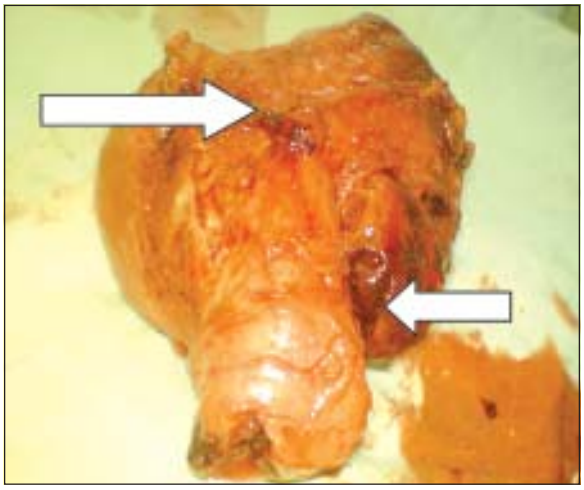

Fig.-1: *Haemorrhagic growth in lat. and ant wall of ut.(case3)*

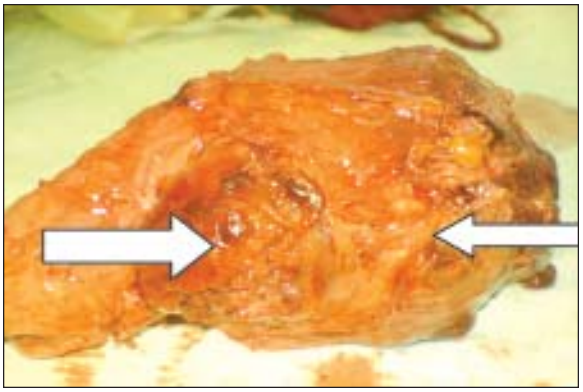

Fig.-2: *Haemorrhagic growth (case4)*

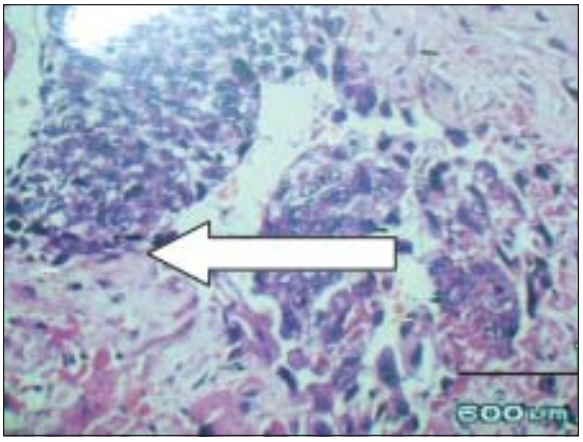

Fig.-3: *Photomicrograph of choriocarcinoma(case4)*

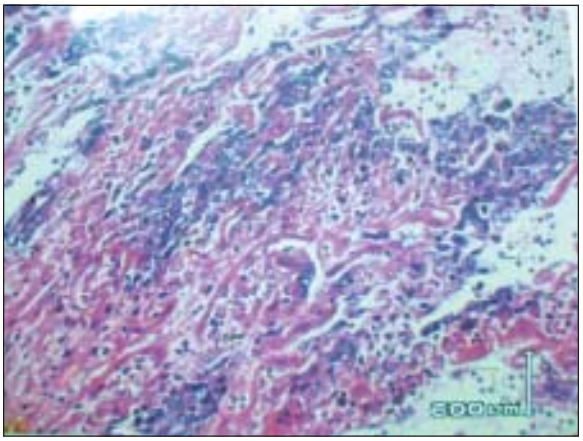

Fig.-4: *Photomicrograph (low power) (case5)*

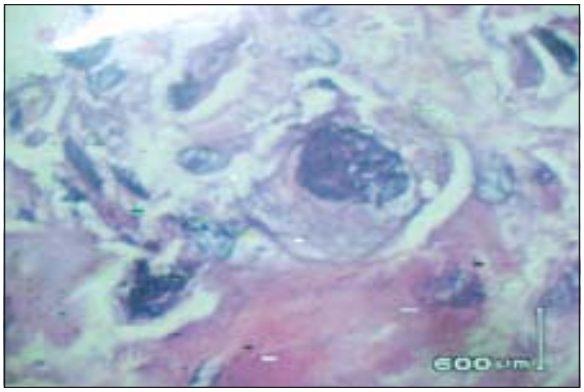

Fig.-5: *Photomicrograph (high power)(case5)*

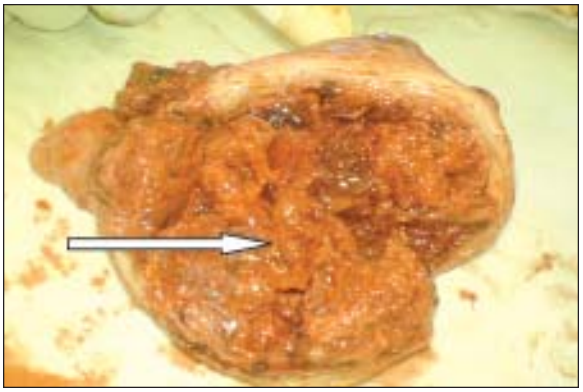

Fig.-6: *Cut section of ut. showing growth(case-6) Fig.7 Growth in vagina.(case-8)*

Table-I

Sociodemographic profile of cases

Case no.	Age	Parity	Socioeconomic condition	Interval of preg. & disease	Antecedent pregnancy	Blood group
1	40	2+0	Poor	13yrs	Term preg.	O
2	20	0+1	Poor	1 yrs	H.Mole	O
3	40	7+0	Poor	7 yrs	Term preg	A
4	20	0+1	Poor	1.6yrs	Abortion	O
5	26	4+0	Poor	1.6yrs	Term preg	O
6	45	8+1	Poor	10yrs	Term preg.	O
7	18	0+1	Poor	3 month	Abortion	A
8	25	1+1	Poor	1yrs	Abortion	O
9	42	3+1	Poor	1.6yrs	Abortion	AB
10	45	10+1	Middle class	2.6yrs	Abortion	A
11	46	7+1	Poor	11 yrs	Term preg.	O

Table showing age of the patient were between 18-46yrs, parity 0-10, mostly following term pregnancy, majority were from poor class family, common blood group were O(OO) .

Table-II

Management outcome of cases-

Case no.	Clinical presentation	Metastasis	Investigations	Treatment	Outcome
1	PVB, Vaginal growth Shock,.	Vagina , Lungs, Brain	β-hCG - 107,000 CXR-pul.matastasis SOL in brain	EMACO RT	good
2	Irreg. PVB, Severe LAP & mass abd.	myometrum	β-hCG - 25,300 USG-Ut.growth (highly vascular)	MTX	good
3	PVB, LAP, mass abd. severe anaemia	Lungs, myometrum	β-hCG - 30,500 USG-RPC/fibroid CXR-pul.matastasis Histopath.-chorio-ca	TAH, EMACO	Lost to follow up
4	PVB, mass abd. Acute abd., shock	myometrum	β-hCG 89,425 USG- ut.mass . Histopath.-chorio-ca	TAH,EMACO	Good
5	PVB, LAP, Severly anaemia mass abd.	Lungs myometrum	β-hCG - 41,600 CXR-pul.matastasis USG- ut.mass . Histopath.-chorio-ca	TAH, Refuse chemo	Lost to follow up
6	PVB, Acute abd. haemoptysis, anaemia	Lungs, myometrum	β-hCG - 711 USG- ut.mas CXR-pul.matastasis Histopath.-chorio-ca	TAH	Expired
7	PVB, fever mass in cx,	Lungs, cervix	β-hCG - 1,60,000 USG-Cx. Fibroid CXR-pul.matastasis	EMACO	Good
8	PVB, cough, resp. distress vag.growth	Lung s Vagina.	β-hCG - 15,00,000 CXR-pul.matastasis. Histopath.-chorio-ca	MTX	Expired
9	PVB, Cough, resp.distress, wt. loss	Lungs, myometrium	β-hCG – 422 USG- Ut,mass CXR-pul.matastasis. Histopath.-chorio-ca	TAH EMACO	Good
10	PVB Enlarged ut..	myometrium	β-hCG - 64,000 USG- Ut.mass Histopath.-chorio-ca	TAH, EMACO	Good
11	PVB Enlarged ut	myometrium	β-hCG - 107,640 USG- Ut.mass Histopath.-chorio-ca	TAH, MTX	Good

Discussion:

11 cases Choriocarcinoma were admitted and studied over a period of 20 months in Sylhet MAG Osmani Medical College Hospital . This study showed a higher frequency of gestational choriocarcinoma in this region.

Most of the patient were from poor socioeconomic class. Higher frequency of choriocarcinoma in this deprived group may be related to poor nutrition.

Association with dietary deficiencies was also reported by Berkowitz *et al* who noted the progressively increasing incidence of GTD with decreasing level of dietary carotene and animal fat. This correlates with the study in Pakistan where similar socioeconomic condition is prevaling[12]

In this study 73.75% (n-8) patients were multipara out of which four were grandmulti. Mean age of the patients were 33.39yrs (range18-46yrs), among them six were > 40yrs of age. Abnormal ovulation and fertilization in older women may predispose to choriocarcinoma. Knowledge of antecedent pregnancy is important because prognosis depends upon it. Choriocarcinoma commonly follows molar pregnancy. But in this study 5 patients had abortion, 5 had delivery at term & only one had molar pregnancy. However 3 of these patients labeled as abortion, no details of clinical findings or histopathology of conceptus were available. So this misdiagnosis causing delay in initiation of treatment and thus influence prognosis. In a study by RN Baergen et. al showed that age greater than 35 years, interval from antecedent pregnancy of >2 years, and prior term pregnancy were the significant prognostic factors. [14]

Haemoptysis in pulmonary metastasis frequently confused with tuberculosis which is common in our country making diagnosis late. Choriocarcinoma is a highly malignant neoplasm that metastasize readily to vagina, lungs, liver & brain. Rarely it can metastasize in intestine, spleen, kidney and lymph nodes.

In this study site of metastasis was lungs (n-7) , vagina (n-2), brain (n-1) and cervix (n-1). Uterine myometrium was involved in 8 cases. βhCG level was high in 9 cases. Two patients (case 6,9) had low β-hcg (<1000iu/L) presented with irregular p/v bleeding, uterine mass & pulmonary metastasis. Case 6 had emergency hysterectomy for severe intra-peritonial haemorrhage but she suddenly expired on 7th POD (? pul. embolism). Case 9 also had hysterectomy & chemotherapy. Both the cases were probably metastatic placental site trophoblastic tumour (PSTT) which is a variant of GTD. In PSTT exaggerated invasion of trophoblastic tissue in the myometrium necessitate treatment by hysterectomy. Metastatic PSTT need chemotherapy in addition to surgery.[13]

Intraperitoneal haemorrhage following spontaneous perforation of uterus may simulate ectopic pregnancy as in case 5. Rapid growth & haemorrhage makes the tumour a medical emergency. In this study, 63.63% (n-7) cases had total abdominal hysterectomy(TAH) which has similarity with the study by RN Baergen where hysterectomy with or without salphingoophorectomy was performed in 85% of cases. . Five cases developed acute abdomen due to intra-peritoneal bleeding needed hysterectomy. 5cases were treated with combined surgery and chemotherapy. Six patients received EMACO therapy and responded well. Two patients died suddenly probably due to pulmonary embolism.

Anatomical staging emerged as the most important prognostic factor. Other significant factors include interval from previous pregnancy, prior term pregnancy, high level, deep myometrial invasion, high mitotic rate, coagulation necrosis. Time interval between antecedent pregnancy and onset of chemotherapy is also a crucial prognostic factor. The number and size of metastasis will obviously influence the response, but the site is also important. Tumour involving the brain, liver and gastrointestinal tract have a poor response. The level of βhCG prior to starting of treatment is important in predicting the response to therapy. Patients with serum βhCG levels above 100,000 miu/ml have a poor response[15].

Conclusions:

Gestational choriocarcinoma is not a rare disease in our country. It is a life threatening disease but complete remission can be obtained in majority of patients by appropriate chemotherapy.

Choriocarcinoma should be suspected when there is irregular uterine bleeding following hydatidiform mole, abortion or pregnancy. Prognosis depends upon early diagnosis and management. High index of suspicion and continued vigilance is required for early detection & treatment in order to reduce choriocarcinoma mortality.

These patients should be managed by team of experts. It is important to individualize treatment for GTN based

upon risk factor. Using less toxic therapy for low risk cases and aggressive multi agent therapy for high risk cases. As choriocarcinoma usually affects poor women, provision of free medical care should be considered to save their lives.

Advanced maternal age is a high risk factor regarding prognosis. Trend of large size families and pregnancy at the extremes of reproductive age should be discouraged by motivation and provision of effective family planning services. Development of Molar Card and its implementation is an essential step for follow up and early detection of post molar complications.

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Verruca: Need to Know about Human Papilloma Virus (HPV) Infection

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Summary:

Verruca or warts are common significant cause of cosmetic concern and frustration of the patient. Social activities may be affected. Verruca are formed by benign proliferations of the skin and mucosa that are caused by infection with Human papilloma virus (HPV). These viruses do not produce acute signs or symptoms but induce a slow, focal expansion of epithelial cells. There are 100 types of Human papilloma virus (HPV). The natural history of common warts is for most of them to spontaneously resolve. But lesions are sometime uncomfortable. Warts typically continue to increase in size and distribution and may become more resistant to treatment over time. A significant proportion of women with genital HPV infection develops low-grade cervical lesions. Most of these low-grade lesions regress spontaneously; one study suggests that approximately 15 percent progress to high-grade cervical lesions within two years. High-grade cervical lesions have a strong malignant potential; one study found that about one-third of high-grade lesions progress to cancer within ten years.

Key words: Verruca, Human Papilloma Virus (HPV), cervical cancer.

(J Bangladesh Coll Phys Surg 2012; 30: 151-158)

Introduction:

Verruca or warts, are benign proliferations of the skin and mucous membrane these are due to infection with Human papilloma viruses. These viruses do not produce acute signs or symptoms but induce a slow focal expansion of epithelial cells. Lesions may remain subclinical for long periods or may grow to large fulminating masses that persist for months or even years. A subset of human papilloma virus (HPV) is known to cause benign warts that may undergo neoplastic transformation.[1]

Human Papilloma Virus (HPV)

Papilloma viruses are a diverse group of small DNA viruses that induce warts in a variety of vertebrates including human. Some papilloma viruses also have malignant potential. Papilloma viruses are highly species specific.[2] Hence, the papilloma virus causing infection in humans is called as human papilloma virus (HPV). Most papilloma viruses have a specific cellular tropism. The lesions can be cutaneous or can involve mucosal squamous epithelium.[3] The virus infects the basal layer of the epithelium, possibly stem cells, but virus replication takes place only in fully differentiated keratinocytes, i.e. cells of the upper stratum spinosum and stratum granulosum.[4] The papilloma viruses are small, non enveloped icosahedral DNA viruses. [5]

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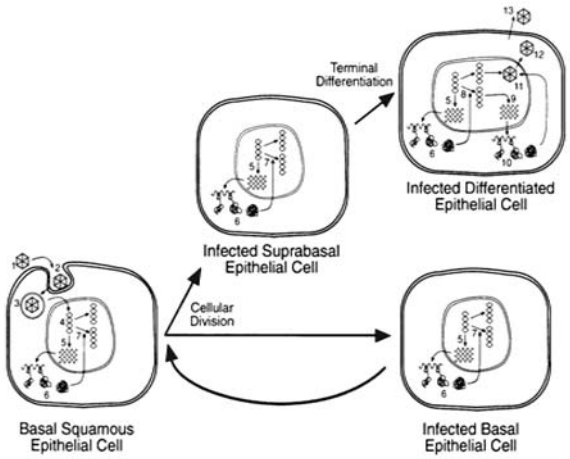
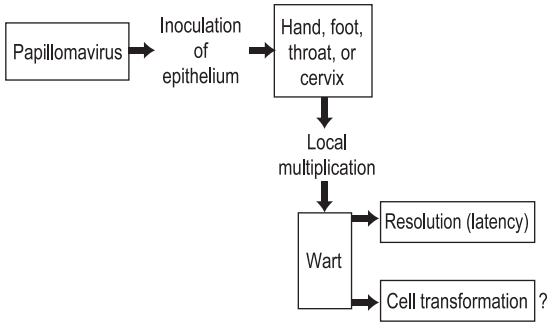


Replication cycle of Papilloma virus: To establish a wart or a papilloma, the virus must infect the basal epithelial cell. Our knowledge is limited about the initial steps in the replication cycle such as attachment (1), uptake (2), Endocytosis (3) and transport to nucleus and uncoating of the viral DNA (4). Early region transcription (5), Translation of the early protein (6), and steady state viral DNA replication (7) an occurring basal cell and in the infected supra basal epithelial cell. Events in the viral lifecycle leading to the production of virion particles occur in the differentiated keratinocytes: Vegetative viral DNA replication (8), Transcription of the late region (9), production of the capsid proteins L1 and L2 (10), assemble of the virion particles (11), nuclear breakdown (12), and release of virus (13). **[From: *Fields Virology. 4th ed.Knipe DM, Howley PM; 2001.p.2197-229.***

Papillomavirus pathogenesis



From: Medical Microbiology, 5th ed. Murray, Rosenthal & P Faller, Mosby inc. 2005.

Types of Human Papilloma Virus(HPV)

More than 120 different HPV types have been characterized and it is believed that there are many additional types that have not yet been discribed.[6] The classification of viral types is based on the species of origin and the extent and degree of related viral genome. The initial classification of the specific type was based on the extent of homology of the DNA genome, using liquid hybridization techniques[7] Depending upon their distinct regional predilection, histopathology and biology, HPV types are separated into three categories(nongenital) types(viz. HPV types 1-4), genital mucosal types (viz. HPV types 6,11,16and 18), and isolates from epidermodysplasia verruciformis (EV) (viz. HPV types 5 & 8).[1] Another important category may be those with a malignant potential. First noted in association with epidermodysplasia verrusiformis (viz. HPV type 5 & 8), association of HPV types 16 & 18 with cervical carcinoma has also been found.[8]

Epidemiology of verruca

It is difficult to determine the overall prevalence of HPV infection. However, it is generally accepted that HPV infections are common and their prevalence has probably increased over the last few decades.[9] Warts occur at any age. Epidemiological data suggested that cutaneous warts are common in children but tend to vary in age distribution according to types.[10] Transmission occurs by means of physical contact with a contaminated object, e.g. the wart itself or toys. The estimated prevalence is 1% in sexually active population in USA. Anogenital warts caused by HPV types 6 and 11, are considered as low risk. High risk HPV types 16 and 18 are found in approximately 40% to 60 % and 10 % to 20 % of all cervical carcinomas, respectively.[11]

Acquisition of HPV depends on several factors, including the location of lesions, the quantity of infectious virus present, and the degree and nature of contact, & the general and HPV specific immunologic status of the exposed individual. Although humoral immunity contributes to resistance to acquisition of infection, host cellular immune reactivity plays an important role in wart regression. Individuals with impaired cell mediated immunity are particularly susceptible to persistent HPV infection, & their infections are notoriously resistant to treatment. Warts are common in renal and solid organ transplant patients

on immunosuppressive therapy, which may contribute to their increased risk of malignancy. Non-genital warts occur most frequently in children and young adults, in whom the incidence may exceed 10 %. Anogenital warts behave as a sexually transmitted condition, and partners can transmit the virus with high efficiency. Penile lesions occur frequently in the sexual contacts of women with cervical intraepithelial neoplasia but not all pearly penile papules are caused by HPV.[1]

Natural history

In many cases of cutaneous warts, spontaneous resolution occurs with in 1 or 2 years. The rate of resolution may be adversely influenced by the HPV type, the extant of duration of warts and the suppression of the host's cell-mediated immune response.[9] Reported clearance rates in children are 23% at 2 month, 30% at 3 months, 65% to 78% at 2 years, and 90% over 5 years.[5]

Deficiencies in cell-mediated immunity can lead to persistence of infection. This can occur as a primary condition e.g. in ataxia-telangiectasia or common variable immune deficiency.[12] Secondary immunodeficiency are also associated with frequent & persistent HPV infection, e.g. hematological malignancies, and acquired immune deficiency syndrome (AIDS). Organ allograft recipients, who are on long term immunosuppressives, also have a higher incidence. In atopic dermatitis, there is an increased occurrence of warts. [13]

Incubation period

The time of acquisition of the infection can seldom be ascertained for common and planter warts, but the incubation period has been estimated to range between a few weeks and more than a year[3], and experimental infections have taken as long as 20 months to produce clinical warts[14]. A prospective study of sexual contacts of patients with genital warts indicate an incubation period of 3 weeks to 8 months (average 2.8 months)[15]. It is believed that perinatally acquired HPV infection may not manifest as genital warts for up to 2 years[16]. Only 57% of cases of laryngeal papilloma in children are diagnosed by 2 years of age[17].

Infectivity & transmission

There is no reliable information on the infectivity of common and plantar warts, but it is low. Warts spread by direct or indirect contact. Impairment of epithelial barrier function from trauma, maceration or both, can predispose to infection with HPV either 'in utero' or during delivery from mother to infant is an important mode of spread of the virus to neonates.[4]

In adults, anogenital warts are transmitted through sexual contact in most patients.[15] Anogenital warts are uncommon in children and hence there are insufficient data to conclusively prove their sexual transmission infection from the mother's genital tract at delivery is regarded as a frequent source of childhood anogenital warts.[18] postnatal transmission from adults with genital warts may occur non-sexually.[19] Other reports suggested a sexual mode of transmission. Thus, both sexual and non sexual routes are significant in the transmission of anogenital warts in children. Absence of other evidence of sexual abuse, location of warts on fully keratinized skin as opposed to genital or anal mucosa, a clinical resemblance to common warts and young age of the child perhaps up to 1-2 years at the onset of warts, would support non sexual transmission. If sexual abuse is suspected, HPV typing may be useful to establish the mode of transmission.[4]

Pathology

The characteristic histological feature of viral warts is vacuolation in cells in and below the granular layer, often with basophilic inclusion bodies composed of viral particles, and eosinophilic inclusions representing abnormal keratohyaline granules. This cytopathic effect may show detailed features typical of the HPV type involved[20] and is most always accompanied by epidermal acanthosis & often papillomatosis.[21]

Histologically, the koilocytic keratinocytes contain nuclear inclusions and "basket weave" appearance is seen in the cornified layer (HE). (fig.1). Verruca vulgaris

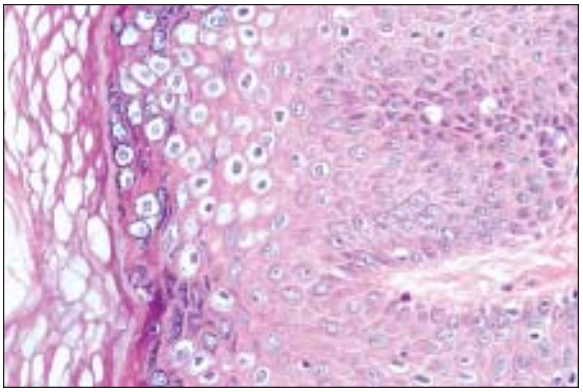


Fig. 1

seen in the forearm of 13 y-o male, showing papillomatosis and hyperparakeratosis with koilocytosis (HE).Hypergranulosis with nuclear inclusions and perinuclear koilocytic changes is evident. Vacuoles remaining in the cornified layer are suggestive of HPV infection. (fig.2)

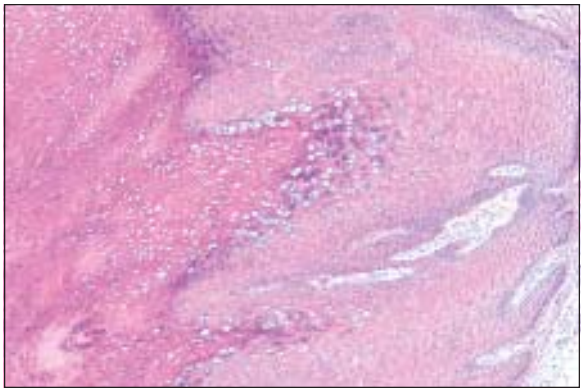


Fig. 2

Immunity to HPV

The viral life cycle appears to have evolved to minimize the exposure of the immune system to viral antigens. However, the course of infection is determined by the immune response of the host.[22] T cell immune responses appears to be most important after the host has been infected, whereas humoral immunity may help prevent the spread of infection to new sites with the host reduces the likelihood of reinfection.[2] Protection appears to be largely type specific.[23] Resistance to re-infection by one HPV type does not appear to confer resistance to re-infection by other types. Cell mediated immunity appears to be the principal mechanism for rejection of warts. In persistent disorders of cell mediated immunity, the prevalence and severity of warts and the incidence of HPV related malignancy are increased.[24]

Clinical features:

HPV infection can occur in many parts of the body such as the skin, and mucous membranes of the genitals and oral cavity. There is some type specificity for involvement of different sites. Some warts may have malignant potential, but almost all resolve spontaneously. Spontaneous recovery depends largely on the individual's immune status, e.g. in immunosuppressed individuals, generally the infection persists for a long time & involves larger areas & may be resistant to therapy; moreover, recurrences are common. On the skin, HPV infection may manifest as common warts, flat warts & filiform warts: depending on the site, there may be palmer & planter warts, anogenital warts, oral warts and conjunctival warts.[4]

Verruca Vulgaris (Common warts):

HPV type 1, 2, 4, 27, and 57. & 63 cause common warts. They occur largely between the age of 5 and 20 and only 15% occur after the age of 35. Frequent immersion of hands in water is a risk factor for common warts. Meat handlers, fish handlers, and other abattoir workers have a high incidence of common warts of the hands. The prevalence reaches 50% in those persons with direct contact with meat.[1] Common warts are usually located on the dorsa of the hands and in children under 12 years of age, on the knees. They also favor the fingers and palms. Periungual warts are more common in nail biters and may be confluent, involving the proximal and lateral nail folds. Common warts may occur anywhere on the skin apparently spreading from the hands by autoinoculation.[4]

Fissuring may lead to bleeding and tenderness. Lesions range in size from pinpoint to more than 1 cm, most averaging about 5 mm. They grow in size for weeks to months and usually present as elevated, rounded papules with a rough, grayish surface, which is so characterized that it has given us the verrucous.[1]

Common warts are usually symptom less, but may be tender specially growing beneath the nail plate. It may disturb in nail growth. Warts on the eye lid may be associated with conjunctivitis or keratitis. About 65% of common warts disappear spontaneously within 2 years and tend to do so earlier in boys.[4]

Planter Warts:

The occurrence of warts on the planter skin is not uncommon. People who have the habit of rubbing their feet against rough surfaces while bathing or otherwise, are more prone to develop such lesions. The lesions are mainly seen over the pressure points such as the heels or metatarsal heads. A planter wart appears as a small, shiny, deep seated papule. Gradually it becomes a sharply defined rounded lesion with rough keratotic surface surrounded by a smooth collar of thickened horn. The common types causing planter warts are HPV types 1, 2, 4, or 57.[4] Planter warts may be confused with callosities or corns. The diagnosis is made by noting

the break in the dermatoglyphic pattern over the lesion, pain on lateral pressure and the appearance of bleeding points on paring. The can also be confused with discrete horny papules punctate keratoderma.

Plane warts (flat warts):

Plane warts, due mainly to HPV-3 and HPV-10, are smooth, flat or slightly elevated and are usually skin-colored or grayish-yellow but may be pigmented. They are round or polygonal in shape and vary in size from 1 to 5 mm or more in diameter. The face and the dorsa of the hands and the shins are the sites of predilection.[25]

Filiform and digitate warts:

Filiform and digitate warts occur commonly in the male, on the face and neck, and are irregularly distributed and often clustered. Digitate warts often in small group, also occurs on the scalp in both sexes, where they are occasionally confused with epidermal naevi. Isolated warts on the limbs often assume a filiform shape.[4]

Anogenital warts:

Anogenital warts are common, with an estimated 1.3 million new cases per year in the USA. They are often asymptomatic, but may cause discomfort, discharge or bleeding. The typical anogenital wart is soft, pink, elongated and sometimes Filiform or pedanculated. The lesions are usually multiple especially on moist surfaces, and their growth can be enhanced during or in the presence of any other local infections. Large malodorous masses may form on vulvar or perianal skin. This classic 'acuminate' form constitutes about two thirds of anogenital warts. The commonest sites, the area frenulum, corona and glans in men, and the posterior fourchette in women, correspond to the likely sites of greatest coital friction.[15]

In children, warts in the anogenital area are often more hyperkeratotic than in adults and may be caused by HPV types associated with cutaneous disease as well as by HPV-6 and HPV-11. The duration of anogenital warts varies from a few weeks to many years. Recurrence can be expected in about 23 % of cases, the interval varying from 2 month to 23 years.[26]

Concept of Cervical Cancer:

Cervical cancer kills approximately 230,000 women annually, with the vast majority of deaths occurring in developing countries. Worldwide, cervical carcinoma is the fifth most common cancer-related cause of death among women; in the developing world, it is the leading cause of cancer death in women. The global distribution of cervical cancer varies, with Africa, Asia, and Latin America bearing a substantial burden of this disease. [11] Research worldwide has clearly shown that virtually all cervical cancer is caused by human papillomavirus (HPV) infection.[23] It is estimated that less than five percent of women infected with HPV who receive no health intervention ultimately develop cervical cancer.[27] Some estimates indicate that more than 50 percent of sexually active adults in the United States have experienced an infection with one or more HPV viral types.[10] One study, using prevalence data among Finnish women, estimated a woman's lifetime risk of HPV infection at 75 percent.[11] One study suggests that in up to 70 percent of those initially diagnosed, the infection is undetectable within two years.[12]

HIV infection:

In HIV infection, common, planter, flat, oral and genital warts are all very common. Warty keratoses at the angle of the mouth, often bilateral are a characteristic and perhaps unique, manifestation of HPV infection in patients with AIDS. The warts are caused predominantly by HPV-2,-27 and -57. Genital neoplasia associated with HPV 16 and -18 occur much more frequently in HIV infected women and homosexual men. HIV infected persons whose helper T-cell count never falls below 200 are more likely to have sustained remission of their warts. Genital warts are increased 15 fold among HIV infected women.[27]

Diagnosis:

1. The clinical appearance and history of acquired, slowly enlarging papules usually lead to the diagnosis of viral wart.
2. Histologic examination can be used to confirm the diagnosis.
3. Application of 3% to 5% acetic acid to genital warts enhances visualization of these lesions. Particularly with colposcopic magnification, although the diagnosis should not rest only on the present of the white lesions as the test is non-specific.
4. Immunohistochemical detection can be used to detect these capsid proteins in clinical materials,

including formalin-fixed tissue, but is sensitive and not routine.

5. PCR techniques detect cutaneous HPV but are generally limited to research & diagnostic laboratories. [1]

Discussion:

It is believed that most people would have claimed to have a verruca at some stage of their lives and they have also accepted the fact that 'the wart infection has increased over the last century with the figures estimated between 7 and 10 per cent in Europe and the USA.[3] Warts are not commonly found in tropical regions, however, they are commonly known to occur in the winter months according to Elliot *et al.*[28]. It is known that,Verruca pedis commonly affect approximately 4.5 per cent of school children in the UK. [29] The incidence of verruca pedis peaks at the ages of 12 and 16 years with females and males being equally affected with the wart virus infection.[30]

It is considered that verruca vulgaris can spread from person to person or when traumatized or fissured skin comes into contact with the virus in communal showers, changing rooms and swimming pools which can also increase the incidence of verruca vulgaris,stated by Elliot *et al.*[28]

Campbell *et al.* (2003) reported that duofilm and cryotherapy was the best choice of treatment employed when a survey was conducted among 85 patients chosen from the public and from the dermatological department in Australia.[29] Bunny *et al*, have been reviewed within the literature and have been reported for treating verrucae pedis and concluded that the most satisfactory treatment was duofilm. However, the success rates differ within many studies. Bunny *et al. r*eported that in their 1969 trial, 296 common warts from 382 patients were treated with salicylic acid. The authors found an 84% cure rate by the end of 12 weeks and concluded that salicylic acid is a suitable method for treating common warts. However, many years later, Bunny disagreed with the fact that salicylic acid is not compulsory for the treatment of warts. There is no evidence to suggest why the author had come to this conclusion. [30]

One study was found to have compared the combination of 17% salicylic acid with 17% lactic acid versus placebo by Sinclair *et al.* in a small sample size of 57 patients in a double blinded study. The age range of the participants between 7-30 years in the active treatment group and 8-34 years in the placebo group were found later in the results section. There was no age variation in the two groups which may have led the reader to think of any patient bias. The cure rates from this study were compared at 6 weeks and 6 months. At 6 weeks the authors reported a high cure rate in the active treatment group (66%) compared to the placebo group (18%). At the end of 6 months the author reported a high cure rate in the active treatment group (83%) compared to the placebo group (54%). The authors reported that duofilm was more significant in the active treatment group (80%) than in the placebo group (43%) during the first week of treatment bit was less significant in the final week of treatment in the placebo group (35%) than in the active treatment group (4%). Furthermore, it was also reported that 60% of the participants had HPV1 IgM antibody detected in their sera where as only 9% were detected with HPV2 IgM antibody. [39]

Several authors have stated that 'the most advocated procedure is the use of liquid nitrogen,' which has a boiling point of -196^0c has shown to have a 91% cure rate by Landsman *et al.*[32] If cryotherapy is applied every three weeks, the effectiveness will be of great significance in the cure rates and this significance was demonstrated by Berth-Jones *et al*. when they compared effectiveness of cryotherapy when treating warts at weekly, 2-weekly and 3-weekly intervals. A sample size of two hundred and twenty five participants had taken part in this study. The cure rates from this study were reviewed at the end 3 months for the weekly group, 6 months for the 2-weekly group and 9 months for the 3-weekly group. The authors reported an overall cure rate of 43% in the weekly group, 37% in the 2-weekly group and 26% in the 3-weekly group by the end of 3 months even more so, the authors reported that after 12 treatments the cure rates were similar in the weekly group (43%), 2-weekly group (48%) and in the 3-weekly group (44%). Participant withdrawal rate was relatively low (24%) before the 3 months compared to the beginning of the 12 treatments (40%). The authors state the reason for this was 'failure to attend'. In the author's findings, blistering and soreness was a common complaint presented among the three treatment groups.[33]

Several authors (Bunny *et al.*) have debated whether a single or a double freeze cycle is suited best when treating warts.[30] Sinclair & Thai (1999) have stated that 'the timed spot freeze technique is one method of standardising the delivery of the desired dose of cryogen to maximise destruction of the lesion, it was concluded that the double freezing had no effect on the hand warts but had a greater effect on plantar warts, although single freezing may be beneficial when treating hand warts. They evaluated the value of a second freeze thaw when treating common warts in three hundred participants presenting with hand and plantar warts.[31]

Bunny *et al.* states that 'the time required to freeze the wart is between 5-30 seconds depending on the thickness of the wart.[30] The actual time to freeze the warts was studied in 2001 by Bazmi *et al.* in a study frame of two hundred participants, 91 males and 109 females, with a mean age of 22 years. The participants were randomly selected to receive a traditional method of freezing or a 10 second sustained freezing with liquid nitrogen. The participants were treated with a single freeze thaw cycle using the 'Brymill Cryogun', and according to the authors this method was easier and it worked more rapidly than did the cotton buds.[34]

Conclusion:

HPV infection (genital) is a sexually transmitted infection (STI) that is very common among young men and women in many parts of the world. More than 30 HPV types are associated with genital warts. Research worldwide has clearly shown that virtually all cervical cancer is caused by human papillomavirus (HPV) infection . Besides cancer of the cervix, genital HPV infection is closely linked with cancer of the glans penis, anus, vulvo-vaginal area and periungual skin. In HIV infection, common, planter, flat, oral and genital warts are all very common. A large portion of genital HPV infection is either subclinical or latent. Subclinical or latent infection are probably responsible for most recurrences, following treatment of genital warts.[27] So knowledge about HPV infection, its early detection and treatment is necessary.

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A Guideline on Developing Effective Multiple Choice Questions and Construction of Single Best Answer format

T BEGUM

(J Bangladesh Coll Phys Surg 2012; 30: 159-166)

Introduction:

The perfect examination would be one in which the student was accurately assessed in his knowledge, comprehension, application, analysis and evaluation of material pertinent to the subject being examined [1, 2]. Although, the essay does determine the candidate's ability to write, assesses powers of logic, original thought and creativity but the use of the essay type question paper as the sole means of assessment has been criticized because of its low reliability and subjective marking [1, 3]. Besides being liable to subjective marking, the area covered by such an examination is very limited and the marking of essays is time consuming.

For several years educationalists of many different disciplines have sought methods of objective testing. In the objective tests the student has to choose the correct response out of one or more alternatives and the marking of the answers is objective [4]. The subjective judgment of the examiner thus plays no part in this form of examination. Multiple choice questions (MCQs) are being increasingly used as objective test for assessment in various fields of education [5, 6, 7].

The characteristics of MCQs are purely objective in scoring and testing, ease of marking, and the ability to test large numbers of candidates with minimal human intervention [8, 9]. Hence, they are cost efficient and feasible. MCQs are time efficient as broad content areas can be tested in a short period of time [1, 4, 5, 8, 9, 10,11] . This allows highly reliable examination.

Disadvantages of MCQs are that they allow for guessing and they are difficult and time consuming to construct [5]. They inhibit students from expressing creativity or demonstrating original thinking. Longer reading time is required and success depends on suitability of distracters [11].

This article will concentrate on providing an overview of established guidelines for writing effective MCQs so that MCQs can continue to have an important role in assessment and a positive effect on learning.

Question types:

The following are example of some of the MCQ format:

1. S**imple true-false question** is a specialized form of the multiple choices format in which there are only two possible alternatives- either true or false. These questions can be used to measure a student's ability to identify whether statements of fact are accurate or not. It is a very efficient method of testing a wide range of material in a short period of time [12].
2. **Multiple true false (MTF)** or multiple response questions is another format in which candidate choose more than one response from a list of possible answers [12, 13]. There are no restriction on the number of answers to which the correct response is 'true' and the number, to which the correct response is 'false'. It allows a series of questions to be asked relating to a single topic [8, 12, 14].
3. **Single best response or answer (SBA)** - This format consists of a list of possible answers, among which, only one is the "best" and the remaining are inferior but not incorrect [8, 13, 15]. The student is instructed to select a single correct answer or best or most appropriate choice from the group of five possible answers [10, 16, 17, 18, 19, 20].
4. **Matching questions-**It consists of two lists of statements, words or symbols, which have to be matched with one another. Information in each column should be homogenous [20]. These formats are well adopted for assessing student's

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understanding of relationship between large amounts of factual information and also application of knowledge [12]. However, it is very difficult to test higher level of cognition with this format [20].

5. **Extended matching question (EMQ)** - as the question is focused on clinical problem, extended matching items aim at assessment of application of knowledge, decision-making or problem solving [12]. The large number of alternatives reduces the effect of cueing. Because the items are relatively short and can be answered quickly, EMQ covers a large knowledge base with a short period of time [12, 13].

7. **Multiple true false completion type-** consists of a stem followed by 4 or 5 true or false statements. Instructions should be clearly given at the beginning [14, 20].

8. **Assertion and reason-** combine elements of true false questions and multiple responses. The question consists of two statements, an assertion and a reason.

The student must first determine whether each statement is true or not. If both are true, the student must next determine whether the reason correctly explains the assertion. There is one option for each possible outcome [12, 21]. This format can be used to explore cause and effect and identify the relationship. Hence, requires a higher level of learning [21].

Among all question types, 3 major formats are being used increasingly, these are:

- Multiple true false (MTF)
- Single best answer (SBA)
- Extended Matching Question (EMQ)

Traditional MTF questions have been considered as most common format historically but increasingly abandoned by many centers over the last decade [22, 23]. MTF format is difficult to write. In order to avoid ambiguity, the writer is pushed to assessing factual recall of isolated fact [21]. Moreover, cueing effect and guessing are major intrinsic drawbacks of this format [9].

In general, Single Best Answer (SBA) format can be invaluable to test application of knowledge, problem solving, judgment and discrimination to a greater extent than other form [9, 15, 18, 21]. These competencies are essential in clinical practice. Furthermore, well-constructed SBA allows the candidate to demonstrate that they know how rather than simply know and this is a fundamental principle of the assessment of clinical skill [9, 15, 24].

Although probably no easier to write than MTF, the format is more flexible and the chance of random guessing can be reduced [15, 20].

In EMQs, one or more correct response(s) is/are selected from a list of possibilities. EMQs are difficult to construct but more reliable, more discriminating and testing time is reduced [15, 21].

Guidelines for writing MCQs:

Several authors have outlined the elements of good MCQs [7, 25, 26]. Different terms are applied to the different components of MCQs. The ***item*** is the entire test question, which consists of a ***stem,*** question or ***lead in*** and several ***options*** [5, 12, 13]. Question should focus on an important concept of curriculum [9].

The ***stem*** consists of a clinical scenario or statement. Compared with MTF questions, in SBA and EMQ, the stem should be long and the options short. It should contain all the relevant information (signs, symptoms, lab test etc.) that is necessary to answer the question.

The possible answers are called ***options, alternatives or choices*** related to the stem. The correct answer is called the ***key*** while rest of the options is called the ***distracters*** or ***foils*** [3, 5, 11].

- Writing stems with example:

The stem is usually the first part. It should be brief and clear. Items which use just one or two words in the stem are better avoided. Direct and complete statement is preferable (e.g. which of the following characteristics are the features of . . . .) as incomplete stems lowers the students' correct response rate by 10 – 15% [27, 28].

The stem for MTF may be:

a) A single ward e.g. Digoxin.
b) A statement e.g. contraindications to the use of Digoxin include –
c) Photograph.
d) X-ray of the chest.
e) ECG
f) Diagram, graphs
g) Biochemistry, hematology or other report.
h) A statement from a text

OR A short description of a problem, which may be a case history or clinical scenario ± pathological data ± radiological findings (not more than 50 words) in case of single best answer question (SBA).

- Writing a question or lead in:

It should be clear and short, asking what is the best answer or a similarly phrased question. e.g. 'the most likely diagnosis is …..'

- Writing the key or correct answer/s:

The correct answer is one or the candidate make a single mark on the answer for each question in case of SBA or it may be more than one in MTF question. The key should be clearly correct, should not be longer than other distracters and should not contain any clue [13].

- Writing distracter:

The distracters may not be completely wrong or incorrect or totally farfetched but for the given scenario, less correct [9]. It should differ from key and should not be so close to the correct answer that may confuse the students who know the correct answer. The most challenging aspect of creating MCQs is designing distracters and it is time consuming [1, 5, 17, 29, 30]. The function of the distracters is to distract those students who are uncertain of the answer [11]. The standard of an objective test is probably best assessed in terms of the quality of its distracters. Distracters should be plausible and attractive alternative to the key and should be homogenous or fall into the same category e.g. signs, diagnosis, risk factors, test, treatment etc. They should appear as similar as possible to the correct answer in terms of grammar, length and complexity [5, 12, 13]. The number of possible answers can be 3 to 10 but the reliability is high with 5 options [31]. The list of options should be arranged systematically (alphabetical, chronological, and numerical). There should be sufficient number of distracters to reduce chance of guessing and they should not contain clues. For a distracter to be useful, it should represent a common misconception among students about the correct answers [30].

Points to be remembered during construction of question:

The examiners should know exactly what he/she wants to ask and they have to select the words or sentences that cannot be misunderstand.

During construction of question, following points need to be remembered [4, 5, 9, 12, 13, 15, 32]:

- The stem and options must be clear, concise, unambiguous and correct in grammar and sentence.
- Questions must not contain clues to the correct answer for the student.
- The options should be continuous with the stem e.g.

  Q. Cyanacobalamin (Vitamin B_{12})-

  X Required for folic acid metabolism

  ✓ Is required for folic acid metabolism
- Options in one item should not reveal information that allows the candidate to automatically know the correct answer to another item. This is referred to as 'cueing' when an option in one item provides a hint to the answer for another item.
- Terms such as 'invariable', 'always', 'must', 'all', 'only', and 'never' should be avoided since they imply absolutes and are therefore likely to be false. e.g.

  a) Haemophilia *never* occur in female

  b) Hepatomegaly is *always* found in PEM
- Similarly ambiguous/ imprecise/ too open term like sometimes, possible, may, often, commonly, rarely, usually, can, a few must also be avoided for MCQs to generate valid scores as these terms are difficult to interpret, have different meaning to different person and the answer tends to be true. E.g.

  a) Weight loss is *sometimes* found in thyrotoxicosis

  b) Weight loss is *commonly* found in thyrotoxicosis

  c) Weight loss is found in *a few* patient with thyrotoxicosis

  d) Malarial parasite *often* found in blood film during febrile phase

  e) The *possible* side effect of digoxin are . . .
- The term 'typical' is a useful one for multiple-choice questions. Its meaning implies 'that which is found most commonly'. 'Characteristic' implies a time honored anatomical feature, and 'recognized' an accepted textbook description. e.g. Mental retardation is a *recognized* features of congenital hypothyroidism OR the *characteristic* feature of hypothyroidism is short stature.
- Should not include the phrases *none of the above or all of the ab*ove [5].

- The question like "*which of the following are correct*?" should not be used, as the question is unfocused
- Eponyms, acronyms or abbreviations without some qualification after each term should be avoided.

  E.g. the most likely cause of BPD is . . . . . .

  Examinees may be unfamiliar with such terms or the terms may have more than one meaning e.g. BPD stands for bi-parietal diameter or broncho-pulmonary dysplasia
- Plausible alternative should be used in options; otherwise it will give a clue to correct answer. e.g

The following vitamin deficiencies are common in children:

a. Folate all- vitamin
b. Riboplavin e- micronutrient
c. Vit A
d. Vit D
e. Zinc

- Avoid *negative* statement in the stem or option.

  e.g. The following *are not* the feature of Addison's disease
- Avoid *double negative* in the stem or option.

  e.g. The following features are *not unusual* in DKA
- Avoid *double statement* in the stem or option as the student may not be certain as what part is true and what other part is wrong.

  e.g. The *ECG* & *serum cholesterol* level are used to diagnose hypothyroidism.
- Avoid *opposite statement* in the stem or option.

  e.g. SIADH is characterized by:

  i) hyponatremia

  ii) hypernatremia
- Options should be placed in logical order. It is advisable to randomize the order. For example, if the answer is a number, the option should begin with smallest value and proceed to the largest value or largest to smallest. If the options are date, they should list in chronological order. If the options are statement, they should follow *alphabetical* order. If the options are ranges of values, the choice can be independent.
- Common element in the option should be included in the stem. E.g.

The risk factors of pneumonia-

a) Includes passive smoking
b) Includes malnutrition
c) ……..

Correct stem is- the risk factors of pneumonia includes-

a) passive smoking
b) malnutrition

- Be specific: Inclusion of more information in the question may result in less confusion. e.g. patient's age or sex or habit. What may be appropriate treatment in a 10 month old child, may not be appropriate in a 60 year old person.
- Be careful in the use of figures e.g. In Bangladesh 54% of under five children are malnourished. Actually it is not our intention to test whether the student knows the figure- 54% or 56%. The question can be constructed in a better way. e.g. In Bangladesh, over half of under five children are malnourished or between 50-60% of the under five children are malnourished
- Ensure that the warding of question is precise e.g. the plasma ACTH is high in Addison's disease. The answer would be 'true' if untreated and in primary cause or 'false' if treated or is secondary to pituitary cause. Good question would be 'Plasma ATCH is high in untreated . . . .'

Construction of test items:

Construction of good test items is pre-requisite in preparing effective MCQs [10, 17, 33].

This requires a sound knowledge on the subject and understanding of the objectives of assessment as well as time and skills of writing good test items [17, 34].

If the question is incorrectly or ambiguously worded or is not concerned with appropriate objectives, it will not be reliable.

The steps are- a) developing educational objectives, b) defining levels of learning for each objective and c) writing effective MCQs that test the learning [5].

A direct relationship between instructional objectives and test items must exist. Thus test items should come directly from the objectives [11]. Understanding of and thoughtfully written objectives are critical to the construction of appropriate test questions and in ensuring adequate assessment of intended learner competence [5].

In 1959, Bloom published taxonomy of cognitive domain, which was described as a hierarchy of knowledge [26]. During test construction, the examiners must decide or have guidance on what subject or aspect of the subject is to be tested. Although MCQs are used frequently to test terminology and factual recall, but they can be used to assess higher order of thinking such as application of facts,

interpretation, analysis of relationship, synthesis, problem solving, clinical judgment, reasoning and even attitudes [15]. Inclusion of different level of learning increases the validity of examination[13, 32].

Following examples are given to explain the different level of learning.

Factual knowledge/ Recall:

Q. The risk factors for respiratory distress syndrome (RDS) are:
   a) Asphyxia in term baby
   b) Caesarian section without labour
   c) Intrauterine growth retardation
   d) Maternal diabetes
   e) Prematurity

Understanding:

Q. The mechanism of respiratory distress syndrome in diabetes mellitus is/are:
   a. Delay in development of lung
   b. Decreased stimulation by adrenergic hormone
   c. Decreased production of phosphatidyl- choline
   d. Increased chance of peri-natal asphyxia
   e. Mutation of surfactant protein C gene

   Application:

Q. "A baby of Rh –ve mother born at 36 weeks of gestation by C/S. His cord blood bilirubin is 7 mg/dl. The previous 2 sibs died of jaundice in 1st week of life. The steps of management include:
   a) Anti D Ig M to the mother
   b) Anti D Ig G to the mother
   c) Blood transfusion
   d) Immediate exchange transfusion.
   e) Photo therapy

Steps of developing Single Best Answer (SBA) MCQs in short: Example-

Specialty: Paediatrics

System: Haematology

Choose a **theme** (e.g. purpura, gum bleeding, **pallor**, lymphadenopathy, splenomegaly, bone pain etc.)

Choose a **sub-theme** (S/S, risk factors, diagnosis, **investigation,** treatment, complication)

Make a **list of 6-10 homologous options** related to theme & sub-theme (brief, similar length)

Select one option with an asterisk *

Write a stem with case scenario

Write lead in question

Reduce option list to 5 (alphabetical)

Case scenario should include-

- Age, gender
- Site of care (OPD, ER, Ward, ICU)
- Presenting complaints, duration
- Physical finding
- Investigations/X- Ray
- Initial treatment

Homologous option list related to theme (pallor) and sub theme (investigation)

1. Hb%
2. Hb electrophoresis *
3. Coomb's test
4. Bone marrow study
5. Reticulocyte count
6. Serum iron
7. Serum ferritin
8. Osmotic frazility test

Clinical case scenario:

A 5 year old boy attended in OPD with complaints of gradual pallor for 3 years. O/E he was found moderately pale with hepatosplenomegaly. His Hb% was 7 gm% & PBF showed microcytic hypochromic picture with fair number of target cell.

Lead in: What investigation you want to do to confirm the dx?

Option list:

a. Bone marrow study
b. Coomb's test
c. Hb electrophoresis
d. Reticulocyte count key- c
e. S. ferritin

Another example:

Scenario: A newborn baby delivered by C/S for breech presentation, on routine checkup, his arm was found in a position of adduction and internal rotation with pronation of forearm.

Lead in: Which of the peripheral nerves are injured in this case?

Options:

a) 3rd, 4th and 5th cervical
b) 5th and 6th cervical
c) 7th and 8th cervical
d) 7th , 8th cervical and 1st thoracic
e) 1st and 2nd thoracic

Any TOPIC can form the basis for options in SBA

List of possible themes:

Arteries	Metabolic defects	Physical signs/ symptoms
Muscles	Electrolyte abnormalities	Diagnoses
Nerves	Hemodynamics	Crucial investigations
Cells	Causative agents	Lab studies
Cell components	Pathological process	Initial management steps
Blood components	Cytokines	Management alternatives
Body fluid	Immune disorders	Risk factors
DNA analysis	Vaccines	
Hormones	Toxic agents	
Enzymes	Drugs/ side effects	
Amino acids	Screening tests	

Procedure for constructing the question paper:
Steps to the followed:-

1. Confirm the type and number of objective questions to be used. Forty 5 stem questions can usually be covered in one hour or sixty questions in one and half hours. If problems are given in the stem, than longer time may be necessary.
2. Determine the content of the examination in terms of subject matter, competences to be tested and level of difficulty.
3. Review each item for accuracy and appropriate formatting. Internal review may not reveal all errors. It can be very beneficial to have a colleague read and respond to the MCQs and offer feedback.
4. A question bank may be prepared from where question can be used in future.

A satisfactory bank of questions takes three to five years to build. After this time the questions can be grouped into sections and, whenever an examination paper is required, questions can be chosen at random from each sections. Continuous updating and revision of this material should be undertaken and new material added regularly.

5. During moderation, the following points should be checked-
   a) Wording of the stem & option.
   b) Competences- from recall of facts to higher level of cognitive domain.
   c) Inclusion of different aspects of subject.
   d) Duplication or overlap by using a text matrix.
   e) The instruction to the student, marking scheme or the method of scoring.
6. After examination, examiner should meet to review the questions and the student performance in each item.

Fig: Summery of guidelines for writing effective MCQs [5]

Test items

- Relate directly to instructional objectives
- Test at the same level of learning as the objectives are designed to assess
- Reflect different levels of learning (recall, comprehension, application and problem solving

Stems

- Provide a complete statement
- Include only relevant information
- Contain as much of the test item as possible
- Ask for the correct, not the 'wrong' answer
- Avoid absolute terms, such as always, never, all, or none
- Avoid imprecise terms such as seldom, rarely, occasionally, sometimes, few or many
- Avoid cues, such as may, could or can
- Define eponyms, acronyms or abbreviations when used

Options

- Keep options grammatically consistent with the stem
- Link options to each other (e.g. all diagnoses, tests, treatments)
- Write distracters similar in grammar, length, and complexity
- Write distracters being plausible but clearly incorrect
- Avoid none of the above and all of the above
- Place options in a logical order (e.g. numerical, chronological)

Scoring:

Multiple questions appear to be the easiest of all to mark [32]. A student is either right or wrong and should be given a mark for the correct answer and nothing for the wrong one. This is the simplest and best method of marking [13].

It can be done by computer or by hand if the number of candidates is small. Whatever the scoring system employed, an MCQ paper can place the student in rank order in terms of their ability to answer that particular paper. The real problem of marking MCQ is that of allowing for guessing [31].

Conclusion:

Assessment of learner's knowledge is an important step in educational process. MCQ is the most efficient form of written assessment, being both reliable and valid by broad coverage of content. Improvement of individual's skill in constructing MCQs is crucial. Flawed MCQs interfere with accurate and meaningful interpretation of test scores and negatively affect student pass rate. Therefore, it is important for test developers to be skilled in effective test item writing to evaluate students' competence.

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Retroperitoneal Plasmacytoma: A Case Report

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Summary:

Solitary Extramedullary Primary Plasmacytoma (SEMPP) is a rare neoplasm. When diagnosed, head and neck region is its most likely location. Rarely, it may occur in the retroperitoneum. We report a case of an elderly male who was admitted in the department of surgery, Dhaka Medical College Hospital (DMCH) with a Solitary Extramedullary Retroperitoneal Primary Plasmacytoma (SEMRPP). Subtotal excision of the mass was done. The patient was referred to the department of Oncology DMC for radiotherapy. The first report of an extramedullary plasmacytoma was in 1905 in Taiwan. To the best of our knowledge, there was no report of a Solitary Extramedullary Retroperitoneal Primary Plasmacytoma (SEMRPP) from Bangladesh.

Keywords: Extramedullary, Plasmacytoma, Retroperitoneum.

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Introduction:

Plasmacytoma, a neoplastic proliferation of plasma cells, may be primary or secondary to disseminated multiple myeloma and may arise from osseous (medullary) or non-osseous (extramedullary) sites. Approximately 80-90% of extramedullary Plasmacytomas (EMPs) involve the Mucosa Associated Lymphoid Tissue (MALT) of the upper airways and 75% of these involve the nasal and paranasal regions.[1] Isolated plasmacytomas are rare, comprising only 4% of all plasma cell malignancies. EMP is an uncommon low grade malignant neoplasm with relatively good prognosis. Rarely, EMP may occur in the retroperitoneum. The first report of an EMP was in 1905 in Taiwan[2]. We report a 60 years elderly man with a Solitary Retroperitoneal Extramedullary Plasmacytoma (SREMP). This is probably the first case reported in Bangladesh.

Case Report:

A 60-year old man was referred to our hospital in March 2008 with the history of a swelling in the left side of upper abdomen for last 1 year, which was not increasing in size, and mild pain in the swelling for last 5 - 6 months. He did not have history of fever, anorexia, weight loss, vomiting and bowel or bladder dysfunction. He had two episodes of sudden sweating, palpitation, with restlessness and anxiety within last one year. Physical examination revealed a non-pulsatile, oval, firm to hard, rough surfaced, slightly tender, intra-abdominal lump (measuring about 15x9cm) occupying the left hypochondriac region without local rise of temperature. There was no pallor; icterus, lymphadenopathy and both testes were normal. Ultrasound report revealed a large solid mixed echogenic retrogenous mass (15.2X11cm) seen in the left upper quadrant of abdomen separated from liver, left kidney, left suprarenal gland and aorta. Body and tail of pancreas were pushed forward by the

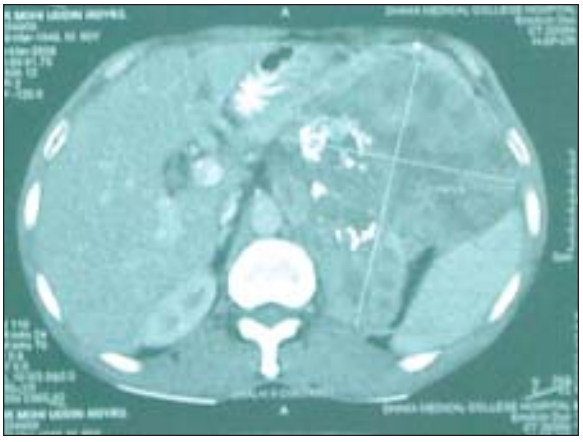

Fig.-1: *Computed tomography revealing a soft tissue between spleen and stomach and anterior to left kidney Distal body and tail of the pancreas are pushed anteriorly by the mass*

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mass. CT scan of abdomen (Figure: 1) revealed a mixed density mass with amorphous calcification measuring about (15X14X12) cm in the left side of abdomen in between spleen and stomach and anterior to left kidney. Distal of body and tail of the pancreas was pushed anteriorly by the mass; showing left sided large retroperitoneal mass. US guided Fine Needle Aspiration Cytology showed the mass compatible with adreno-cortical adenoma / carcinoma.

Investigations revealed Haemoglobin 10.5 gms/dl, Erythrocyte Sedimentation Rate (ESR) 120 mm in 1st hour, Total Leukocyte Count (TLC) was normal. Renal function tests, hepatic enzyme levels, serum electrolytes, serum calcium were within normal limits. Plasma protein electrophoresis revealed polyclonal gammopathy. Skeletal survey was normal. Bone marrow aspiration and biopsy revealed myeloid hyperplasia. Subtotal excision of the retroperitoneal mass (Figure 2 & 3) was done, leaving small upper portion of the mass that was firmly adhered with great vessels, spleen and left dome of the diaphragm. Post operative recovery was uneventful.

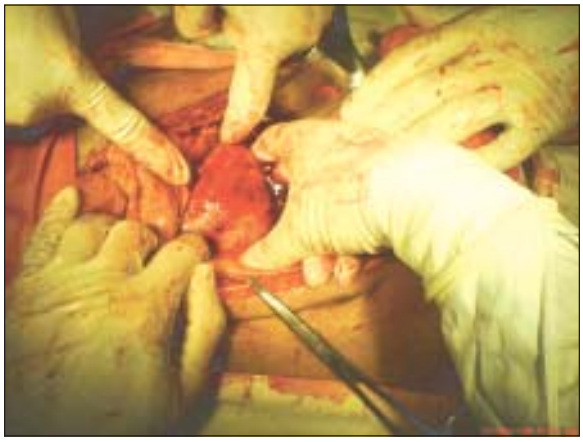

Fig.-2 & 3: *Figure showing huge retroperitoneal mass with piecemeal resection.*

Histopathology revealed sheets of mature and immature plasma cells (Figure: 4) suggestive of plasmacytoma. A final diagnosis of solitary retroperitoneal extramedullary plasmacytoma was made.

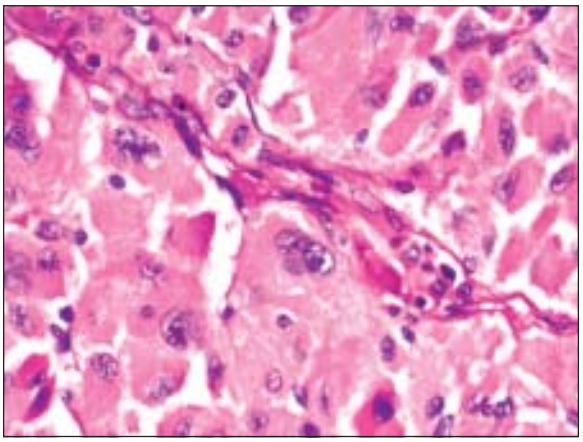

Fig.-4: *Showing picture of the retroperitoneal plasmacytoma under microscope.*

Discussion:

Extramedullary Plasmacytoma (EMP) constitutes 4% of plasma cell tumours. It is defined as a solitary tumour composed of monoclonal proliferation of cells with plasmacytic differentiation in an extramedullary site.[3] It is classified as either primary EMP (when there is absence of coexisting multiple myeloma) or secondary EMP (when it is associated with multiple myeloma). EMP most commonly occurs (>90%) in head and neck region. Other documented sites include gastrointestinal tract, CNS, urinary tract, thyroid, breast, testis, parotid glands and lymph nodes.Solitary EMP in the retroperitoneum is very rare. Marks [4] reported bilateral renal vein occlusion with renal failure and fatal haemorrhage due to tumour erosion and vena caval perforation in case of a RPEMP. Kobayashi et al [5] has reported tumour thrombus within the renal vein in case of RPEMP involving kidney.

The differential diagnosis of RPEMP includes lymphoplasmacytic lymphoma and immunoblastic lymphoma. Many cases of gastrointestinal plasmacytoma were misdiagnosed as low grade B-cell lymphoma with plasma cell differentiation.[6] Immunohistochemistry using CD45 and CD20 negative stains is specific for plasma cells. [7]

There are no clear guidelines for treatment of RPEMP due to its variable presentation and rarity. All 3 modalities, surgery, radiotherapy and chemotherapy have been tried with the variable results. Radiotherapy has been effective in achieving long term local control.[8] However it is associated with high morbidity particularly when used for large retroperitoneal tumours. Tanaka et al [9] have tried chemotherapy before and after surgical resection (which was incomplete). Their patient progressed later and died 33 months after initial treatment. Chen et al [10] has reported in a case of retroperitoneal extramedullary plasmacytoma with obstructive jaundice who showed complete response to treatment with sequential radiotherapy and chemotherapy.

We first treated our patient by doing subtotal excision of the mass (as complete excision was not possible as it was adherent with great vessels). Then we referred the patient to the department of Oncology in DMCH for radiotherapy.

In summary, we have presented a rare case of primary extramedullary plasmacytoma in the retroperitoneum. Extramedullary Plasmacytoma should be kept in mind as a differential diagnosis of abdominal haematolymphoid malignancy. Surgical resection is also an important treatment option in such patients .[11]

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Expectant Management of Ectopic Pregnancy - A Case Report

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Summary:

A patient with suspected ectopic pregnancy was managed successfully with expectant approach using serial serum ²hCG monitoring. Expectant management can be a useful form of treatment for ectopic pregnancy in selected patients.

Key words: Pregnancy, ectopic pregnancy expectant.

(J Bangladesh Coll Phys Surg 2012; 30: 170-172)

Introduction:

Ectopic pregnancy is a disaster in human reproduction. It is one of the most important causes of death during the first trimester of pregnancy. Ectopic pregnancy is more threatening for women than normal vaginal delivery and induced abortions [1] . If it is not diagnosed and treated expeditiously, it may also take the life of the mother or at the very least, compromise her future ability to reproduce.

Ectopic pregnancy effects approximately 2% at all pregnancies [2] . Currently over 90% of ectopic pregnancy can be visualized on Transvaginal scan (TS). This means that early ectopic pregnancy can be detected in asymptomatic women [3] by TVS and the rapid immunoassay of serum ²hCG. The advent of modern diagnostic technique, the treatment modalities of ectopic pregnancy has changed dramatically.

Case Report:

A 30 years old housewife was referred to our hospital on May 08, 2008 with complains of intermittent pervaginal spotting over the preceding 3 weeks. Her last menstrual period was on February 12, 2008. Pregnancy test was positive at 6 weeks of gestation. This was her planned pregnancy. Ultrasonography was done – at 10 weeks of her gestation outside our hospital. It did not show any intrauterine gestational sac but there was presence of an adnexal mass, the size of which could not be mentioned.

She had complicated past obstetric and gynecological history. In 2001, she had a ruptured right tubal pregnancy and right sided salpingectomy was performed. There were extensive pelvic adhesions with pelvic endometriosis which were noted in the operation note of the patient.

On admission, her general condition was stable. The abdomen was soft and non tender. Some brownish old blood was seen on vaginal speculum examination and the cevical os was closed and non tender.

The hemoglobin level was 11gm/dl. Transabdominal and transvaginal ultra sonogram were performed with the following findings: the uterus was bulky with thick endometrial echo. There was no evidence of an intrauterine pregnancy. A complex mass measuring 4 cm in diameter was seen around the left adnexa. Vascular flow signals were detected within and surrounding the mass. There was no free fluid in the pouch of Douglas. So, clinical diagnosis was in favour of tubal pregnancy. Serum ²hCG was done which revealed increased value. (In May 09, 2008 ²hCG – 7092 miu/ml).

But the patient remained asymptomatic apart from minimal vaginal spotting and there was no sign of ruptured ectopic pregnancy. So there was no option for surgical treatment. Only follow-up of the patient was done by serial ²hCG. There was a falling level of serum ²hCG over 48 hours from 7092 miu/ml (may 09) to 3915 miu/ml (may 11). In view of the above finding, and those at previous operation, expectant management was planned.

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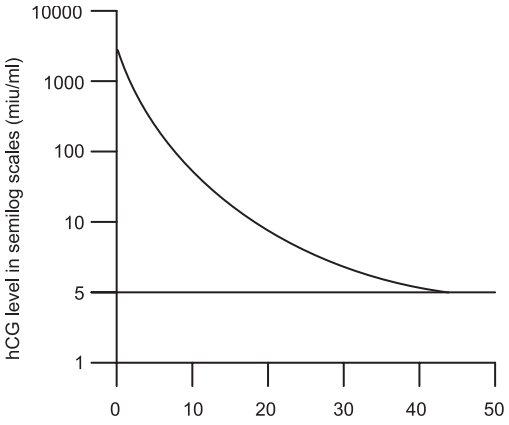

Fig-1: *Serial hCG level versus number of days after initial diagnosis.*

She had to come back regularly for follow up with ²hCG monitoring. We had to explain the risk of ruptured ectopic pregnancy and the need for emergency surgical intervention if this occurred. She was advised to come back immediately if there was any abdominal pain or vaginal bleeding.

She then remained asymptomatic and the serum ²hCG level decreased to 24 miu/ml on June 04, i.e. day 28 of her initial diagnosis (Fig- 1). Menstruation returned on the same day. The serum ²hCG level decreased further to less than 5 miu/ml (²hCG level less than 5 miu/ml is considered to be normal for the non pregnant status) on June 24, i.e. day 48 after the initial diagnosis. A follow up ultra sonogram was performed on June 29 (Day 53). The decrease in the size of the mass could still be seen in the left adnexa, but no vascular flow signal was detected within or surrounding the mass.

Discussion:

Early diagnosis of unruptured ectopic pregnancy has become more common with the improvement of the diagnostic tools including radioimmunoassay of hCG (human chorionic gonadotropin) and transvaginal sonography. As a result, apart from traditional surgical treatment of ectopic pregnancy, medical treatment (e.g. methotrexate, prostagladins) and even expectant management are possible in well selected patients.

The rationale of expectant management is based on the observation that spontaneous resolution of ectopic pregnancy can occur with preservation of tubal patency.

This was first reported by Lynd in 1995 [4] .Depending on the selection criteria, the percentages of patients with ectopic pregnancy that are suitable for expectant management vary from 20% to 29% [5-8].

The most common criteria include:

1. No symptom or sign of rupture or acute bleeding.
2. A falling level of serum ²hCG at a 48 hours interval.
3. The diameter of the suspected ectopic pregnancy <4cm shown on the pelvic ultrasonogram.

Our patient fulfils the first 2 criteria although a complex adnexal mass measuring 4cm in diameter was shown by the pelvic ultrasonogram. We postulated that this size might have been due to preexisting tuboperitoneal adhesion and the size of the suspected ectopic pregnancy was most probably less than 4 cm. The persistence of adnexal mass though in decreased size by the follow up ultrasonogram on day 53, even when the hCG level returned to normal supported this postulation. The disappearance of vascular flow signal within and surrounding this mass was compatible with resolution of the tubal ectopic pregnancy inside a complex mass of tuboperitoneal adhesions. Further follow up ultrasonogram will be performed.

Trio in 1995 presented the first report evaluating the ability of the hCG levels and sonographic finding to predict successful expectant management [9]. The following factors were identified.

1. An initial hCG level < 1000 miu/ml appeared to be the best independent predictor of a spontaneous resolution of ectopic pregnancy.
2. Ultrasonographic finding at the time of diagnosis did not seem to have any individual predictive value after controlling the initial hCG level and the trend in hcG levels.

In our patient, the initial hCG level was 7092 miu/ml. Expectant management was adopted because we believed that the trend in hCG levels, particularly the decrease in the first 48 hours time interval was more important than the absolute value of the initial hCG level. The absolute hCG level would depend on the radioimmunoassay that was used and on which international standard it is calibrated against. Our patient had an acceptable decrease in hCG level (Fig-1) despite the initial hCG level being greater than 1000 miu/ml.

The benefit of expectant management of ectopic pregnancy is the possibility of avoiding invasive surgical

treatment (laparoscopy/laparotomy). The main disadvantage of expectant management is that of rupture of ectopic pregnancy. Other disadvantages of expectant management include the risk of additional tubal damage and blood loss, the need for an emergency operation, the cost of serial hCG measurements and ultrasonograms and the emotional cost from the anxiety of waiting for the spontaneous resolution of the ectopic pregnancy. As a result we recommend that a substantially favourable risk: benefit ratio has to be demonstrated before the expectant approach is to be adopted.

With successful expectant management the patient remains clinically stable and decreasing hCG levels with no ultrasonographic evidence of an enlarging adnexal mass. The waiting period ranges from 5 to 51 days [6,9,10] and the success rate of expectant management ranges from 46% to 92% [5,8,11].

Conclusion:

Adequate explanation to the patient and judicious follow up of the patient are the essential components for the expectant management of ectopic pregnancy. The advent of modern diagnostic modalities has changed the clinical scenario of ectopic pregnancy from one possible disaster to one potential success. So, in conclusion, expectant management can be a useful form of treatment for ectopic pregnancy in selected patients.

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Pleuro-Pulmonary Blastoma: A Rare Cause of Pleural Effusion in a Young Girl

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Summary:

Pleuropulmonary blastoma (PPB) is a rare, primitive primary neoplasm of the thorax that affects children. We present a case of a girl of 11 years who was admitted in National Institute of Diseases of the Chest and Hospital (NIDCH) with the complaints of high grade continued fever and shortness of breath. Initial physical examination and chest radiograph was suggestive of left sided massive pleural effusion. Along with pleural effusion, chest CT depicted a large heterogeneous mass occupying most of the left hemithorax. Computed tomography and bone scintigraphy suggested the mass to have a primary pulmonary origin. Cytologically the lesion was consistent with pleuropulmonary blastoma. Due to pleural involvement and presence of large inoperable mass, we considered chemotherapy as the first modality of treatment prior to surgery and managed thereby.

Key wards: Pleuropulmonary blastoma, pleural effusion, pulmonary blastoma of childhood

(J Bangladesh Coll Phys Surg 2012; 30: 173-176)

Introduction:

Pleuropulmonary blastoma is an aggressive tumor accounting for less than 1% of all primary malignant lung tumors in the paediatric population[1]. Manivel et al. suggested that PPB is a rare, distinctive intrathoracic/ pulmonary neoplasm, where both the blastematous and sarcomatous components coexist as compared to the typical biphasic epithelial-stromal morphology seen in classic adult type pulmonary blastoma[2]. PPB in children differs from its counterpart in adults because of its variable anatomic location, primitive embryonic-like blastema and stroma, absence of a carcinomatous component and potential for sarcomatous differentiation[2]. We herein report a case of PPB (suggestive of type III), presenting with radiological feature of large mixed density pulmonary mass with pleural effusion[2].

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Presentation of the case:

An 11-year-old girl, student of class-VIII was admitted in NIDCH on 12th July, 2008 with fever and shortness of breath. She developed high grade continued fever and cough productive of mucoid sputum for two weeks. She experienced heaviness of the left side of the chest and progressively worsening respiratory distress for about 10 days. At the time of presentation, she used to become breathless while walking on the flat surface at her own pace at close distances and developed inability to lie down on right lateral position. She was in her junior high school study. She had no significant past medical history and there was no history of tumors in her close relatives.

She was a thin, alert, young girl with preferred left lateral decubitus. Her temperature was 101ÚF, pulse was 110 beats per minute, respiratory rate was 26 breaths per minute, blood pressure was 100/70 mm Hg, and her oxygen saturation was 96% while she was breathing room air. She had no cyanosis, clubbing, lymphadenopathy or bony tenderness. Trachea was shifted towards the right side and apex beat was impalpable. The left hemithorax was immobile with dull

on percussion and absent breath sound, both anteriorly and posteriorly. The remainder of the physical examination was normal.

Complete blood count revealed the hemoglobin level was 8.8 g/dl, erythrocyte sedimentation rate was 105 mm in 1st hour. She had a negative tuberculin skin test. Staining for acid fast bacillus was negative on three sputum specimens as was Gram's staining. Chest radiograph showed an apparent left sided pleural effusion with mediastinal shift to the right side.

A thoracocentesis was performed according to ATS guideline and removed about 1000 ml of haemorragic fluid which was exudative, lymphocyte predominant without showing any AFB and malignant cell. Pleural biopsy was taken by Abrahm's needle but failed to detect any granulomatous or malignant lesion. Fibre-optic broncoscopy revealed no endobronchial growth, but left lower lobe bronchus was narrowed due to external compression. Bronchial washings were negative for malignant cells. After 3 days, patient developed severe respiratory distress and left chest drainage was given.

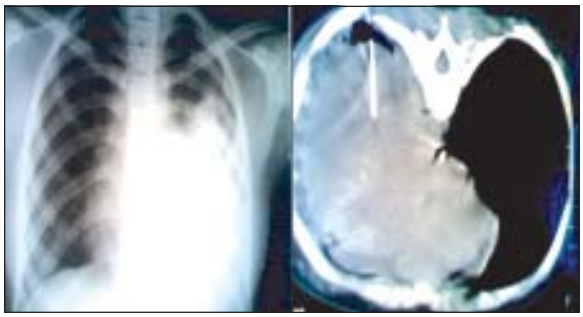

Fig.1. (A): *Chest X-Ray P/A view with a mass lesion involving the left upper and mid zone.* ***(B)*** *CT scan of chest showing a large mixed density mass in the left lung medially merging with the mediastinum, in situ FNAC needle is also seen.*

Repeat chest X-Ray after thoracocentesis revealed a mass lesion involving the left upper and mid zone (Figure 1A). Computed tomography (CT) scanning of thorax was performed for further delineation of the lesion. A large mixed density mass lesion was seen in the left lung medially merging with the mediastinum. (Figure 1B) Small left sided pleural effusion was also noted. There was no hilar or mediastinal lymphadenopathy.

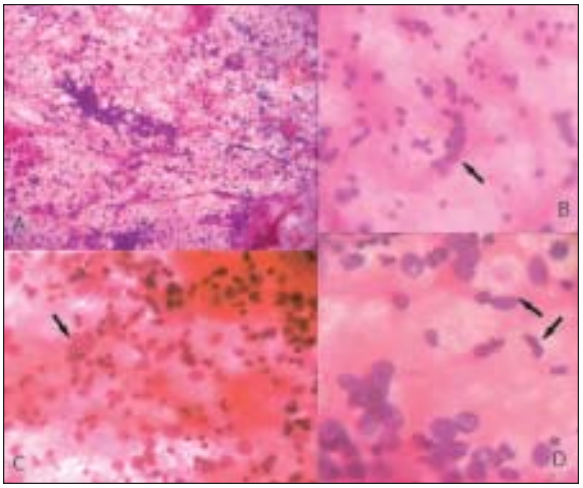

Fig.2. (A): *Light microscopy of the smear shows cluster of primitive appearing cells. (H&E, ×100)* ***(B) &(C)*** *Group of small primitive appearing cells having round to oval nuclei and scanty cytoplasm. (H&E, ×400)* ***(D)*** *Arrow shows individually dispersed spindle shaped cells with elongated nuclei. (H&E, ×400)*

A CT guided FNAC was performed. Smear showed group of small primitive appearing cells having scanty cytoplasm with indistinct borders and round to oval nuclei with finely granular, evenly distributed hyperchromatic chromatin and inconspicuous nucleoli; on a background of necrotic material. (Figure 2A-C) A less frequent second cellular population consisted of individually dispersed, elongated or spindle-shaped cells with similar-appearing nuclei was also found.(Figure 2D) There was no evidence of neoplastic epithelium within the smears. Morphologically this finding is quite consistent with PPB.

Presence of metastasis was verified by whole body bone scan and MRI of brain, but there was no active lesion. Ultrasonography of abdomen also revealed no abnormality. Due to presence of inoperable huge tumor, after consulting with thoracic surgeons, patient was referred to medical oncologists for further management.

Discussion:

Pleuropulmonary blastoma is a rare malignant dysontogenetic neoplasm primarily affecting children[3]. It was previously known as cystic rhabdomyosarcoma, pulmonary blastoma of childhood or rhabdomyosarcoma arising in a cystic adenomatoid malformation. This neoplasm occurs not only in lung,

but also may arise from mediastinum, diaphragm and/or pleura[4]. PPB is classified into three categories by gross and microscopic examination - type I (purely cystic), type II (cystic and solid) and type III (purely solid)[5]. These three types of PPB are presumed to have histogenetic linkage with the potentials of progression into other forms[3]. The PPB in the present case has predominantly solid blastematous component and belongs to the type III subcategory.

Pleuropulmonary blastoma occurs almost exclusively in children under the age of 12 years[6], usually by the age of 4 years, with a median age of 2 years[7]. Type I tumours occur in the youngest children, type III in the oldest [8]. This is consistent with our recent case. The lower lobe of the lung is most commonly involved than the upper and middle lobe. The disease is usually unilateral, although bilateral lesions have been reported[5].

According to the clinic-pathological study conducted by Priest et al, the commonest clinical presentation is respiratory distress[8], as seen in the present case. Other symptoms include fever, cough, chest or abdominal pain, malaise and anorexia[5]. A suspected pulmonary infection is the most frequent clinical suspicion in these patients. Radiographically, type III PPB is typically a heterogeneous solid mass with or without involvement of chest wall or mediastinal structures. The entire hemithorax may be opacified by the mass. We have similar radiological finding in our case.

Histologically, PPB is characterized by a biphasic neoplastic population of primitive appearing small round cells and larger elongated or spindle-shaped sarcomatous elements, but a malignant epithelial component does not occur[9], a key morphologic point in differentiating PPB from the adult pulmonary blastoma. A proportion of these cancers may also manifest rhabdomyosarcomatous, chondrosarcomatous or liposarcomatous differentiation[4]. Immunohistochemical positivity with vimentin, muscle-specific actin, desmin, S-100 protein etc. can strengthen the diagnosis in such a case[10].

The cytopathologic findings of PPB may represent some or all of its histopathologic components[9]. In our case, the two major cell types-the primitive blastemal elements and spindle-shaped cells-were represented in the aspiration smears. But there was no recognizable differentiation in the blastemal or mesencymal component, also any evidence of neoplastic epithelium within the smears. All together goes in favour of PPB.

A significant feature is that up to 25% of patients with PPB or their young relatives have associated dysplastic or neoplastic lesions, such as pulmonary cyst, cystic adenoid malformation, cystic nephroma, medulloblastoma, and thyroid neoplasia; this is called the PPB family cancer syndrome.[1,11] In our patient there was no such positive history. Several cytogenetic studies have shown the detection of numerical and structural chromosomal abnormalities of 2 and 8 in isolated cases.[3,12] Thus, once the diagnosis of PPB is made, a thorough search for tumors should be initiated in the close relatives.

For the metastatic propensity, the CNS metastasis rate was 44% of all recurrences in the study of 50 cases of PPB by Priest et al, and patients with pleural or mediastinal involvement fared significantly worse than those without such involvement[8]. Other common metastatic sites include bone, lymph nodes, liver, pancreas, kidney, and adrenal glands[4]. Presence of pleural effusion suggests involvement of pleura in our patient, although evidence for distant metastasis was absent.

Complete tumor ablation is essential to prevent local recurrence and for survival, so the main goal of therapy should be radical surgery, followed by chemotherapy. Some authors suggest that chemotherapy should be given with local radiotherapy in the majority of type II and type III patients[10,13] Unfortunately our patient was an inoperable one and we referred the patient for chemotherapy.

There is a better outcome of type I PPB compared to the other two types; most type I PPB patients have 80-90% five year disease-free survival[10]. At present, type II and III patients have less than 50% five year survival[10]. Like our patient, those with pleural, mediastinal or extrapulmonary involvement at the time of diagnosis have worse prognosis than others without such involvement [13].

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Congenital Absence of Gall Bladder

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Summary:

Congenital absence of gall bladder is a very rare entity found in clinical practices. Due to miss interpretation of sonographic findings as they are not familiar with the condition it possess a great difficulty in management the patient.

Though the patient present with the feature of acute cholecystitis, conservative treatment is enough to cure the disease. Modern radiological intervention make the diagnosis confirm, thus preventing unnecessary surgical procedure.

Here we report two cases of Congenital absence of gall bladder presenting as acute cholecystitis ultimately diagnosed and treated.

(J Bangladesh Coll Phys Surg 2012; 30: 177-180)

Introduction

Biliary system variants are relatively common but is isolated gallbladder agenesis is a rare entity with an estimated incidence of 10–65 per 100,000. Females are more commonly affected (ratio 3:1), typically presenting in the 2nd or 3rd decade of life. Despite an absent gallbladder, half of patients present with symptoms similar to biliary colic, which is poorly understood. Symptomatic congenital absence of gall bladder puts the diagnostic dilemma and treatment difficulties.

Case Report:

1. A 35 years old woman, mother of two children, of Noakhali District. Bangladesh, presented with severe upper abdominal pain, bouts of vomiting, slight abdominal distention. She was non-icteric, mildly anaemic.

Physical examination revealed good health, remarkable tenderness over the Right. hypochondriac region. Murphy's sign was positive. She was mildly dehydrated. Patient was normotensive and non diabetic. Examination of other systems revealed normal findings.

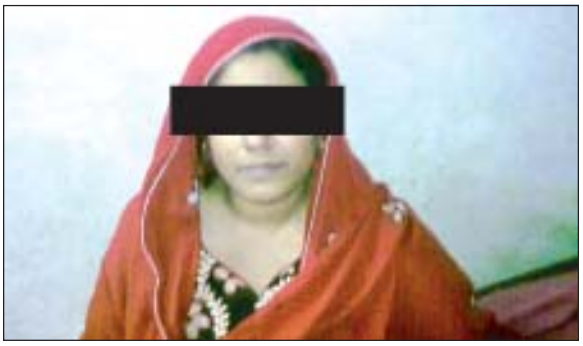
Routine laboratory examinations (Complete Blood Count, Erythrocyte sedimentation rate, blood biochemistry Panel) revealed nothing abnormal except Neutrophilic lucocytosis.

Liver function tests, serum Creatinine, Random blood sugar were within normal limit.

Ultrasonographic scan done but the comment was "gall bladder could not visualized may be due to bowel gas" (Fig.-1)

Contrast enhanced computed tomography (Fig.-2) revealed absence of gall bladder without any remarkable change in the extra and intra hepatic biliary apparatus.

Common bile duct was normal in diameter with no calculus present. Magnetic Resonance Cholangio Pancreatography done later (Fig.-3) which revealed absent gall bladder, normal intra and extra hepatic biliary channels. Common bile duct normal in diameter.



1st Patient (Printed with Permission)

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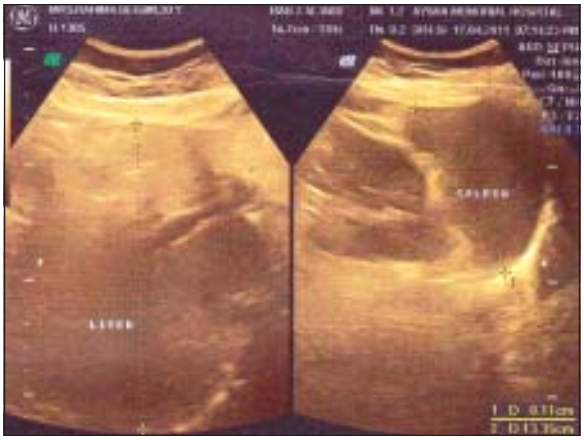

Fig.-1: *Ultrasonographic Scan*

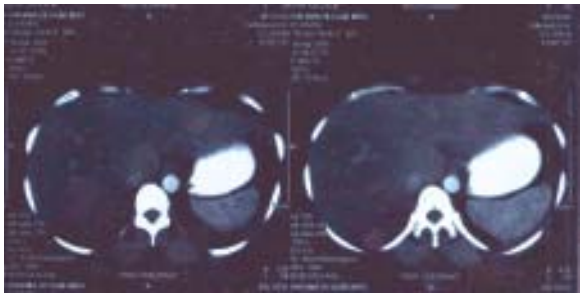

Fig.-2: *CT Scan*

Fig.-3: *MRCP Scan*

Diagnostic laparoscopy done and gall bladder could not found. Common bile duct and Right and Left hepatic duct were found normal.

No other congenital abnormalities like annular pancreas or atresia found. The patient was treated conservatively with nothing per oral, intravenous fluid, Broad spectrum antibiotics, Nasogastic Suctions, Analgesics and antispasmodics.

2. The second patient 32 years old Bangladeshi woman, mother of two children, of Comilla District Bangladesh, admitted in a local clinic with severe upper abdominal pain, fever,nausea, and anorexia. Physical examination revealed good health, remarkable tenderness over the Right. hypochondriac region. Murphy's sign was positive. She was mildly dehydrated. Patient was hypertensive, non insulin dependent diabetic. Examination of other systems revealed normal.

Routine laboratory examinations revealed nothing abnormal except Neutrophilic lucocytosis.

Liver function tests, serum Creatinine were within normal limit.

Ultrasonographic scan done and the comment was "contracted gallbladder " (Fig.-4)

The patient underwent laparotomy but during the procedure gall blader was absent.The extra hepatic billiary apparatus were normal.

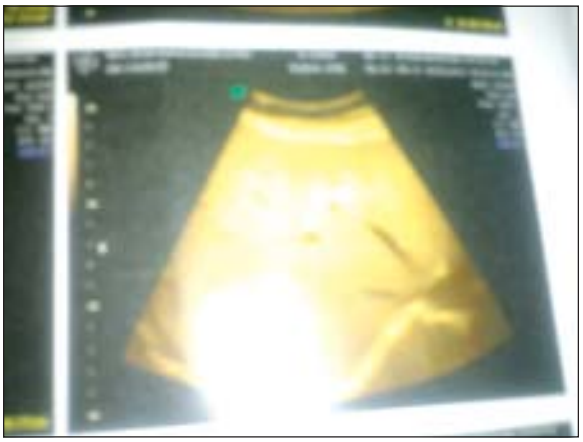

Fig.-4: *Ultrasonographic Scan*

Fig.-5: *CT Scan*

Discussion:

Gallbladder agenesis is a rare entity with an estimated incidence of 10–65 per 100,000[1,2]. The incidence is noted to be higher (up to 90 per 100,000) in studies based on autopsy reports[3]. The first reports of cases of gallbladder agenesis date back to 1701 and 1702 by Lemery and Bergman[1,2,4]. The pathogenesis is related to embryonic development due to failure of the gallbladder and cystic duct to bud off from the common bile duct during the fifth week of gestation[1].

Prior authors have classified patients into three groups. The first group consists of asymptomatic anatomical abnormalities seen incidentally on autopsy. The second group presents with symptoms of biliary colic (54%), dyspepsia (34%) and/or jaundice (27%), and the third presents in childhood with other associated severe fetal anomalies[2,4].

The exact prevalence of each of the three groups is variable based on published reports. It is thought that approximately 70% of cases are usually isolated anomalies, although some cases appear to be familial and are associated with more severe anomalies[5,8,9]. In an interesting series of 34 cases (29 children and 5 adults) of congenital gallbladder agenesis, the most common anomalies associated were involving the genitourinary tract followed by gastrointestinal and cardiovascular malformations. Family history was negative in all, suggesting a sporadic occurrence[10].

Historically, all cases were identified intraoperatively. In a review of 9 cases by Cho et al.[11], all patients underwent a laparotomy, which failed to identify the gallbladder. However, now with the increased frequency of advanced imaging, cases are being diagnosed more often and, more importantly, before any surgical intervention.

However, given that patients with gallbladder agenesis tend to present symptoms suggestive of biliary colic, a number of them are still diagnosed intraoperatively. Due to a lack of awareness of the diagnosis, this entity remains a diagnostic challenge[2,12]. In those cases which are diagnosed intraoperatively, patients often are exposed to complications from prolonged exploration[13], and it is suggested to abort the procedure rather than complete further exploration if a gallbladder is not found on laparoscopy since open exploration for possible ectopic gallbladder increases the risk of complications[14]. Intraoperative ultrasound can demonstrate an ectopic gallbladder but is not always available[13]. A follow-up with more advanced imaging techniques should be the next option to truly identify gallbladder agenesis as the sole abnormality to guide management further.

It is therefore important to consider the presence of this unusual entity when the nonvisualization of the gallbladder is suggested on ultrasound[15]. However, as is known, ultrasound is highly dependent not only on the operator but also on other factors such as body habitus or presence of bowel gas obscuring visualization. Cases of gallbladder agenesis have been reported as 'contracted/fibrotic gallbladder' on ultrasound[14].

HIDA scans, which are also usually performed in patients with cholecystitis, in this case are unhelpful since nonvisualization of the gallbladder remains typical of cystic duct obstruction, as well as of agenesis[13], MRCP is considered the test of choice if there is suspicion. It is also helpful in demonstrating an ectopic gallbladder along with other possible anomalies of the biliary tract system[8] In terms of treatment, there are no specific guidelines on how to manage these cases. Interestingly, one author notes that 98% of patients had resolution of symptoms after exploratory, nontherapeutic surgery[5]. It is unclear how these patients would have had symptom resolution in the absence of exploration.

Conclusions:

Gallbladder agenesis presents as a significant diagnostic challenge. With the advances in imaging, more cases of gallbladder agenesis are being diagnosed incidentally and outside of the operating room. Clinicians should have a strong index of suspicion if nonvisualization is suggested by an ultrasound. A positive HIDA scan can be seen in the presence of gallbladder agenesis in the absence of cholecystitis. MRCP is considered the investigation of choice if there is suspicion. It is also helpful in demonstrating an ectopic gallbladder along with other possible anomalies of the biliary tract system. Management is usually conservative with smooth muscle relaxants.

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Primary Vaginal Carcinoma in Prolapsed Uterus

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(J Bangladesh Coll Phys Surg 2012; 30: 181-182)

Primary carcinoma of vagina is a rare entity in gynaecological oncology [1]. Carcinoma of vagina in prolapsed uterus is extremely rare .A tumour should be considered as a primary vaginal cancer when the cervix is uninvolved .

A 65 years old (para 6) menopausal lady presented with retention of urine , pervaginal bleeding ,pelvic pain and irreducible uterovaginal prolapse .On vaginal examination , a large fungating growth (5-6cm)occupying the middle part of anterior and right lateral wall of vagina was found . Physical examination including digital rectal examination showed no involvement of parametrium, urinary bladder or rectum .Inguinal lymphnodes were not palpable. Biopsy was taken from the fungating growth. Histopathology examination diagnosed the case as squamous cell carcinoma of vagina. Paps smear of cervix and X ray chest revealed no abnormalities. IVU showed bilateral hydroureter and hydronephrosis ,CT scan of abdomen revealed procidentia with no parametrium or lymph node involvement . The patient was staged as having a FIGO stage I vaginal carcinoma and TNM(T1N0M0)

The treatment performed was radical vaginal hysterectomy and excision of the whole vagina .Histopathology confirmed the squamous cell carcinoma of vagina . All the resection margins of the surgical specimen were clear. There was not lymphvascular space involvement. Her postoperative period was uneventful. After the operation the patient received external radiotherapy.

The primary therapeutic consideration encompasses surgery , radiotherapy and chemotherapy .Surgical approach may be curative in stage I [1,2,3,4]. Due to early invasion of bladder or rectum and particularly in older patients primary radiotherapy is most common therapeutic modality, although surgery may be implemented in early stage.[2,3,5]

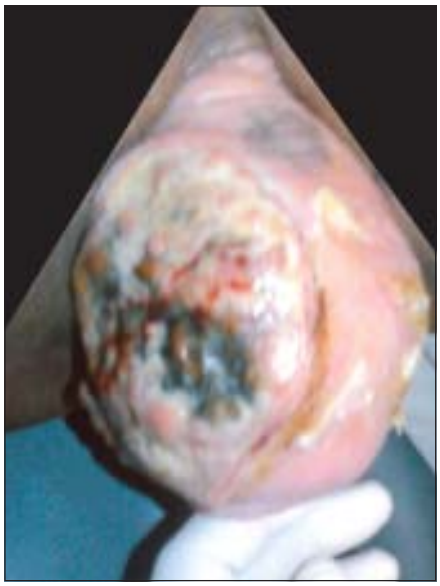

Fig. : *Primary vaginal carcinoma in prolapsed uterus. (Consent for publishing the photograph was taken from patient).*

Carcinoma of vagina is considered the rarest gynaecological neoplasms. It represents less than 1-2% of gynaecological malignancies. Its incidence peaks during 60s[1,2,3]. Among them 85% are squamous cell carcinoma.

Few cases of vaginal carcinoma associated with uterine prolapse are reported[5-8]. Common factors that may

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increase a women's chance of developing vaginal carcinoma are age factor (over two-thirds of women are 60 years old or older during diagnosis), smoking habit, infection with human papillomavirus(HPV), Human Immunodeficiency Virus(HIV)infection. Other risk factors include: exposure to diethylstilbestrol (DES) as a fetus (mother took DES during pregnancy, vaginal adenosis ,vaginal irritation or uterine prolapse, previous cervical dysplasia or invasive lesion .Drinking alcohol may increase the risk of vaginal carcinoma .

In our case , the patient had a history of prolapse for more than 10 years . It is suggested that , patients with procidentia of 10 years duration are more likely to develop malignant transformations [8]

Vaginal cancer is often asymptomatic. Postmenopausal vaginal bleeding or vaginal discharge is the most common presenting feature, however urinary tract disturbances and pelvic pain may occur. An ulcerative lesion in vagina may occur following an inflammatory reaction due to prolonged retention of a pessary or other foreign body. Direct invasion to bladder and rectum may occur .The incidence of lymphnode metastases is directly related to the size of tumour. Tumours from the lower third of vagina metastasizes to inguinal lymphnodes .and from the upper vagina to common iliac and presacral lymph nodes.

The treatment of patient with simple invasive vaginal carcinoma primarily consists of combined external beam and internal radiation therapy .In stage 1 and IIA ,also in young woman where coitus is an important factor surgery should be considered .The 5 –year survival rate for stage I is 70% . The size and stage of the disease is the most important prognostic indicators in squamous cell cancers .

As few published cases of combined uterine prolapse and vaginal carcinoma , there have been no published reports that assess the management of primary invasive carcinoma of vagina associated with vaginal prolapse.

Any fungating or ulcerative lesion in vagina or decubitus ulcer not responding to treatment should be considered as malignant until proved otherwise .

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LETTER TO THE EDITOR

(J Bangladesh Coll Phys Surg 2012; 30: 183)

To Editor in Chief Journal of Bangladesh College of Physician and surgeon

At first I would like to thank The Editor for publishing an original article on "The Ten Step Vaginal Hysterectomy- A Newer and Better Approach" (April Vol 30, no2,2012; Page71-77) in your most prestigious journal in Bangladesh.

Though prevalence of uterine prolapsehas decreased in the urban areas, but still now it is a big problem in rural areas of our country. Vaginal hysterectomy remains the accepted surgicaltreatment for women with symptomatic uterine prolapse.

The vaginal route should always be considered when hysterectomy is indicated, because of a quicker recovery, lack of abdominal scar and shorter hospital stay[1,2]. In order to find out whether vaginal hysterectomies can still be optimized and simplified after so many years of practice and accumulated experience, a re-evaluation of 'Ten-Step Vaginal Hysterectomy' was initiated[3]. This method is anatomically logical, easier to learn, perform and teach. It reduces operating theater time and analgesic use[4]. Only ten instruments and ten sutures are needed and it was shown that this reduces the operation time[5].

In this article the author nicely and appropriately mentioned the steps and the procedure. It would encourage the gynaecologist to adapt this procedure. I specially thankthe author as she has performed this in a district level hospital and shared her experience with us.

Prof. Neke Akhter
Prof. and Head
Department of Gynaecology& Obstetrics
Bangladesh Medical College.

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Author's reply:

First of all, I would like to thank the Editor of the most honourable and prestigious journal, as well as, my dear colleague Prof. NekeAkhter who gave such an impressive comment on my original article on "The Ten Step Vaginal Hysterectomy- A Newer and Better Approach" (April Vol. 30, No. 2,2012; Page: 71-77) on "The Ten Step Vaginal Hysterectomy- A Newer and Better Approach" (April Vol. 30, No. 2, 2012; Page: 71-77).

In fact, this is a new approach in comparison to the traditional method and we do not have enough study in this case. So in my point of view, more gynaecologists are needed to practice this method of vaginal hysterectomy. So that we can identify the week points of this method and then rectify and modify the operation in collaboration with other colleagues. Because our target is patients centered care and always do the best for the patients.

Thanks a lot for your time and convenience.

With best regards,

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COLLEGE NEWS

(J Bangladesh Coll Phys Surg 2012; 30: 184)

News on Continuing Professional Development program (CPD) Continuing Professional Development (CPD) is a multi-professional educational activity that helps professionals to keep their knowledge and skills up-to-date in response to the changing needs of the community and profession.

Present CPD committee, BCPS has organized one CPD program at BSMMU and 2nd CPD day. You all know that the 1St CPD day was organized by CPD committee on 2010. It was a memorable day for BCPS where 474 post graduate doctors and students were there as participants.

In CPD program, tow papers were presented. The program was chaired by Prof. Selimur Rahman, Professor of Hepatology, BSMMU and Prof. Md. Salahuddin Al-Azad, Professor of Radiology & Imaging, BSMMU. Dr. Md. Abul Kalam Azad, Associate Professor of Medicine, BSMMU conducted the session as moderator.

Papers presented were:

1. Practice guideline for the management of chronic Hepatitis B. Speaker -Dr. Md. Sahinul Alam, Associate Prof, Hepatology, BSMMU
2. Role of Ultrasound in chest lesions. Speaker- Dr. Md. Delwar Hossain, Associate Prof, Radiology & Imaging, NIKDU

We have also organized CPD day, a day long program on 5 April, 2012 at BCPS premises, where we had 355 participants were with us. Thirty two papers from different disciplines were presented over the session.

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

We have a plan to arrange our next program at Shaheed Suhrawardy Medical College in September.

FROM THE DESK OF EDITOR in CHIEF

(J Bangladesh Coll Phys Surg 2012; 30: 185)

Dear Fellows

Another quarter has past and we are with a new issue of our favourite journal. We the editorial team have been working hard over this period for gradually build up this journal into one of the most prestigious periodical of this region. In this regard we have now updated the information for authors section of the journal. This will help to improve the quality of the writing as well as develop an uniform format for articles printed in JBCPS.

We are also working on developing a reviewer's guideline which is almost ready and hope that we will be able to make it available for you by the next quarter. In the mean time I would hope that my dear fellows will be along our side and help us reach our desired goal.

Prof. HAM Nazmul Ahasan
Editor-in-Chief

Obituary

(J Bangladesh Coll Phys Surg 2012; 30: 186)

The following Fellows who died June 2012

Professor Abul Hasnat Mohammad Firoz

Professor Abul Hasnat Mohammad Firoz died on 5th June 2012. He passed fellowship in Psychiatry in July, 1988 from Bangladesh College of Physicians and Surgeons (BCPS).

Professor M.A. Matin

Professor M.A.Matin died on 13th June 2012. He awarded fellowship without Examination in Ophthalmology in, 1974 from Bangladesh College of Physicians and Surgeons (BCPS). He was president of Bangladesh College of Physician & Surgeons from 1st March to 28th February 1985. He was Councillor of Bangladesh College of Physician & Surgeons from 5th March 1975 to 28th February 1985.He was Member of the Parliament, Ex.Minister of the following Ministries: Ministry of Health and Family welfare, Ministry of Home Affairs, Ministry of Education, Ministry of Communication and Ex. Deputy Prime Minister,Govt.of the Peoples Republic of Bangladesh.

Professor Dewan Eklimur Raza Chow.

Professor Dewan Eklimur Raza Chow died on 16th June 2012. He passed fellowship in Surgery in January, 1974 from Bangladesh College of Physicians and Surgeons (BCPS).

Professor Alamgir Mohiuddin Kabir

Professor Professor Alamgir Mohiuddin Kabir died on 21th June 2012. He passed fellowship in Medicine in January, 1973 from Bangladesh College of Physicians and Surgeons (BCPS).