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INFORMATION FOR AUTHORS

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Guide to Authors

MH Samorita Medical College Journal provides rapid publication (twice in a year) of articles in all areas of different subjects. The Journal welcomes the submission of manuscripts that meet the general criteria of significance and scientific excellence.

The manuscripts should be submitted addressing Editor-in-Chief.

The Journal of MH Samorita Medical College only accepts manuscripts submitted as triplicate hard copy with a soft copy.

Papers must be submitted with the understanding that they have not been published elsewhere (except in the form of an abstract or as part of a published lecture, review, or thesis) and are not currently under consideration by another journal (**International or National)** or any other publisher.

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

The cover letter

Cover letter is expected to be submitted along with manuscript. Use the cover letter to explain why the paper should be published in the Journal of MH Samorita Medical College. The cover letter should include the corresponding author's full address, telephone/ fax numbers and e-mail address.

Ethical aspects

- Ethical aspect of the study is considered very carefully at the time of assessment of the manuscript.
- Any manuscript that includes table, illustration or photograph that have been published earlier should accompany a letter of permission for re-publication from the author(s) of the publication and editor/ publisher of the Journal where it was published earlier.
- Permission of the patients and/or their families to reproduce photographs of the patients where identity is not disguised should be sent with the manuscript. Otherwise the identity would be blackened out.

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 MH Samorita Medical College Journal (MHSMCJ) and may not be reproduced by any means in whole or in part without the written consent of the publisher.
- It is the author's responsibility to obtain permission to reproduce illustrations, tables etc. from other publications.

Article Types

Four types of manuscripts may be submitted.

Editorials: It should preferably cover a single topic of common 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 and its volume should **not exceed 5000 words** or equivalent space including title, summary/abstract, main body, references, table(s) and figure(s).

Review Articles: Submissions of reviews 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) and should **not exceed 5000 words**. It should be focused and must be up to date.

Case Reports: This should cover uncommon and/or interesting cases and should **not exceed 1000** words or equivalent space.

Review Process

All manuscripts are initially screened by editor and sent to selective reviewers. Reviewers are requested to return comments to editor within 3 weeks. On the basis of reviewers' comments the editorial board decides whether the articles are accepted or send for re-review the manuscripts. The MH Samorita Med Coll J editorial board tries to publish the manuscript as early as possible fulfilling all the rigorous standard journal needs.

I. Preparing a Manuscript for Submission to MH Samorita Med Coll J

Editors and reviewers spend many hours reading and working on manuscripts, and therefore appreciate receiving manuscripts that are easy to read and edit. The following information provides guidance in preparing manuscripts for the journal.

I A. Preparation of manuscript

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

Preparation

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

- Title page
- Abstract
- Main body/Text: Introduction, Materials and Methods, Results, Discussion and conclusion (For an original article/ Systematic review)
- Acknowledgement
- References
- Tables and legends

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

I A. 1. General Principles

- The text of observational and experimental articles is usually (but not necessarily) divided into the following sections: Introduction, Materials and Methods, Results, and Discussion(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.
- Authors need to work closely with editors in developing or using the publication formats and should submit supplementary electronic material for peer review.
- Double-spacing all portions of the manuscript— including the title page, abstract, text, acknowledg- ments, references, individual tables, and legends— and generous margins make it possible for editors and reviewers to edit the text line by line and add comments and queries directly on the paper copy.
- If manuscripts are submitted electronically, the files should be double-spaced to facilitate printing for reviewing and editing.
- Authors should number on right upper all of the pages of the manuscript consecutively, beginning with the title page, to facilitate the editorial process.

I A. 2. Title Page

The title page should have the following information:

- The title should be brief, relevant and self explanatory. It should reflect the content of the article and should include all information that will make electronic retrieval of the article easy. Subtitles should not be used unless they are essential.
- Title should not be phrased as questions.
- The names of the authors should appear below the title that should include full names of all authors **(no initial).**

Example: Md MA Hamid **(correct form);** Hamid MA **(incorrect).**

The affiliations and full addresses of all authors should be mentioned in the title page.

- Contact information for corresponding authors: The name, mailing address, telephone and fax numbers, and e-mail address of the author responsible for correspondence about the manuscript.
- The name and address of the author to whom requests for reprints should be addressed or a Statement that reprints are not available from the authors.
- Source(s) of support in the form of grants, equipment, drugs, or all of these.

I A. 3. Abstract

Original Article: Structured abstracts are essential for original research. Structured abstract includes introduction, objective(s), materials and methods, results and conclusion. Should be limited to 250 words. The abstract should provide the introduction of the study and blinded state and should mention the study's purpose, basic procedures including selection of study subjects or laboratory animals, main findings (giving specific effect sizes and their statistical significance, if possible) and the principal conclusion. Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion that many readers read, it should accurately reflect the content of the article; so, authors need to be careful about that.

Review Article: is expected to contain background, objective(s), main information and conclusion in brief form. Without any subheading the content should be described in a single paragraph.

Case Study: needs to have background, case summary and conclusion. The content should be described in a single paragraph.

Do not put references in the abstract.

I A. 4. Main body

I A. 4 a) Original article

The body of the text should be divided into the following sections: i) Introduction, ii) Materials and methods, iii) Results, iii) Discussion and iv) Conclusion.

i) Introduction

Should not exceed **500 words**. This section includes background of the problem (that is, the nature of the problem and its significance). It should be very specific, identify the specific knowledge in the aspect, reasoning and what the study aim to answer. Only pertinent primary references should be provided and no data or conclusions should be included from the work to be reported. **Justificatio**n of the study and its **objective(s)** should be mentioned at the end of this section. All information given in this section must have references that to be listed in the reference section.

ii) Materials and methods

The Methods section should be written in such way that another researcher can replicate the study. The type of study (study design), study period, sampling technique, sample size, study population, data collection technique and tool as well as data handling, processing and data analysis should be briefly mentioned in this section.

ii a) Selection and Description of Participants

Describe selection of the observational or experimental participants (patients or laboratory animals, including controls) clearly, including eligibility (inclusion) 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 etc. 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.

ii b) Technical Information

- Describe methods, apparatus (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow others to reproduce the results.
- Cite references to established methods, including statistical methods. 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.
- For a systematic review article include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

ii c) Statistics

- Describe statistical methods with enough detail to enable a know- ledgeable 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).
- Cite references for the design of the study and statistical methods (standard for the work) when possible.
- Define statistical terms, abbreviations, and most symbols.
- Specify the computer software used.

iii) Results

Results should be described in past tense.

- Present results in logical sequence in the text, tables, figures and illustrations, giving the main or most important findings first. Maintain the sequence of results with the specific objectives selected earlier.
- Do not repeat all the data in the tables or illustrations in the text; emphasize or summarize only the most important observations.
- When data are summarized in the result section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them.
- Restrict tables and figures to those needed to explain the argument (relevant to objectives) and to assess supporting data. Use graphs as an alternative to tables with many entries; do not duplicate data in figures (graphs/ charts) and tables. **Example:** Age range of the studied respondents should be appeared **either in table or in figure**.
- Avoid nontechnical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlations," and "sample."

iv) Discussion

The discussion must be described in **past tense.** This section should reflect the author's comments on the results.

- Emphasize the new and important aspects of the study and the conclusions that follow 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 those findings.
- Compare and contrast the results with other relevant studies and potential argument for discrepancy and consistency should be given here.
- 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, 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.

v) Conclusion

It should be described in **present tense**. Conclusion should be the main message and the authors' impression from the results of the study. The article should be concluded briefly (**not more than 100 words**). Recommendation(s) can also be included in this section which should not exceed 30 words.

I A. 4 b) Review article

For a systematic review or meta-analysis the body of text should be divided into the following sections (Like an original article): i) Introduction, ii). Materials and methods, iii) Findings/Results, iii a) Main information about the topic, iv) Discussion and v) Conclusion. For a general review article section No. ii (Materials and methods) and iii (Findings/Results) iv) (Discussion) are not relevant. So, for a general review article section No. i). Introduction, iii a). Main Information about the Topic and v). Conclusion are required.

i) **Introduction**: should not exceed **500 words**. This section will include background of the topic. At the end of the review, why the author want to publish the topic on the article ie., the objective should be mentioned.

ii) **Material and methods**: How the review was done, what sorts of articles were searched, how they were searched, the total number of articles reviewed should be mentioned here. This section is not required for a general review article.

iii) **Results/findings**: The findings on the topic after reviewing the articles should be compiled, analysed and described here like an original research article. This section is not required for a general review article.

iii a) **Main Information about the Topic**: The main information about the topic should be described and discussed elaborately with the help of published literatures in this section but the subtitles should be relevant to the topic(Title) for a general review article. This section may not be required for a systematic review or meta-analysis.

iv) **Conclusion:** The article should be concluded briefly (**not more than 100 words**).

I A. 4 c) Case Report

The body of the text should be divided into the following sections: i) Introduction, ii) Case Report (Description of the case), iii) Discussion and iv) Conclusion.

i) **Introduction**: A brief description should be given on the topic of the case with the help of published literatures.

ii) **Case Report**

- The findings (history, clinical examination and investigations) should be described here.
- Management (if any) can also be given.

iii) **Discussion**

- The discussion should be started by briefly summarizing the main findings of the case reported, then possible explanations for those findings should be explored.
- The findings of the case should be compared with other relevant studies and potential argument for discrepancy and consistency should be given here.

iv) **Conclusion**

- The article should be concluded briefly (**not more than 100 words**).
- The main findings of the reported case should be emphasized which the readers can consider as a clue to suspect a diagnosis for a rare case in future.

I A. 5. Acknowledgement

Acknowledge advisor(s) and/or any one who helped the researcher(s)

- Technically
- Intellectually
- Financially

I A. 6. References

I A. 6 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.
- Abstracts should not be used as references. References to papers accepted but not yet published should be designated as "in press" or "forthcoming"; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication.
- Information from manuscripts submitted but not accepted should be cited in the text as "unpublished observations" with written permission from the source.
- Citing a "personal communication" should be avoided unless it provides essential information not available from a public source, in which case the name of the person and date of

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

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

I A. 6 b) Reference Style and Format

➢ **Reference Style**

Author should follow **Vancouver style**.

- R**eference list** should appear at the end of the article and should be numbered consecutively in the order as they are cited in the text, which is done by **superscript** (single press of 'ctrl shift +') in numerical form **(citation number).**
- When **multiple references** are cited at a given place in the text, use a **hyphen** to join the first and last numbers that are **inclusive**. Use **commas** (without spaces) to separate **non-inclusive** numbers in a multiple citation.

  Example: 2,3,4,5,7,10,12 are abbreviated to **(2-5,7,10,12**).
- **Do not** use a hyphen if there is no citation numbers in between 2 numbers that support your statement.

  Example: 1-2 (**in correct form).** 1,2**(correct form)**
- As a general rule, citation numbers in the text should be placed **outside full stops and commas**, inside colons and semicolons (applicable for any part of the document).

  Example: Masud Alam,1 Selim Khan[2]

  Example: Over the past decades public health relevance of mental health condition 'in children and adolescents has been of growing concern'.[1-3,5,6]
- 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.

➢ **Reference Format**

1. Citing a Book

The essential details required are (in order):

1.1 Name/s of author/s, editor/s, compiler/s or the institution responsible.

- Where there are **6 or less authors** you must list **all authors**.
- Where there are **7 or more author**s, only the **first 6 are listed** and **add "et al"** (after a **comma**).
- Put a comma and 1 space between each name. The last author must have a full-stop after their initial(s).

  Format: surname (**1 space**) initial/s (**no spaces or punctuation between initials**) (**full-stop OR if further names comma, 1 space**)

  Example: Smith AK, Jones BC, Bloggs TC, Ashe PT, Fauci AS, Wilson JD, et al.
- **When author/s is/are editor/s :**Follow the same methods used with authors but use the word **"editor"** or **"editors"** in full after the name/s. The word editor or editors must be in small letter. (**Do NOT** confuse with "ed."used for edition.)

  Example: Millares M, editor. Applied drug information: strategies for information management. Vancouver (WA): Applied Therapeutics Inc; 1998.

Sponsored by institution, corporation or other organization (including PAMPHLET)

E**xample**: Australian Pharmaceutical Advisory Council. Integrated best practice model for medication management in residential aged care facilities. Canberra: Australian Government Publishing Service; 1997.

1.2. Title of publication and subtitle if any

- Italics or underlining should be avoided.
- Only the first word of the titles (and words that normally begin with a capital letter) should be started with capital letter (except proper noun).

Format: title (**full-stop, 1 space**)

Example: Harrison's principles of internal medicine.

Example: Physical pharmacy: physical chemical principles in the pharmaceutical sciences.

Example: Pharmacy in Australia: the national experience.

1.3. Edition (other than the first)

Number of edition **other than first one** should be mentioned as **2nd, 3rd,10th ed.**

Example: Blenkinsopp A, Paxton P. Symptoms in the pharmacy: a guide to the management of common illness. 3rd ed. Oxford: Blackwell Science; 1998.

1.4. Place of publication (if there is more than one place listed, use the first one)

- The place name should be written in full.
- If the place **name is not well known**, add a comma, 1 space and the state or the country for clarification. For places in the USA, add after the place names the 2 letter postal code for the state. This must be in upper case. eg. Hartford (CN): (where CN=Connecticut).

Format: place of publication (**colon, 1 space**)

Example: Hartford (CN):

Example: Texas (NSW):

Example: Kyoto (Japan):

1.5. Publisher

The publisher's name should be spelled out in full.

Format: publisher (**semi-colon, 1 space**)

Example: Australian Government Publishing Service;

Example: Raven Press;

Example: Williams & Wilkins;

1.6. Year of publication

Format: year (full-stop, add 1 space if page numbers follow).

Example: 1999.

Example: 2000. p. 12-5.

1.7. Page numbers (if applicable).

- Abbreviate the word "page" to "p.".

Note: do not repeat digits unnecessarily

Format: p (**full-stop, 1 space**) page numbers (**full-stop**).

Example: p. 122-9 (**correct**); p. 122-129 (**incorrect**).

Example: p. 1129-57 (**correct**); p. 1129-157 (**incorrect**).

Example of citing a book: Lodish H, Baltimore D, Berk A, Zipursky SL, Matsudaira P, Darnell J. Molecular cell biology. 3rd ed. New York: Scientific American; 1995.

(*Name/s. Title. Edition(other than first). Place of publication: Publisher; year of publication. p. Page no*)

2. Citing a Chapter in an Edited Book (to which a number of authors have contributed)

- Name/s of author of the chapter
- Title of chapter followed by, In:
- Editor
- Title of book
- Series title and number (if part of a series)
- Edition (if not the first edition)
- Place of publication (if there is more than one place listed, use the first named)
- Publisher
- Year of publication
- Page numbers

(*Title of Chapter. In: Editor(s). Title of book and number. Edition (other than first). Place of publication: Publisher; year of publication. p. Page no*)

Example of citing a chapter in an edited book:

Porter RJ, Meldrum BS. Antiepileptic drugs. In: Katzung BG, editor. Basic and clinical pharmacology. 6th ed. Norwalk (CN): Appleton and Lange; 1995. p. 361-80.

3. Citing a Journal Article from a Print source

The essential details required are (in order):

- **Name/s of author/s of the article.**
  See step 1 of "Citing a book" for full details.
- **Title of article.**
  See step 2 of "Citing a book" for full details.

Example: Validation of an immunoassay for measurement of plasma total homocysteine.

- **Name of journal (abbreviated).**

- Abbreviate the name of the journal according to the style used in Medline.
- A list of abbreviations can be found at: http://w**ww.ncbi.nlm.nih.gov/entrez/query.fcgi?db=journals**

  Note: No punctuation marks are used in the abbreviated journal name.

Format: journal title abbreviation (1 space)

Example: Bang J Psychiatry

- **Year of publication (month or day should be omitted).**

Format: year (**semi-colon, one space**)

Example: 1996; 12(5): 127-33.

- **Volume number (and issue/part)**

  Format: volume number (**colon, one space**)

Example: 1996; 12(5): 127-33. Or
1996; 18: 1237-8.

- **Page numbers**

Note: Do not repeat digits unnecessarily

Format: page numbers (full-stop)

Example: 5310-5.

Example of citing a journal: Russell FD, Coppell AL, Davenport AP. In vitro enzymatic processing of radiolabelled big ET-1 in human kidney as a food ingredient. Biochem Pharmacol 1998; 55(5): 697-701.

Name(s). Title. Name of the Journal Year of publication; Volume Number (Session/Issue Number): Page Number.

- **No author given in article**

  Example: Coffee drinking and cancer of the pancreas [editorial]. BMJ 1981; 283: 628.

- **Journals with parts and/or supplements**

Examples

- **Volume with supplement**

  Environ Health Perspect 1994; 102Suppl 1: 275-82.

- **Issue with supplement**

  SeminOncol 1996: 23(1 Suppl 2): 89-97.

- **Volume with part**

  Ann ClinBiochem 1995; 32(Pt 3): 303-6.

4. Citing a Journal Article from Internet and Other Electronic Sources

This includes software and internet sources such as web sites, electronic journals and databases.

The **basic form** of the citations **follow the principles listed for print sources** (see above).

In the case of sources that may be subject to alteration it is important to acknowledge the **Date The Information Was Cited.** This is particularly true for web sites that may disappear or permit changes to be made and for CD-ROMS that are updated during the year.

4.1. Citing a Journal Article from the Internet

Note: Follow the same procedure for citing print journals as for electronic journals regarding date, volume pages and journal title

Format: Author/s (full-stop after last author, 1 space) **Title of article** (full-stop, 1 space)

Abbreviated title of electronic journal (1 space) **[serial online]** (1 space) **Publication year** (1space) **month(s)** - if available (1 space) **[cited year month (abbreviated) day]** - in square brackets (semi colon, 1 space) **Volume number** (no space) **Issue number** if applicable in round brackets (colon) **Page numbers or number of screens** in square brackets (full-stop, 1 space) **Available from** (colon, 1 space) URL:**URL address underlined**

Examples:

- Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] 1995 Jan-Mar [cited 1999 Dec 25]; 1(1):[24 screens]. Available from:URL: http://www/cdc/gov/ncidoc /EID/eid.htm
- Garfinkel PE, Lin E, Goering P. Should amenorrhoea be necessary for the diagnosis of anorexia nervosa? Br J Psych [serial online] 1996 [cited 1999 Aug 17]; 168(4):500-6. Available from: URL:http://biomed. niss.ac.uk

4.2. Citing a Journal Article from WWW site

(If the author is not documented, the title becomes the first element of the reference.)

Format: Author (full-stop after last author, 1 space) **Title** (full-stop, 1 space) **[Online]** (full stop, 1 space) **Publication Year** (1 space) **[cited year month (abbreviated) day]** (semi colon) **Number of screens in square brackets or pages** (full-stop, 1 space) **Available from** (colon, 1 space)

URL: (no space) **URL address underlined**

Note: The number of screens is not necessary. Put a semi colon and 1 space after the cited date if no pages or screen numbers are listed.

When the date is approximated, indicate that by following the date with a question mark and inserting the statement in square brackets. Eg. [2001?]

Examples: National Organization for Rare Diseases [Online]. 1999 Aug 16 [cited 1999 Aug 21]; Available from: URL:http://www.rare diseases.org/

Royal College of General Practitioners.The primary health care team.[Online]. 1998 [cited 1999 Aug 22];[10 screens]. Available from:URL: http:// ww. rcgp.org.uk/informat/publicat/rcf0021.htmZand J. The natural pharmacy: herbal medicine for depression [Online]. [1999?] [cited 2001 Aug 23];[15 screens]. Available from:

URL:http://www.healthy.net/asp/templates/Article.asp?PageType=Article&Id=920

Important Points For Reference List

- For **online material**, please cite the **URL**, together with the **date you accessed** the website
- **Online journal** articles can be cited using the Digital Object Identifier **(DOI)** number

Samples of Reference List

A list of references contains details of those works cited in the text.

The references are listed in the same numerical order as they appear in the body of the text

1. Getzen TE. Health economics: fundamentals and flow of funds. New York (NY): John Wiley & Sons; 1997.
2. Millares M, editor. Applied drug information: strategies for information management. Vancouver, WA: Applied Therapeutics, Inc.; 1998.
3. Australian Government Publishing Service. Style manual for authors, editors and printers. 5th ed. Canberra: Australian Government Publishing Service; 1994.
4. Australian Pharmaceutical Advisory Council. Integrated best practice model for medication management in residential aged care facilities. Canberra: Australian Government Publishing Service; 1997.
5. Bennett GL, Horuk R. Iodination of chemokines for use in receptor binding analysis. In: Horuk R, editor. Chemokine receptors. New York (NY): Academic Press; 1997. p. 134-48. (Methods in enzymology; vol 288).
6. Coffee drinking and cancer of the pancreas [editorial]. BMJ 1981;283:628.
7. Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] 1995 Jan-Mar [cited 1996 Jue 5]; 1(1):[24 screens]. Available from: URL:http:// www. cdc.gov/ ncidoc/EID/eid.htm

I A. 7. Conflict of interest

All authors are requested to disclose any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations.

It is important to be consistent when you are referencing.

I A. 8. Tables and Illustrations (Figures)

I A. 8 a) Tables

- In tables, capture information concisely and display it efficiently.
- Use tables /fig that are relevant to the study.
- Try to limit the number of tables/figures.
- 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.

I A. 8 b) Illustrations (Figures)

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).

- Review the images of such files on a computer screen before submitting them to be sure that 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.

- If a figure has been published previously, acknowledge the original source and submit written permission from the copyright holder to reproduce the figure. Permission is required irrespective of authorship or publisher except for documents in the public domain.
- For illustrations in colour, MH Samorita Med Coll J accept coloured illustration when it seems essential. This Journal publish illustrations in colour only if the author pays the additional cost. Authors should consult the editorial board of the journal about requirements for figures submitted in electronic formats.

I A. 8 c) Legends for Illustrations (Figures)

- Type or print the legends for illustrations using double spacing, starting on a separate page, with Arabic numerals corresponding to the illustrations.
- When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend. Explain the internal scale and identify the method of staining in photomicrographs.

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- Authors should report laboratory information in both local and International System of Units (SI).
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- Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers.
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- Title page contains all the desired information
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- Uniformity in the language
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- Not more than 200 words for case reports and 250 words for original articles
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- **Introduction**
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- Ethical approval
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- Avoid unnecessary explanation of someone else' work unless it is very relevant to the study
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- Mention about limitation of the study
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- Use reference at the end of the sentence after the full stop with superscript
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Editorial

Emergence of COVID-19 as a Pandemic

Alam MU

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by a virus, the severe acute respiratory syndrome Coronavirus-2 (SARS-Cov-2) is proven to be the biggest public health crises of recent times.[1] SARS-Cov-2 is a newly discovered virus that is closely related to bat coronaviruses, Pangolin coronaviruses and SARS-Cov. The first known case was identified in Wuhan in China's Hubei Province in December 2019.[2] Attempts to contain it there failed, allowing the virus to spread world wide. The virus is thought to be of natural animal origin, most likely through spillover infection. According to official Chinese sources, on 31st December Chinese Disease Control Centre reported 27 cases of patients with Pneumonia of uncertain aetiology. These were mostly linked to the Huanan seafood wholesale market, which also sold live animals.[3]

By December 2019, the spread of infection was almost entirely driven by human-to-human transmission.[4] During the early stages of the outbreak, the number of case doubled approximately every seven and half days. In early and mid-January of 2020, the virus spread to other Chinese Provinces, helped by the Chinese New Year migration. Wuhan was a transport hub and major rail interchange.[5]

On January 30, 2020 the WHO declared COVID-19 a Public Health Emergency of International Concern.[6] Earlier on January 7, 2020, the causative agent was identified as a new coronavirus (2019-n Cov), and the disease was later named as COVID-19 by the WHO. WHO officially declared COVID-19 infection as a Pandemic on March11,2020.[7] Also, WHO risk assessment classified COVID-19 as a "Very-high-risk"global Pandemic.On 31st January the first published modelling study warned of inevitable "independent self- sustaining outbreaks in major cities worldwide " and called for "large-scale public health interventions".[8]

Apart from China, the ministry of Public Health, Thailand witnessed and reported its first laboratory confirmed COVID-19 case on January 13,2020. On the same day, the Ministry of Health, Labour and Welfare, Japan and National IHR Focal Point (NFP),Republic of Korea reported their first COVID-19 case .Both the identified cases in Thailand and Japan were imported cases from Wuhan, China.[9] Later, SARS-Cov-2 cases were reported from Macau Special Administrative Region, United States of America, Hong Kong Special Administrative Region, Taipei Municipality wherein all reported cases had a travel history to Wuhan. Based on the data reported until January 26, 2020, WHO released its 6th situation report on COVID-19 Pandemic, in which 29 confirmed cases were reported worldwide in ten different countries apart from China.

COVID-19 rapidly transformed from being a severe problem seemingly continued to China, to a global health emergency overnight. At the beginning of the outbreak, China was reporting thousands of new cases per day, which has reduced to dozens by March. In Europe, cases were rising rapidly day by day, with Italy recording what was an unprecedented 250 deaths in the 24 hour period between March12-13.As a result, on March13, the WHO declared that Europe had become epi center of the pandemic. On the same day, the US declared a state of emergency.[10] Italy overtook China as the country with the most deaths on 19 March 2020.By 26 March the United States had overtaken China and Italy with the highest number of confirmed cases in the world. Research on Coronavirus genome indicates that majority of COVID-19 cases in New York came from European travellers, rather than China or other Asian countries.

In April 2020,Russia sent a cargoplane with medical aid to the United States.[11] During April a dramatic increase in coronavirus cases in Moscow, pushed to city's health care system to its limits. Iran announced its first two Coronavirus cases on February 19.Less than a week later; the country declared it had 61 coronavirus cases and 12 deaths, more than any other country at the time but China. A number of other

countries in the Middle East have reported cases that have been linked back to Iran.

Latin America reported its first case in Brazil. Brazilian health officials announced a 61 year old man, who had recently returned from a business trip from Italy, tested positive for the coronavirus.

The first South Asian County to report confirmed cases was Nepal, which documented the first case on 23 January 2020, in a man who had returned from Wuhan on 9 January 2020.[12] The virus was confirmed to have spread to Bangladesh in March 2020. The first three known cases were reported on 8 March 2020 by the country's epidemiology institute IEDCR. The first reported death was on 18 March 2020. Since then, the pandemic has spread day by day over the whole nation. Bangladesh became the second most afiected country in South Asia, after India.[13] India was the first South Asian country to overtake China in terms of the number of coronavirus cases.

The number of known cases across the globe grew faster than ever by June 2020, with more than100,000 new infections a day. Densely populated, low-and middle income countries across the Middle East, Latin America, Africa and South Asia were hit the hardest. The WHO said it took Africa 98 days to reach 100,000 coronavirus cases, but only 18 days for that figure to double. Even the developed and high income countries were also affected in the same manner.

The entire world is experiencing the desolation and devastation of a deadly virus, the new disease of COVID-19, has spread throughout the world, affecting more than 210 countries and territories with alarming morbidity and mortality in figures. The pandemic has once again tested the world's preparedness for dealing with such outbreaks. In the coming month and years, we can expect to gain further insights into SARS-Cov-2 and COVID-19.

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Correlation of Serum Transaminase and Gamma Glutamyl Transferase with Hepatic Histological Activity Score Improvement in Nonalcoholic Steatohepatitis Patients Treated with Sitagliptin and Lifestyle Modification

Ghosh J[1], Alam S[2], Mustafa G[3]

Abstract:

Introduction: *Nonalcoholic steatohepatitis (NASH) is the progressive form of nonalcoholic fatty liver disease (NAFLD) which progress to cirrhosis and hepatocellular carcinoma. The study aimed to evaluate the correlation of serum transaminase and gamma glutamyl transferase (GGT) with hepatic histological activity score improvement in NASH patients treated with sitagliptin and life style modification.*

Materials and methods: *In this randomized controlled trial study, total 30 biopsy proven NASH patients irrespective of diabetes mellitus were included. 20 patients were treated with sitagliptin and life style modification (SL) and 10 patients were treated with only lifestyle modification (L) for one year. After completing one year of treatment second liver biopsy were done. NAFLD activity score (NAS) improvement ≥2 and fibrosis score improvement ≥1 was defined as histological responder. Among 20 patients of SL group 13 patients were histological responder and in L group only 2 patients among 10 were histological responders. Finally, 15 patients of histological responders and 15 patients of histological non-responders were evaluated. ALT, AST and GGT improvement were compared between responders and non-responders after one year of treatment.*

Results: *Mean NAS score improvement in responders was 2.6 ± 0.73 and 0.06 ± 0.70 in non-responders. The difference of response between SL group and L group was statistically significant (P=0.02). Mean AST improvement was 20.3 ± 26.3 U/L in responders and 4.3 ± 10.7U/L in non-responders. AST improvement was statistically significant in responders (P=0.037). Mean ALT improvement was 43.7 ± 48.9 U/L in responders and 19.5 ± 23.6U/L in non-responders. There was no statistically significant difference of ALT improvement in responders and non-responders (P=0.095). Mean AST/ALT ratio improvement was – 0.51 ± 0.52 in responders and -0.53 ± 0.28 in non-responders. Mean GGT improvement was 29.8 ± 30.9 U/L in responders and 2.2 ± 19.2 U/L in non-responders. There was statistically significant difference of GGT improvement in responders than non-responders (P = 0.006).*

Conclusion: *AST and GGT improvements correlate with hepatic histological activity score improvement rather than ALT. Further study in large sample is recommended to confirm these findings.*

Keywords: *Fatty liver, NASH, NAFLD activity score, Sitagliptin, Transaminase, Gamma glutamyl transferase.*

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is a common health problem worldwide. The prevalence of NAFLD has doubled during last 20 years, whereas the prevalence of other chronic liver diseases have remained stable or even decreased. Nonalcoholic

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steatohepatitis (NASH) is the progressive form of NAFLD. It is characterized by hepatocellular ballooning, lobular inflammation and liver fibrosis that can progress to cirrhosis and hepatocellular carcinoma[1]. Prevalence of NAFLD in western countries ranges from 24% to 42% [2] and in Bangladesh it is 33.9%. NAFLD and NASH are more prevalent in western males and Hispanics[3] but in Bangladesh females are predominant sufferers of NAFLD[4,5,6].

NAFLD is diagnosed by clinical history, laboratory tests, radiological imaging and liver biopsy. Hepatic steatosis in ultrasonogram is enough to diagnose NAFLD but to detect NASH liver biopsy is still now gold standard test. Elevated ALT and AST indicates hepatocellular injury but it may remain normal in many patients with NASH. Gamma glutamyl transferase may also be elevated in NASH. Some studies revealed that GGT is the good predictor of hepatocellular injury than transaminase[7,8,9].

There are currently few approved drugs for treatment of NASH. Life style modifications are well accepted management of NASH with control of concomitant disease e.g., hyperlipidemia, hypertension and type 2 diabetes mellitus. NASH is more frequent in diabetic patient[10]. Sitagliptin is a highly selective dipeptidyl peptidase-4 enzyme (DPP-4) inhibitor for the treatment of patients with type 2 diabetes mellitus. This enzyme breaks down the glucagon like peptide-1 (GLP-1) and glucose dependent insulinotropic polypeptide (GIP) released in response to a meal[11]. By preventing GLP-1 and GIP inactivation, they are able to increase the secretion of insulin and suppress the release of glucagon by the pancreas. This drives blood glucose levels towards normal. Hepatic DPP-4 expression in NAFLD is directly associated with hepatic lipogenesis and liver injury[12,13,14]. Sitagliptin stimulates peroxisome proliferator activated receptor (PPAR) - alpha in liver by inhibiting expression of DPP-4 enzyme. This PPAR-alpha stimulates hepatic beta oxidation (mitochondrial and peroxisomal) which prevents hepatic fat accumulation[15].

This study evaluated the correlation between liver transaminase and gamma glutamyl transferase with the hepatic histological activity score improvement in NASH patients treated with Sitagliptin and lifestyle modification.

Materials and Methods:

Type of Study: It was a randomized controlled trial (RCT) study.

Place of Study: Department of Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU).

Duration of Study: January 2014 to December 2016.

Study Population: Patients of Nonalcoholic fatty liver disease (NAFLD) who had attended at outpatient and inpatient department of Hepatology, BSMMU.

Sampling technique : Non-probability convenience sampling was done.

Sample size determination: Sample size was determined by power analysis for a single proportion. Total 60 patients with NAFLD were biopsied. Among them 34 patients were found to have NAS ≥5. Finally, 30 patients of NASH were enrolled for analysis.

Inclusion criteria: Patients of 18 to 65 years old who had NAFLD activity score (NAS) ≥5 in liver biopsy irrespective of diabetes mellitus with normal or elevated level of transaminase and GGT were selected as sample of this study.

Exclusion criteria: We excluded the following patients - 1. chronic viral hepatitis (HBV, HCV), Wilson's disease, hemochromatosis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, biliary obstruction or any other causes of chronic liver disease, 2. history of significant alcohol intake, 3. history of taking drugs that may cause fatty liver (i.e., tamoxifen, valproic acid, amiodarone, methotrexate) or that have shown benefit in previous NASH pilot studies (i.e., vitamin E, metformin, thiazolidinediones, fibrates), 4. patient with CKD, IHD, malignancy, 5. patient with hypothyroidism.

Study procedure: Patients with evidence of fatty liver in ultrasonogram were selected for this study. Venous blood of all patients was collected after 12 hours overnight fasting for laboratory tests (CBC, FBS, 2HABF, ALT, AST, GGT, PT with INR, TSH, Fasting lipid profile, HBsAg and Anti HCV). Total 60 patients with NAFLD were selected for biopsy. Informed written consent was taken prior to liver biopsy. NAFLD activity score (NAS) was detected according to Kleiner et al.[16]. Biopsy specimen was stained with hematoxylin and eosin stain for

detecting NAS and Masson's trichrome stain was done to assess fibrosis. After receiving liver biopsy report patients were grouped into NASH and Non-NASH. Patients with NAS score 5-8 were enrolled as nonalcoholic steatohepatitis (NASH) and 0-4 were enrolled as non-NASH fatty liver (NNFL). NNFL patients were excluded from study and NASH patients were included in study. Total 34 NASH patients were selected and divided into two groups randomly by lottery.

22 patients were selected in SL group (Sitagliptin plus life style modification) and 12 patients were selected in L group (only life style modification). Patients of these two groups were followed up for next one year. As liver biopsy is an invasive procedure, 4 patients were incompliant. They dropped from study due to their lack of interest for 2nd biopsy. Total 30 NASH patients (20 in SL group and 10 in L group) were considered for final analysis.

Sitagliptin 100 mg was given once daily in SL group patients and no Sitagliptin for the L group patients for one year. Life style modification was advised for both groups of patients. Patient was encouraged for moderate exercise that was walking 30 minutes a day. Dietary advice to avoid saturated fat, excessive sugar containing diet, soft drinks, fast food and refined carbohydrate were given to both groups of patients. After one year, liver biopsy was repeated for both groups. The primary parameters that compared between first and last visit were systolic blood pressure, diastolic blood pressure, waist circumference, body mass index (BMI), ALT, AST, GGT, HOMA-2 IR, Cholesterol, TG, HDL, LDL, FBS, 2HABF, NAS and fibrosis score. NAS improvement ≥2 or Fibrosis score improvement ≥1 were considered as histological responder. NAS improvement < 2 or Fibrosis score improvement <1 was considered as histological non-responder. ALT, AST, ALT/AST ratio, GGT, NAS and fibrosis score were compared between responder and non-responder group of patients.

Statistical analysis

All data were analyzed by SPSS (version 20). Quantitative data were presented as mean ± SD and qualitative data were presented in percentage. Qualitative data were analyzed by Chi-square test and quantitative data were analyzed by student´s t-test. Pretreatment and end treatment data within group were compared by paired t-test. All quantitative and qualitative data were analyzed between responders and non-responders. A statistically significant result was considered when *P* value was less than 0.05.

Ethical consideration

Ethical clearance for this study was taken from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. This study was conducted with good clinical practice and followed the principles of the Helsinki's Declaration. Prior to commencement of the study, the aim and objectives of the study along with procedure, risk and benefit of the study were explained to the patients. It was assured that all information and records would be kept confidential.

Results:

Baseline characteristics of patients: Total 30 NASH patients were evaluated. Among them 20 patients belonged to SL group and 10 patients in L group. Mean age of patients were 41.5 ± 9.2 years in SL group and 38.7 ± 6.8 years in L group. 25 patients were females and 5 patients were males. In SL group 16 (80%) patients and in L group 9 (90%) patients were female. Mean AST was 49.2 ± 25.2 U/L in SL group and 32.2 ± 13.4 U/L in L group. Mean ALT was 70.7 ± 41.7 U/L in SL group and 50.6 ± 21.8 U/L in L group. Mean AST/ALT ratio was 0.65 ± 0.22 in SL group and 0.47 ± 0.18 in L group. Mean GGT was 64.5 ± 38.5 U/L in SL group and 32.8 ± 9.3 U/L in L group. The baseline liver function tests did not differ significantly in both group patients. Mean NAS score was 5.7 ± 0.81 in SL group and 5.4 ± 0.69 in L group. Mean Fibrosis score was 1.8 ± 0.69 in SL group and 1.9 ± 0.87 in L group (Table-1).

Results after completion of treatment: After one year of treatment with sitagliptin and life style modification, mean NAS score improvement was 1.8 ± 1.4 in SL group and 0.22 ± 0.97 in L group. The difference of NAS improvement between the two groups was statistically significant (P= 0.003). Mean Fibrosis score improvement was 0.15 ± 1.22 in SL group and 0.11 ± 1.16 in L group. Fibrosis score improvement was not statistically significant between the two groups (P=0.932).

Mean AST improvement was 16.1 ± 23.9 U/L in SL group and 1.4 ± 10.8 U/L in L group. Mean ALT improvement was 38.0 ± 44.9 U/L in SL group and

19.7 ± 24.9 U/L in L group. Mean AST/ALT ratio improvement was 0.44 ± 0.47in SL group and -0.55 ± 0.30 in L group. Mean GGT improvement was 22.8 ± 25.1 U/L in SL group and 2.9 ± 22.3U/L in L group. GGT improvement was statistically significant in SL group (Table-2).

Comparison between histological responders and non-responders group of patients

Total 15 patients were responders and 15 patients were non-responders. Among responders 13 (86.7%) patients were in SL group and 2 (13%) patients in L group. Among non-responders 7 (46.7%) patients were in SL group and 8 (53%) patients in L group. The difference of response between SL group and L group was statistically significant (P=0.02) (Table-3). Mean NAS score improvement in responders was 2.6 ± 0.73 and 0.06 ± 0.70 in non-responders. Mean Fibrosis score improvement was 0.33 ± 1.29 in responders and 0.06 ± 1.16 in non-responders (Table-4).

Mean AST improvement was 20.3 ± 26.3 U/L in responders and 4.3 ± 10.7 U/L in non-responders. AST improvement was statistically significant in responders (P=0.037). Mean ALT improvement was 43.7 ± 48.9 U/L in responders and 19.5 ± 23.6 U/L in non-responders. There was no statistically significant difference of ALT improvement in between responders and non-responders (P=0.095). Mean AST/ALT ratio improvement was – 0.51 ± 0.52 in responders and -0.53 ± 0.28 in non-responders. Mean GGT improvement was 29.8 ± 30.9 U/L in responders and 2.2 ± 19.2 U/L in non-responders. There was statistically significant difference of GGT improvement in responders than non-responders (P = 0.006) (Table-4).

Table 1. Baseline characteristics of patients (n=30)

Variables	SL group(n=20)	L group(n=10)	*P* Value
Age (Years)	41.5±9.2	38.7±6.8	0.402^{ns}
Sex (Male/Female)	4 /16 (20%/80%)	1/9 (10%/90%)	0.448^{ns}
*Obese (yes/no)	14/6 (70.0%/30.0%)	4/6 (40.0%/60.0%)	0.025^{s}
*WC increased	15/5 (75.0%/25.0%)	3/7 (30.0%/70.0%)	0.024^{s}
*Diabetes (yes/no)	11/9 (55.0%/45.0%)	4/6 (40.0%/60.0%)	0.438^{ns}
*Hypertension	8/12 (40.0%/60.0%)	4/6 (40.0%/60.0%)	0.655^{ns}
BMI (kg/m2)	27.1±4.7	27.4±4.8	0.397^{ns}
WC (cm)	96.0±8.7	95.9±11.2	0.978^{ns}
FBS (mmol/L)	7.2±3.9	5.6±1.3	0.220^{ns}
2HABF (mmol/L)	10.3±4.7	8.5±2.5	0.269^{ns}
HbA1c%	7.6±1.5	6.7±1.2	0.302 ^{ns}
Cholesterol (mg/dl)	222.8±53.7	205.8±64.9	0.415^{ns}
LDL (mg/dl)	139.8±44.0	144.4±73.3	0.831^{ns}
HDL (mg/dl)	38.6±10.0	33.9±7.0	0.195^{ns}
TG (mg/dl)	207.0±103.9	230.0±135.2	0.609^{ns}
AST (U/L)	49.2±25.2	32.2±13.4	0.056^{ns}
ALT (U/L)	70.7±41.7	50.6±21.8	0.166^{ns}
HOMA-IR	2.5±1.8	2.8±1.6	0.659^{ns}
GGT (U/L)	64.5±38.5	32.8±9.3	0.016^{s}
NAS score	5.7±0.81	5.4±0.69	0.325^{ns}
Fibrosis score	1.8±0.69	1.9±0.87	0.734^{ns}

Table 2. Characteristics of patients after completion of treatment (n=30)

Improvement	SL group(n=20)	L group (n=10)	*P* Value
BMI (kg/m2)	0.37±1.1	0.35±0.68	0.958^{ns}
WC (cm)	1.55±5.6	0.38±1.65	0.526^{ns}
Weight reduction e" 7%	4/16 (20.0%/80.0%)	3/7(30.0%/70.0%)	0.428^{ns}
FBS (mmol/L)	1.8±3.4	0.4±1.7	0.232^{ns}
2HABF (mmol/L)	3.5±4.3	2.4±3.5	0.490^{ns}
HbA1c%	1.0±0.9	0.5±0.2	0.938 ^{ns}
Cholesterol (mg/dl)	56.5±61.0	31.4±60.4	0.295^{ns}
LDL (mg/dl)	37.7±51.6	68.1±86.3	0.236^{ns}
HDL (mg/dl)	-4.5±16.6	-2.3±5.0	0.687^{ns}
TG (mg/dl)	51.5±80.9	-47.4±28.4	0.001^{s}
AST (U/L)	16.1±23.9	1.4±10.8	0.076^{ns}
ALT (U/L)	38.0±44.9	19.7±24.9	0.242^{ns}
AST/ALT ratio	-0.44±0.47	-0.55±0.30	0.646^{ns}
HOMA-IR	0.93±1.2	1.0±2.1	0.907^{ns}
GGT (U/L)	22.8±25.1	2.9±22.3	0.023^{s}
NAS	1.8±1.4	0.22±0.97	0.003^{s}
Fibrosis score	0.15±1.22	0.11±1.16	0.932^{ns}

Table 3. Comparison of baseline factors between responders and non-responders

Baseline factors	Responders (n=15)	Non-responders (n=15)	*P* Value
SL group / L group	13/2 (86.7%/13.3%)	7/8 (46.7%/53.3%)	0.020^{s}
Age (in years)	41.3±10.2	39.8±6.6	0.636^{ns}
Sex (Male/female)	4/11(26.7%/73.3%)	3/12(20.0%/80.0%)	0.500^{ns}
*Obesity	7/8 (46.7%/53.3%)	3/12(20.0%/80.0%)	0.121^{ns}
*WC increased	4/11(26.7%/73.3%)	4/11(26.7%/73.3%)	0.659^{ns}
*Diabetes mellitus	7/8 (46.7%/53.3%)	4/11 (26.7%/73.3%)	0.255^{ns}
*Hypertension	7/8 (40.0%/60.0%)	5/10 (33.3%/66.7%)	0.456^{ns}
BMI (kg/m2)	26.1±4.5	28.4±4.6	0.177^{ns}
WC (cm)	95.1±8.7	96.8±10.3	0.629^{ns}
FBS (mmol/L)	7.2±4.5	6.1±1.3	0.370^{ns}
2HABF (mmol/L)	10.5±5.4	9.0±2.5	0.337^{ns}
AST (U/L)	50.9±28.2	36.2±14.7	0.084^{ns}
ALT (U/L)	76.1±44.7	51.8±23.2	0.072^{ns}
GGT (U/L)	64.1±38.0	43.7±29.6	0.112^{ns}
NAS score	5.8±0.8	5.3±0.7	0.079^{ns}
Fibrosis score	1.9±0.7	1.8±0.8	0.718^{ns}

Table 4: Comparison of dynamic factors between responders and non-responders

Dynamic factors	Responders (n=15)	Non-responders (n=15)	*P* Value
*Weight reduction ≥7 (kg)	5/10 (33.3%/66.7%)	2/13 (13.3%/86.7%)	0.194^{ns}
Waist circumference (cm)	2.5±6.1	0.23±2.17	0.185^{ns}
FBS (mmol/L)	-15.1±4.7	-15.9±11.7	0.001^{s}
2HABF (mmol/L)	4.4±4.3	1.4±3.1	0.036^{s}
AST (U/L)	20.3±26.3	4.3±10.7	0.037^{s}
ALT (U/L)	43.7±48.9	19.5±23.6	0.095^{ns}
AST/ALT ratio	-0.51±0.52	-0.53±0.28	0.896^{ns}
HOMA-IR	0.99±1.30	0.95±1.77	0.944^{ns}
GGT (U/L)	29.8±30.9	2.2±19.2	0.006^{s}
NAS score	2.6±0.73	0.06±0.70	0.001^{s}
Fibrosis score	0.33±1.29	0.06±1.16	0.551^{ns}

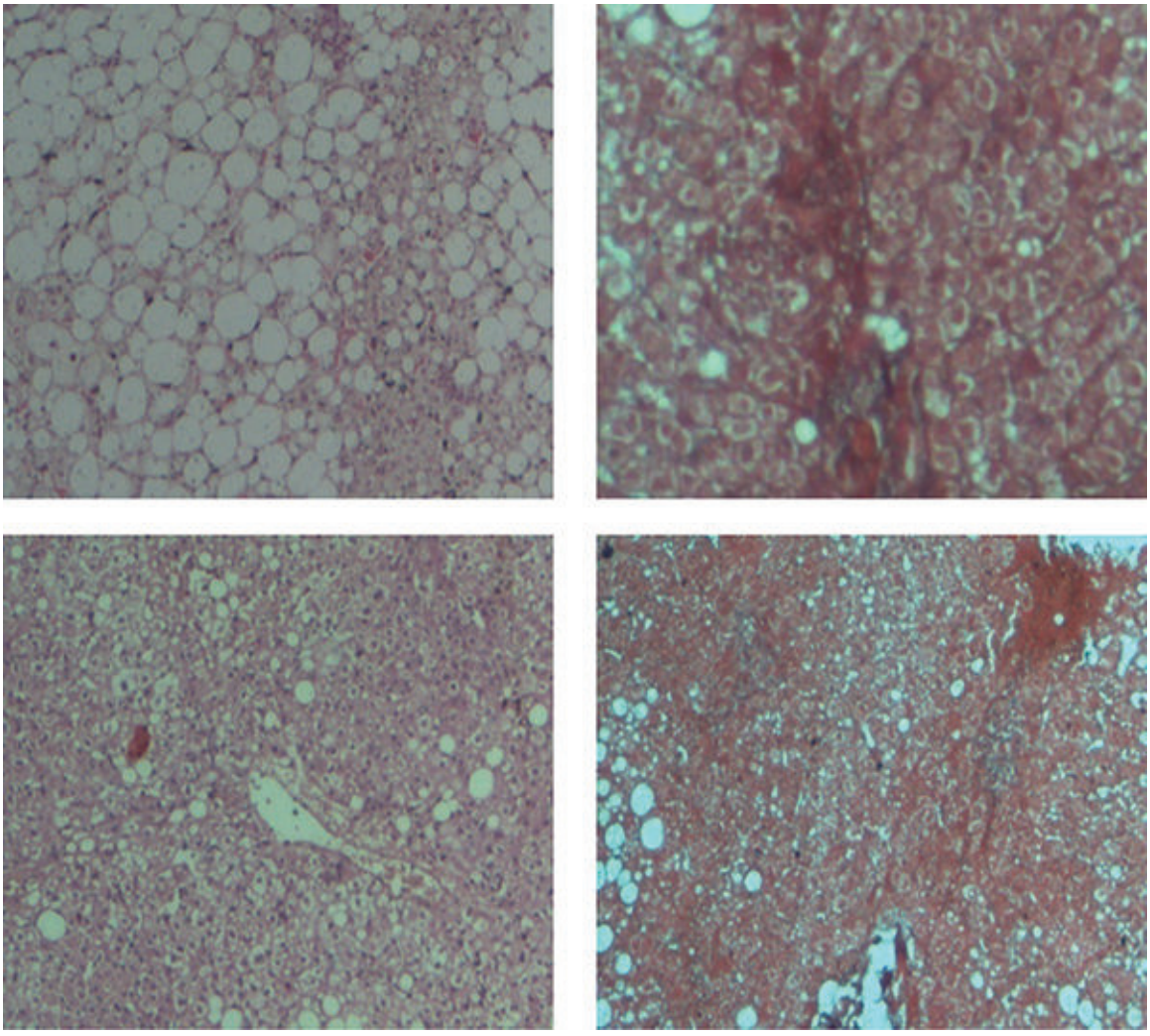

Fig. 1: *Histological improvement between index and end study liver biopsy. Upper panel showed 1st biopsy and lower panel showed 2nd biopsy of same patient. NAS score improvement from 6 to 4 and fibrosis score improvement from 2 to 1.*

Discussion:

NAFLD has considered the hepatic manifestation of a metabolic syndrome[10]. The burden of NAFLD is increasing day by day in the world. Currently NAFLD treatment is directed at the components of metabolic syndrome and also aims to reverse liver injury. To date, the principal treatment for NASH is life style modification by diet and exercise[17]. This study included life style modification in both groups because it is the standard approach of patient management. New therapies with strong experimental evidence are currently being trialed in human NASH, and may provide hope of a targeted pharmacotherapy. Sitagliptin is one of the dipeptidyl peptidase-4 inhibitors that has been recently studied for a role in the treatment of NAFLD. To date, there is one pilot study conducted in human examining the effect of sitagliptin on biopsy- proven diabetic NASH patients[18]. ALT, AST and GGT elevated in NASH due to hepatocellular injury but these enzymes may remain within normal limit despite of liver injury[9].

This study evaluated the correlation of transaminase and gamma glutamyl transferase with hepatic histological activity score improvement. The most significant changes in hepatic histology induced by sitagliptin and lifestyle modification in this study were reflected by the decrease of NAS score. In this study NAS ≥2 improvements occurred in 65% patients in SL group and 20% Patients in L group. Total 15 patients were histological responders among two groups. The difference of NAS improvement between the two groups was statistically significant (P=0.003). In SL group, fibrosis score ≥1 improvement occurred in 25% patients, whereas, in L group, it occurred in 20% patients. The difference between the two groups did not reach statistically significant level (P=0.932). Yilmaz et al[18]. in a pilot study showed that after one year treatment of 15 diabetic patients with NASH, Sitagliptin caused significant reduction in ballooning (P=0.014) and NAS (P=0.04), while the reduction in steatosis score was borderline statistically significant (P= 0.054) but lobular inflammation and fibrosis score improvement was not significant [17]. Total 15 patients were diabetic among 30 patients in present study. There was no significant difference in histological response between diabetic and nondiabetic patients (P=0.255). In this current study, improvement of AST and GGT was observed in histological responders but ALT did not improve in responders. These findings were not consistent with the findings of Zein et al. and Sanyal et al. In these two RCT, histological improvements were consistent with serum ALT improvement [19, 20]. This present study showed that improvement of AST and GGT correlates with hepatic histological activity score improvement.

Limitations of the study: Sample of this study was small and included patients were only Bangladeshi nationality. For this reason, that result might not be applicable to populations with different ethnic background.

Conclusion:

AST and GGT correlates with hepatic histological activity score improvement rather than ALT. Further study in large sample and different ethnicity is recommended to confirm these findings.

Abbreviations:

*Y/N: Yes/ no, ns: not significant, s: significant, WC: Waist circumference, BMI: Body mass index, ALT: Alanine transaminases, AST: Aspartate transaminases, GGT: Gamma glutamyl transferase, FBS: Fasting blood sugar, 2HABF: 2 hours after breakfast, HOMA IR: Homeostatic model assessment of insulin resistance, LDL: Low density lipoprotein, HDL: High density lipoprotein, TG: Triglyceride.

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Sex Estimation Using a Discriminant Functional Analysis from Maximum Length of Fully Ossified Dry Human Left Calcaneus

Zaman F[1], Ara JG[2], Akter M[3], Jahan I [4], Badhon NM[5], Nahar Y[6], Rahman MM[7]

Abstract:

Introduction: *For the forensic anthropologist sex determination is one of the major challenges within a medico-legal context; it is considered an early step in personal identification from skeletal remains and it is indispensible for applying procedures to define race and age at the time of death.*

Objectives:*The aim of this study was to collect data regarding maximum length of fully ossified dry human calcaneus and to find out possible variations in male and female.*

Materials and methods:*An analytical study was done on one hundred and fifty five (155) fully ossified dry human left calcaneus of unknown sex in Bangladesh at Department of Anatomy, Sir Salimullah Medical College, Dhaka, Bangladesh from January 2014 to June 2015. The study sample were distributed in male and female sex group by discriminant function analysis technique.*

Results: *Among 155 calcaneus 51.61% were male and 48.38% were female. The mean (±SD) value of maximum length of calcaneus were greater in male than female which was statistically significant ($p<0.01$).*

Conclusion: *Maximum length of calcaneus were greater in male than female. The difference in maximum length can be useful in sex differentiation.*

Key words: *Maximum length; calcaneus; sex; discriminant function analysis technique.*

(MH Samorita Med Coll J 2020; 3(2): 52-55)

Introduction:

The calcaneus is a weight bearing tarsal bone. It belongs to proximal row and forms the posterior pillar of two longitudinal arches of foot. It articulates with the talus above and cuboid in front[1]. It is a rectangular block of bone characterized by sustenticulum tali, a shelf that projects from the upper border of its medial surface[2].

Since calcaneus bone is located at the rear portion of foot, it is most vital in bearing weight of body. Approximately 50% of body weight is distributed through subtalar joint to calcaneus, with remaining 50% transmitted across metatarsal heads. Calcaneus supports leg and helps in easy walking and standing. Functions like rotating and bending foot are possible on calcaneus[3].

In the upper surface calcaneus forms talocalcaneal joint with talus. There are three facets over the upper side of talocalcaneal joint: anterior talar facet, middle and posterior. These facets articulate with the head of the talus and the incidence of which varies with race and sex[4].

It is widely been recognized that skeletal characteristic vary among populations. So each

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population should have specific standards to optimize the accuracy of identification. Preservation of bones is a very important factor for anthropological and forensic investigation. Calcaneus bones are relatively more durable than other bones and such estimates are very useful in cases of poor preservation.[5]

Materials and methods:

Sex estimation from calcaneus has potentially significant importance for forensic community. Specifically measurements of calcaneus provides an additional reliable method for sex estimation via discriminant function analysis.[6]

One hundred and fifty five (155) dry left sided adult human calcaneus were collected from medical students of Sir Salimullah Medical College (SSMC), Dhaka and Dhaka National Medical College. Then the sexes of collected calcaneus were determined by discriminant function analysis. This linear discriminant function analysis technique was applied to the collected data as follows-

As discriminant function $Z = b_1 \times MAXL + b_2 \times MAXB + c$

Here, Z = Discriminant function
c = Constant,
b_1 and b_2= Discriminant co-efficient,
MAXL= Maximum length
MAXB= Maximum breadth

In this study the value of Z for each specimen was calculated by substituting the values of variables in linear function. A sectioning point was created by using mean discriminant scores which were also known as group centrioid. To assign the case to either male or female sex the product Z was compared to the sectioning point derived by discriminant function analysis. A value higher than sectioning point was considered to be male and a value below it was considered to be female. The values of co-efficient (b_1 and $b_{2)}$ were obtained by using standard computer program.

Afterwards though calcaneus is an irregular bone, maximum length of this bone was measured with the help of digital slide caliper and then the straight measurements at values were considered. For the measurement of maximum length of calcaneus a coloured marker was used with red and blue. A red dot was given on anterior most point of calcaneus and blue dot was given on posterior most point of calcaneal tuberosity. The fixed jaw of digital slide caliper was placed on anterior most point of calcaneus and sliding jaw was fixed on posterior most point of calcaneal tuberosity. The distance between two dots which is represented by MAXL was measured by digital slide caliper and recorded.[7] (Fig-1)

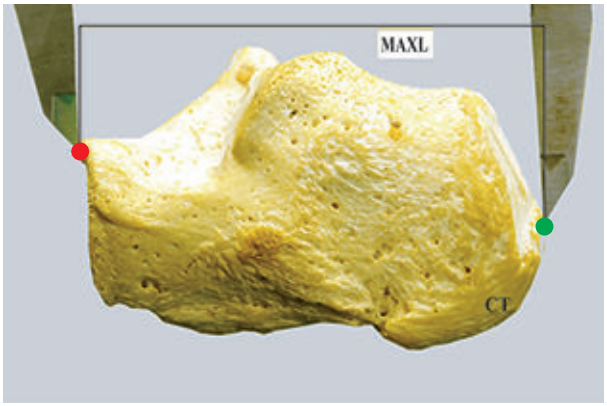

Fig. 1: *Photograph showing maximum length measured by digital slide caliper. red dot- anterior most point of calcaneus and blue dot-posterior most point of calcaneal tuberosity [CT=Calcaneal tuberosity].*

After collection of data the statistical analysis were done by unpaired Student's 't' test. The comparison between male and female was done by unpaired Student's 't' test. All the statistical analyses were done by using Computer based Software, Statistical Package for Social Science (SPSS) Version 20.0.

Ethical clearance:

This thesis work was carried out after approval of research protocol by Institutional Ethics Committee (IEC) of Sir Salimullah Medical College, Dhaka.

Results:

The fully ossified dry human left calcaneus were grouped into male and female by discriminant function analysis. (Table -1)

Table 1: Maximum length of calcaneus in male and female

Sex	Number of study samples after discriminant function analysis (n)	(%)
Male	80	51.61%
Female	75	48.38%
Total	155	100%

The range of maximum length of calcaneus was 71.00-86.00mm in male and 66.40-75.40mm in female. The mean (±SD) maximum length of left calcaneus was 78.57 (± 3.96) mm and 69.78 (± 2.80) mm in male and female. The mean (±SD) maximum length was greater in male than in female. There was significant difference between maximum length (p=0.000)

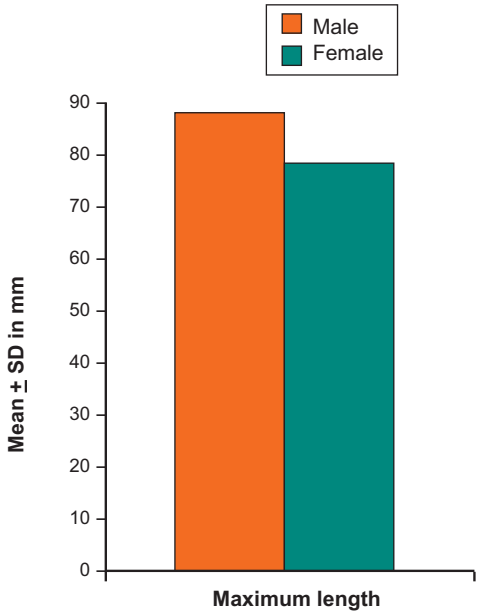

Fig 2: *Mean Maximum length of Lt Calcaneus*

Discussion:

In the present study mean (±SD) maximum length was found greater in male than that of female which was statistically significant (p<0.01). The values of present study coincide with a study conducted by Kumar A et al. (2004) on calcaneus for sex determination using maximum length[8]. In that study 50 were male and 50 were female. The mean (±SD) maximum length was 79.21±3.89 mm and 71.21±2.34 mm in male and female respectively.

In 2011, Sakaue K. worked on 143 calcaneus of both sides. Among them 72 were male and 71 were female and age ranged between 14 to 78 years. Average age was 38.7 years. The mean (±SD) maximum length was 73.8±3.7 mm in male and 67.8±3.0mm in female. There was statistically significant difference (p=0.001) between male and female[9].

A study was carried out by Introna, F. et al in 1997. Total 80 dried human calcaneus were examined in which 40 were male and 40 were female. They reported that maximum length was 79.1±3.7 mm in male and 72.5±5.3 mm in female[5].

The present study was carried out in calcaneus collected from Bangladesh. Skeletons that are available in Bangladesh also come from neighboring countries. Bangladeshis are mixed race of Caucasoid, Negroid, Mongoloid and Australoid group. However the maximum length in present study was nearly similar to the mean values of other researchers.

Conclusion:

The maximum length of calcaneus is by far the best single variable for estimation of sex. No citable published research works on calcaneus in Bangladesh has been found. This study was undertaken to measure the maximum length of calcaneus and to evaluate the difference in length of same between male and female. Osteometric measurements of calcaneus improves the knowledge of anatomy, treatment and diagnostic procedures of orthopaedic surgery, kinesiology, physical treatment and rehabilitation sections.[4].

The present study was an attempt to construct data on maximum length of left sided human calcaneus which will serve as a reference value in the field of Anatomy. Maximum length of left human calcaneus were higher in male than that of female. Further radiographic study of living calcaneus and comparison of the radiographic findings of fully ossified dry human left calcaneus might be beneficial in this study.

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Seroprevalence of Dengue Infection in MH Samorita Hospital and Medical College during 2019 Outbreak in Dhaka, Bangladesh

Akhter R[1], Zahan NA[2,] Khanam S[3]

Abstract:

Intoduction: *Dengue fever is a seasonal, re-emerging acute mosquito borne arbo-viral illness. As worldwide epidemic, this Aedes mosquito-transmitted pathogen is considered one of the most important arboviral infection and growing public health problem affecting tropical and sub-tropical countries including Bangladesh.*

Objective: *The present study was undertaken to detect dengue virus infection among the clinically suspected patients attended at MH Samorita Hospital and Medical College.*

Materials and Methods: *This cross sectional study was conducted to determine the sero- prevalence and clinical feature of dengue virus infection among the clinically suspected patients attended at MH Samorita Hospital and Medical College during July to September 2019. The study was carried out on 955 clinically suspected Dengue patients attended in MH Samorita Hospital and Medical College during July to September 2019 having fever with temperature >39°C. Blood sample was collected during acute febrile phase of patients and separated sera were tested for NS1 dengue antigen and IgM and IgG antibodies using commercial test kits (NS1 by OMC Healthcare (Pvt.) Ltd & IgM antibody by Omega Diagnostics Ltd.)*

Results: *Of the total 955 patients number of positive case were 230(24.08%). Among them 196(85.22%) were NS1Ag positive, 13(5.68%) were IgM positive, 08(3.47%) were IgG positive, both IgM & IgG positive 09 (3.91%) and 04 (1.72%) were both NS1Ag and IgM positive.*

Conclusion: *Outbreak of dengue fever is continuing every year and now a days patients present dengue fever with atypical presentation. Fever with arthralgia and retro-orbital pain were major clinical manifestations in the present dengue outbreak instead of headache and rash with fever. A large number of suspected dengue cases were negative by dengue tests for antigen NS1 and IgM,IgG antibodies concludes that other infections of similar clinical presentations are becoming prevalent in Bangladesh. The dengue situation in Bangladesh was getting worse in the year of 2019 as the number of affected people were more than doubled since July to September, compared with the same period last year.*

Key Words: *Dengue Fever; Dengue NS1 antigen, IgM antibody, IgG antibody, Clinical feature of Dengue.*

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Introduction:

Dengue fever (DF) is the most rapidly spreading mosquito-borne arboviral disease and the major public health challenge worldwide.[1] Almost 2.5 billion people are at risk of infection in the tropical and subtropical regions.[1]More than 50 million infections occur globally and 25000 deaths being reported annually.[2.]

Global prevalence of dengue has grown dramatically and get worse in recent years as the disease is

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spreading to new areas and its epidemiological pattern and clinical manifestations are gradually changing.[3,4,5]However, dramatic changes in this pattern have occurred and currently dengue ranks as the most important mosquito-borne viral disease in the world.[6] It may give rise to an undifferentiated fever, classical dengue fever, dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).[7]

In Bangladesh Dengue cases were first detected in 1964 and the outbreak was known as 'Dacca Fever.[7] A long period after that, dengue cases were undetected due to lack of investigation opportunity. A few cases were reported in the year of 1999. In 2000, 5,551 cases and 93 dengue-related deaths were reported in different hospitals of Bangladesh. Since then, Bangladesh has experienced small or large scales dengue fever every year.[6,8, 9,10]

Dhaka is the worst-hit city in the country and the districts in Dhaka Division are among the most affected regions. Dengue virus is a member of the family Flaviviridae and genus Flavivirus. It contains an enveloped particle containing a 10.7 kb single-stranded RNA genome of positive polarity,[11]transmitted primarily by the bite of *Aedes aegypti* and *Aedes albopictus*.[10,12] Infections can also be transmitted through blood transfusion, organ transplantation and possibly vertically from mother to child.[13,14] Dengue syndrome composed of four clinical stages including undifferentiated fever (UF), dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[15] Dengue shock syndrome (DSS) is a severe complication form of dengue which is often caused by a secondary infection with a different virus serotypes.[15]

There are four serotypes of dengue viruses (DENV1, DENV2, DENV3, DENV4) of the genus flavivirus and different serotypes have capability to produce severity of different intensities.[16] These four serotypes are genetically similar and share approximately 65.0% of their genomes. A fifth variant DENV-5 has been isolated in October 2013.[17] Infection in human by one serotype produces life-long immunity against re-infection by the same serotype.[2,18] Primary infection with any of the serotypes is typically mild and self-limiting called Classical Dengue Fever.[3,18] Classical Dengue fever presents as a fever of 5-7 days with headache, retro-orbital pain, backache, skin rashes, arthralgia and myalgia.[19,20] Recovery from infection one of four serotype is generally complete, each generating a unique host immune response and confers serotype specific lifelong immunity. However, secondary infection with a heterogeneous serotype often creates devastating outcomes, which may be due to antibody-dependent enhancement resulting production cross reacting antibody against previous different serotype named 'Orginal Antigenic Sin'.[3,20] Secondary infection with other dengue serotypes may produce severe form of life threatening disease; Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS).[3] Primary infection may rarely produce DHF and DSS.[21]

World Health Organization guideline for dengue suggested for establishment of a surveillance system for detection of dengue and DHF/DSS to prevent and control the progression of this disease which relies on the precise and early diagnosis of dengue infection. Thus, a rapid and accurate dengue diagnosis is very important for effective control of dengue outbreaks. [10,11]

In both primary and secondary dengue infected cases detection of anti-dengue IgM indicates recent infection which typically appear approximately 5-6 days after onset of fever. Anti-dengue IgM develops earlier than IgG in primary infection and is usually detectable by day 5 of illness and wanes after 1-2 months.[20,22] In 93-99% of cases IgM antibody become detecctable by day 6 to 10 which delay in early diagnosis of dengue infection.[23] Dengue virus NS1 antigen is detectable in blood from first day after onset of fever up to day 7.[24] So detection of dengue NS1 antigen represents an important approach to the diagnosis of acute dengue virus infection at earlier stage. As a result, this test serves as an aid in the clinical laboratory diagnosis of early dengue infections prior to the presence of IgM or IgG antibodies in patients with clinical symptoms consistent with dengue infection. In a dengue patient, detection of only dengue specific IgM antibodies provides only partial information, denoting that the patient is suffering from acute dengue at least 5 days after the onset of fever. So the patient cannot be diagnosed at an early stage of the disease before that and also it cannot be classified whether he is suffering from primary or secondary dengue infection.

Therefore, in the present study both methods were used to diagnose acute dengue infection.

The objective of the present study was to explore positive patients of acute dengue infection among the suspected febrile patients presenting at MH Samorita

Hospital and Medical College Hospital, Bangladesh to determine the prevalence of DF patients and to inform the present clinical symptoms of dengue infection among clinically suspected patients.

Materials and Methods:

A total of 955 clinically suspected cases of dengue were selected who were sent by the physician during rainy season (July - September). After taking all strict aseptic precaution 5 ml of venous blood sample was collected from each patient in MH Samorita Hospital and Medical College laboratory and transferred to a properly labeled sterile clot activated tube. Serum sample was collected in labeled eppendorf tubes within 2-3 hours of blood collection by centrifugation of the blood sample and after proper inspection of sample that there was no haemolysis. The serum samples were preserved in a -20°C fridge until the testing for NS1 antigen, IgM, IgG by Immuno chromatographic test (ICT) method according to the instruction of the manufacturer. Dengue NS1 Ag kit (OMC Healthcare (Pvt.) Ltd, Canada) was used for NS1 and anti-dengue IgM (Omega Diagnostics Ltd, UK) kit was used to perform tests in patient's samples. According to our case definition, dengue positive cases diagnosed by NS1antigen and or anti-dengue IgM, IgG Immuno chromatographic test (ICT) positive tests. Cases with both NS1 and anti-dengue IgM Immuno chromatographic test (ICT) negative tests were considered to have other febrile illness. The details of NS1, IgM,IgG dengue antibody test results including the day of performing the tests were documented for analysis of result

Results:

Out of 955 clinically suspected dengue patient number of positive cases were 230(24.08%) and negative cases 725(75.91) (Table 1). Among them,196 (85.22%) were NS1Ag positive, 13(5.68%) were positive for IgM, 08(3.47%) were IgG positive, both IgM & IgG positive 09 (3.91) and 04 (1.72%) were both NS1Ag and IgM positive shown in Table 2.

Table-1: Distribution of clinically suspected dengue patients with number of positive and negative cases-

Total number of patients	Positive cases		Negetive cases	
955	No	%	No	%
	230	(24.08)	725	(75.91)

Out of the 230 dengue positive patients 171(74.33%) were male and 59 (25.62%) were female (Figure1). The present study demonstrated that males were predominantly affected by dengue fever than females(171 male vs 59 female). Among males maximum 157(68.26%) cases occurred in the age group of 11-40 years.(Table-3)

Table-2: Distribution of serologically positive dengue cases (n=230)

Test method	Number of positive cases	Percentage%
NS1 antigen Positive	196	(85.22.%)
Anti dengue IgM positive	13	(5.68%)
Anti dengue IgG positive	08	(3.47%)
Both IgM& IgG positive	09	(3.91%)
Both NS1 antigen and Anti dengue IgM positive	04	(1.72%)
Total	230	100%

Table-3: Age and Sex distribution among acute dengue positive patients.

Age	Male	Female	Total
0-10 years	05(2.17%)	02(0.86%)	07(3.03%)
11-20 years	43(18.69%)	14(6.08%)	57(24.77%)
21-30 years	87(37.83%)	22(9.56%)	109(47.39%)
31-40 year	27(11.74%)	13(5.65%)	40(17.39%)
41-50 years	05(2.17%)	07(3.04%)	12(5.21%)
51-60 years	03(1.30%)	01(0.43%)	04(1.73%)
>60 years	01(0.43%)	0(00%)	01(0.43%)
Total	171(74.33%)	59(25.62%)	230(99.95%)

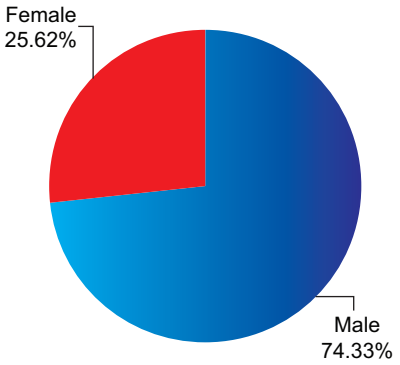

Fig. 1: *Sex distribution of Dengue seropositive cases*

Discussion:

The incidence of dengue has increased dramatically around the world in last few decades. The actual number of dengue cases are under recorded and many cases are not classified consequently. Uncontrolled population growth, unplanned and uncontrolled urbanization are the major factors identified, especially in tropical developing countries.[25,26] Dengue infection is also associated with climate variation. Increased rainfall favors vector's growth,and high temperatures promote mosquito development.[27] Dengue cases are found more during wetter and warmer months indicating seasonal potentiality. However, the incidence of dengue infection depends not only on climate heterogeneity but on, circulating Dengue virus serotypes, and virus–host interactions.[28]With the widen incidence of dengue and the absence of vaccine for prevention of the disease, it is important to detect early dengue virus infection for management of patients as well as for effective public health control of dengue outbreaks. Various studies have confirmed the detection of dengue, among them NS1 antigen is useful for early diagnosis of dengue infections.[29,30] Dengue NS1 antigens has allowed for early detection of dengue fever. Usually detectable dengue antigen remain in the blood for 5 days after onset of fever and rapidly disappear after formation of specific antibodies.[31] IgM antibodies start to appear in blood approximately 5-6 days after onset of fever. In 93-99% cases IgM antibody become detectable by day 6 to 10 which delay in early diagnosis of dengue infection.In the present study, out of 955 clinically suspected patients only 230 (24.08%) patient's sera were positive for NS1 antigen or IgM,or IgG antibody. This low percentage of positive result may indicate other viral infections like Chikungunyia having similar clinical presentation were prevailing at that time. Outbreak of Chikungunya in 2019 is supporting the assumption of fever having similar clinical manifestations was present at the similar season and was spreading by a common mosquito vector Aedes-aegeypti.[32]

The dengue seroprevalence rate in this study was 24.08%, whereas in Delhi, India it was found 44.56% serological confirmed cases in 2006 which is relatively higher than present study.[33] It was found in another Indian study that 31.3% patients were serologically positive for dengue infection which is also comparatively higher than present study.[34] Similar study in Chittagong found 34.3% seropositive dengue patients in 2000.[35]During the year 2015-2016, a study carried out in one of the private Medical College in Dhaka, it was observed that 52.05% NS1 antigen positivity among the clinically suspected Dengue patients whrereas NS1antigen positive was 85.22% in our study, the rate of NS1antigen positive test for dengue was higher in present study and also predicted that NS1 antigen plays an important role in diagnosis of acute dengue infection.[25] In Medical College Hospital in Chittagong, Bangladesh in 2009-2010 showed that 42.59%, 39.96%, 17.45% positivity of Dengue IgM, IgG antibodies & both IgM, IgG among clinically suspected cases where the rate of positive test for Dengue IgM, IgG antibodies & both IgM, IgG positive were significantly higher than the present study. Another study from Chittagong found that 63% anti-dengue IgM positive and 68% anti-dengue IgG positive cases in 2001 which is different from our studies.[32] In another study in Pakistan showed 73% anti-dengue IgM positive patients in 2011 which had no similarity with our study.[36]In Delhi found 25.05% anti dengue IgM positive cases in the year of 2003.[34] This dissimilarity of findings may be due to the rapid unplanned urbanization with unchecked construction activities and poor sanitation facilities contributing to a fertile breeding ground for mosquitoes. It is also true that an increase in the alertness among medical professionals following the initial epidemic and the availability of diagnostic tools have contributed to the increased detection of cases.[36]The present study showed infection occurred predominantly in young adult age group (20-40)149 (65.78%) positive cases. Another Bangladesh's study showed the predominance in the adult with the mean age about 29.2±12.9 years and age range was

20-29 years of age.[8] Similar findings were observed in many other studies in Bangladesh and neighbouring countries.[5,37]

In the present study, 74.33% were male and 25.62% were female where showing male predominance . Most of them 65.78% were in the age group of 20 to 40 years. Studies in Singapore, India and Bangladesh showed similar male predominance in occurrence of infection which is also compatible with the present study.[37,38,5] However, this gender difference may not indicate more susceptibility of male to dengue infection, because females in these areas get less priority and may not obtain equal chance to have proper treatment for fever. There was no significant difference in sex among dengue cases in 2000 outbreak in Dhaka Bangladesh.[8] Moreover, reports from South America showed either equal proportions of male and female dengue cases or a greater proportion of female cases.[39,40]

Conclusion:

Dengue NS1 antigen detection assay is very useful, and sensitive for early diagnosis of dengue virus infection associated with anti-dengue IgM, IgG test in the laboratories. In our country there is limitation of resources, personnel, lack of viral culture or RT-PCR facilities in most of the laboratories. Monitoring of current serotype circulating should be done to get early warning for new dengue viral outbreak in the country. The transmission of dengue occurs year-round, even during cooler, drier months. Public health preparedness should nevertheless be focused during peak months to help cope with potentially large influxes of patients.

Limitation

There were some limitations in the present study that we could not exclude Chikungunya, other mosquito borne Flavivirus infections and we could not also able to observe IgG antibody rising titre between acute and convalescent sera to differentiate primary from secondary dengue infection due to lack of patients compliance. A large scale study will have to be conducted in the future to describe the risk factors for the acquisition of dengue infection such as specific environmental, virological and human behavioral practice which could contribute in the changing epidemiology of dengue in Bangladesh.

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MH Samorita Hospital Medical College Laboratory.

Conflict of Interest: None

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A Study of Death Caused by Stab Wound with Its Nature & Severity

Biswas M[1], Khan RH[2], Jahan KD[3], Naiem J[4], Akter N[5]

Abstract:

Introduction*: Criminal attack involving stab injuries are common as homicidal method all over the world. Stab wounds are of major importance in Forensic Medicine as these are extremely common. Stab can note purposeful action by an assassin or murderer, but sometimes, one can accidentally stab himself by the motion of the object used in a stabbing generally moves perpendicular directly into the victim's body, rather than being drawn across it.*

Objectives*: The main objective of this study was to evaluate pattern of stab injury which are fatal & causes death by its nature & severity.*

Materials & Methods*: This was a descriptive type of cross-sectional study which included 57 number of deceased. The studied data were collected from Rangpur Medical College at Forensic Medicine Department from July 2017 to June 2018. During that period 57 autopsies were assayed to evaluate the pattern of stab injuries which caused death.*

Results*: Among the 57 deceased, majority of the cases were constituted by male gender 53 (93%) & females were 4 (7%). In most of the cases the motive was assault in which robbery- 19 (33.3%), property dispute- 15 (26%), familial problem- 8 (14%), business rivalry- 13 (23%), & others- 2 (4%) occurring at home or in public street which involved chest, abdomen, upper limb, head, neck, face, lower limb.*

Conclusion: *Increasing security measures may help to reduce stab wound injury events in urban places where criminal attacks are seen more frequently. Here is a discussion where 57 victims were murdered by inflicting one or multiple stab wound over different parts of the body & all the injuries collectively contributed to cause death. The nature & severity of the wound was also evaluated.*

Key words*: Stab injury, death, injury site, nature & severity of assault.*

(MH Samorita Med Coll J 2020; 3(2): 62-66)

Introduction:

Trauma is one of the leading causes of death in all age groups in most developed countries[1, 2] & globally an estimated five million people die every year from trauma injuries that are in most cases preventable & thus it has become a public health problem. Among all kinds of trauma, stab injuries are seen as life threatening events worldwide indicating urgent intervention.

Stab wound (Punctured wound) is an injury caused by a pointed weapon when it is driven in through the skin & its depth is the greatest dimension. Such weapon includes a knife, dagger, needle, spear, arrow, scissor, ice pick etc[3]. As stab wound caused by a sharp pointed & cutting instruments has clean cut edge, which are almost parallel but slightly curved to each other like an ellipse & have sharp angles at the two extremities. So, by definition, stab

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wound is deeper than its length & due to the depth of the injury these are often fatal.

Most often stab wounds occur because of domestic disputes or street violence. In fact, millions of violent acts occur around the globe but a limited number of such accidents are reported to the health care facilities or law enforcement[4].

Like all other parts of the world, criminal attacks by stab wound is the most common method of homicide in Bangladesh. The motives are usually due to robbery, property dispute, familial problem, business rivalry & others. All these motives along with their circumstantial evidence plays a major role in drawing conclusion about fatal outcome[5]. That is the reason for stab wound is of major importance in Forensic Medicine. Most deaths from stab wounds are homicidal. Stab wound which have fatal outcome not necessary to be multiple. Single stab wound in a vital point is enough to bring death.

These types of injuries are referring sharp force injury as caused by the thrust of a sharp & pointed weapon[6]. Stab wounds may result in penetrating & perforating injuries[7]. A penetrating injury refers to a puncture wound when the weapon pierces the body cavity, while a perforating wound occurs when the weapon enters from one side of the body surface & exit from the other side.

Penetrating stab injuries especially deep injuries involving internal organs & large vessels in the chest or abdomen can lead to infection, shock, exsanguination & death[8]. During stabbing, there is often considerable relative movement between the assailant & victim. The shape of the entry wound may thus therefore sometimes not correspond to the weapon used. It may have an atypical appearance may also result when the injury is caused by a relatively blunt edged weapon due to simultaneous cutting & tearing of the skin during the process of stabbing.

Materials & Methods:

This was a descriptive type of cross-sectional study conducted among 57 number of victims of stab wound and was carried out at Rangpur Medical College Morgue from July 2017 to June 2018. We have observed the pattern & incidence of traumatic injuries on the victims with their nature & severity. Cases of abdominal & thoracic penetration were included in the study. Demographic characteristics, wound site, peculiarity, injured organs were examined retrospectively. The inclusion criteria of this study were both male & female gender with age range between 10-60yrs.

Results:

During the study period from July 2017 to June 2018 total number of autopsies were 647. Among them 57 cases were due to stab wound. Among 57 cases, 53 (93%) were male & the rest 4 (7%) were female (Figure-1).

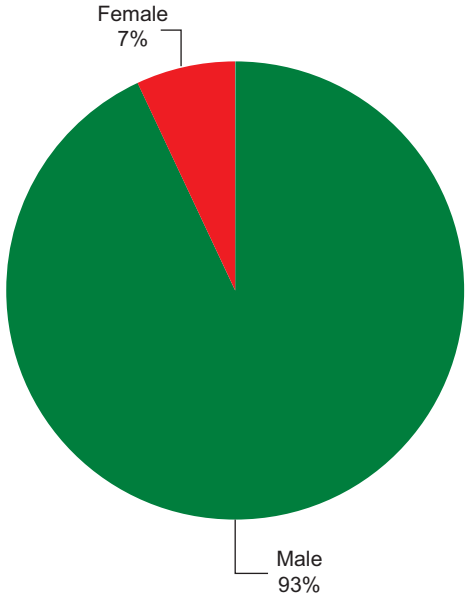

Fig. 1: *Distribution of the deceased by sex*

Table 1: Age distribution of deceased (n=57)

Age	Number	Percentage
10-20yrs	06	10%
20-30yrs	17	30%
30-40yrs	21	37%
40-50yrs	08	14%
50-60yrs	05	09%
Total	57	100%

Table 1 shows commonest age group involved in stab injuries were 30-40yrs (37%). Second most common age group were 20-30yrs (30%).

Among the victims age range was between 10-60yrs.

The distribution of the stab wound was also recorded. The occurrence of stab wound was highest in region of the abdomen about 58%, then chest 49%, upper & lower back 9%, 7% and lower limbs 4% (Table-2). As mentioned earlier, the pattern of

injuries that found to be most common was the penetrating type of stab wound of the abdominal injuries either stomach or liver. Some victims also had multiple injuries on different parts of body.

Second most common injury patterns were the penetrating type of stab wound of the chest with the involvement of either heart or lung. Another pattern was widely scattered multiple stab wound both on front, back & lower limb which sometimes causing division of major vessels.

Table-2: Distribution of stab wound

Stabbing Zone	Number	Percentage
Chest	28	49%
Upper back	05	9%
Abdomen	33	58%
Lower back	04	7%
Lower limb	02	4%

The study shows more prone to having stab wound in abdominal region though it is a vast area without any bony outline. So, way to enter a sharp pointed weapon without friction.

The occurrence of neurovascular & bone injury was also documented. Among the number of victims 98% of them had multiple small vessel damage. (Table-3)

Table-3: Vascular Injury

Injured vessel	Number	Percentage
Large vessel	30	53%
Small vessel	49	86%
Multiple small vessel	56	98%

Table-4: Bone & Joint Injury

Injury to bone & joint	Number	Percentage
Femur	5	9%
Knee	1	2%
Spine	4	7%

Table-4 shows highest (9%) victims had injury to femur followed by spine injury about (7%) & knee (2%).

Total number of injured organs as detected in 57 cases are as follows: small intestine: 8, liver: 7, colon: 3, spleen: 2, stomach: 2, diaphragm: 4, heart: 18, lungs: 4. In accordance of the injured organ Injury Severity Score has been made which was shown as below.

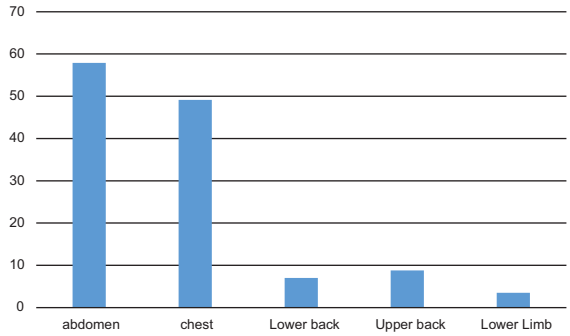

Fig-2: *Injury Severity Score means in relation of stabbing zone.*

The means of the Injury Severity Score were seen to be highest in abdominal region with involvement of small guts, liver etc. Second most common was chest. Other patterns were widely scattered stab wound on whole back, limbs with or without division of major blood vessels. (Fig-2)

Discussion:

Stab wound is the commonest method for homicide worldwide resulting from fight, domestic violence & street crimes. Inter personal violence & fight are major problem all over the world, resulting in physical & psychological consequences[9,10]. Penetrating injury can be seen after different kinds of events including stab wounds, gunshot wounds, industrial accidents, fall from height, traffic accidents etc. The name of the organs wounded & characteristics of injury is subject to change in every particular cases. The outcome of the penetrating injuries are mostly devastating & life threatening.

In this study, the range of age was between 10-60yrs. The commonest age group was 30-40yrs. Here, the study showed that the young adult people (30-40 yrs.) were more frequently apprehended to stab injuries. With advancing the age range, the occurrence was declined. The study also revealed that most of the victims were male (93%). The sex variation may be due to their mobile life style, involvement with different kinds of crime, peer influence, drug abuse, alcohol, weapon availability, increase political corruption & instability, disharmony in family[11]. These young people also tend to be involved in a wide range of antisocial

behavior, committing more non-violent offences than violent offences[12, 13]. Stab wound may also result major disabilities, affecting the victim's daily routine, while increasing the health care burden. *Al Wahbi et al* conducted a cross sectional study that included 32 patients with vascular injury associated with limb loss in KSA[14].

According to WHO report on Violence & health Summary Geneva 2002 an estimated 1.6 million people lost their lives due to violence in 2000[15]. About half were suicide, one third were homicide & one fifth were casualties. Considering the injury pattern, 100% of victim of this study had multiple abrasion, bruise all over their body. Number of stab with their site is an important factor in determining the nature of the wound. The most common site for stab wound was abdominal region about (57.89%) followed by chest cavity (49.12%), then upper back region about (8.77%) subsequently lower back (7.01%) & lower limb (3.5%). Most commonly used weapon was knife. The frequent association of combined chest and abdominal injuries demonstrated in this study suggested that the injuries in this group are particularly violent.

For most of the stab wounds all over the world & for several decades abdomen & chest remain the most common site for fatal stab injury[16]. The abdominal lesions were consisted of different site at gastrointestinal injuries (small bowels, colon, stomach, liver, spleen, diaphragm) shown as Injury Severity Score (ISS). The small bowel was the single most frequent intra-abdominal injury (30.7%), then liver (26.9%), colon (11.5%), stomach (7.6%), spleen (7.6) and diaphragm (15.3%). Second most common site for thoracic lesion were heart (81.8%), lung (18.1%). There were about 15 victims who had multiple regional injuries. So, the multiple number of wounds that widely scattered & deeply penetrating associated with small other injuries when present on the vital site of the body indicates intention of the assailant to confirm death.

Many overseas medical literatures have showed that not only in Bangladesh stab wound is a great problem worldwide. According to UN global study on homicide knife violence is not as common in the United States and the Western Hemisphere as it is in Europe and other countries in Asia. The UN also reports that a man in the Americas is six times as likely to die by firearm as by a knife; however, a man in Asian countries is almost as likely to die by a knife as a firearm. China had large knife attacks resulting in many injuries and deaths. In 2014, about 10 men and women wielding knives in a Kunming train station, injuring more than 130 people and resulting in 28 deaths. Other Asian countries that have experienced frequent knife violence include Japan and South Korea.[17]

In Bangladesh perspective Stab injury information is not available in an organized form. Snatching, robberies are very common in our country. This is a common picture of Dhaka city & generally increasing day by day. For better protection of ourselves we should be aware about different types of life-threatening attacks & would encounter in such events.

Conclusion:

Increasing the security measures may help to reduce stab wounds events in urban place where criminal attacks are seen frequently. Preventing the injured & accused people from facing each other & re-involving in the criminal events by psychological approach may affect personal behavior positively.

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A Review on Pharmacovigilance

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Abstract:

All medicines have the potential to cause Adverse Drug Reactions (ADRs). Pharmacovigilance is very important for evaluation of medicine. *It deals to improve public health and contribute to the assessment of benefit, harm, effectiveness and risk of medicine. Spontaneous reporting is very important for effective pharmacovigilance though under reporting is a limitation. Inadequate knowledge and attitude of health professionals greatly related to under reporting. Under reporting can be improved by appropriate educational intervention. It is difficult to prevent adverse drug reactions, but an effective pharmacovigilance system will definitely help in minimizing the further occurrence of similar adverse drug reactions and may ensure better health care and safe use of medicines.*

Key words: *Adverse Drug Reactions, pharmacovigilance, safe, medicine.*

(MH Samorita Med Coll J 2020; 3(2): 67-70)

Introduction:

Every drug is associated with beneficial as well as undesirable or adverse effects. Adverse drug reactions (ADRs) is defined as 'a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function'[1]. Adverse drug reactions are global problem of major concern. In some countries, adverse drug reactions (ADRs) rank among the top 10 leading causes of death and are associated with a significant morbidity and mortality [1, 2]. Pharmacovigilance is defined as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem'[2]. It plays a vital role in ensuring that doctors, together with the patient, have enough information to make a decision when it comes for choosing a drug for treatment [3]. The ultimate aim of pharmacovigilance is to ensure safe and rational use of medicines. A most important outcome of pharmacovigilance is the prevention of patients being affected unnecessarily by negative consequences of pharmacotherapy [4].

Each year 41,000 older adults are hospitalized and 3,300 of those die from ulcers caused by NSAIDs (non-steroidal anti-inflammatory drugs, usually for treatment of arthritis). Each year 32,000 older adults suffer from hip fractures attributable to drug-induced falls, resulting in more than 1,500 deaths. In one study, the main categories of drugs responsible for the falls leading to hip fractures were minor tranquilizers (30%), antipsychotic drugs (52%), and antidepressants (17%). All of these categories of drugs are often prescribed unnecessarily in older adults by the physician or by the pharmacist or by the patients. Approximately 163,000 older Americans suffer from serious mental impairment (dementia) either caused or worsened by drugs. It was found in one study conducted in

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Washington state that 46% of the patients reported drug-induced mental impairment caused by minor tranquilizers, 14% by high blood pressure drugs and 11%, by antipsychotic drugs respectively. Two million older Americans are addicted or at risk of addiction to minor tranquilizers because they have used them daily for at least one year. Drug-induced tardive dyskinesia has developed in 73,000 older adults; this condition is the most serious adverse reaction to antipsychotic drugs, and it is often irreversible. Tardive dyskinesia is characterized by involuntary movements of the face, arms and legs. About 80% of older adults receiving antipsychotic drugs do not have schizophrenia or other conditions that justify the use of such drugs, so many of these patients have serious side effects from drugs that were prescribed inappropriately. Drug-induced Parkinsonism has developed in 61,000 older adults also due to the use of antipsychotic drugs such as haloperidol, chlorpromazine, thioridazine , trifluoperazine and fluphenazine. Pharmacovigilance improve patient care and safety, public health, assessment of benefit, harm, effectiveness and risk of medicines, promotes understanding, education and clinical training [5]. In this review we will discuss about role, benefits and challenges of pharmacovigilance and its future consideration in healthcare sectors.

Aims of pharmacovigilance

1. Improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions.
2. Improve public health and safety in relation to the use of medicines.
3. Detect problems related to the use of medicines and communicate the findings in a timely manner.
4. Contribute to the assessment of benefit, harm, effectiveness and risk of medicines, leading to the prevention of harm and maximization of benefit.
5. Encourage the safe, rational and more effective (including cost-effective) use of medicines.
6. Promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public [6].

Role of health care professionals in Pharmacovigilance

Physicians are frontline healthcare givers in a community. They may play a pivotal role in maintaining the well being of society by active participation in pharmacovigilance. Preventing ADRs is an integral part of routine clinical work of any physician. Spontaneous monitoring is the foundation of successful pharmacovigilance. Post marketing surveillance of drugs is very important in analyzing and managing the risk associated with drugs once they are available for the use of the general population.The contribution of health professionals in this regard to ADRs database is enormously significant and has encouraged ongoing ascertainment of the benefit risk ratio of some drugs as well as contributed to signal detection of unsuspected and unusual ADRs previously undetected during the initial evaluation of a drug [7,8,9]. Their active involvement in spontaneous reporting of ADRs is essential for the effective implementation of National Pharmacovigilance Program.

Professionals working in healthcare are the preferred source of information in pharmacovigilance. These include medical practitioners (general, specialists), nurses and pharmacists and pharmacy technicians. Other health workers and family members can play an important role in the stimulation of reporting and in the provision of additional information (e.g. on co-medication and previous drug use). Pharmaceutical manufacturers, applicants and research organizations have to ensure that suspected adverse reactions to their products are reported to the competent authority [10].

Type of reaction should be reported

- For "new" drugs- report all suspected reactions, including minor ones.
- For established or well-known drugs- report all serious and unexpected suspected ADRs.
- Report if an increased frequency of a given reaction is observed.
- Report all suspected ADRs associated with drug-drug, drug-food or drug-food supplements (including herbal or complementary products) interactions [11].

- Report ADRs in special fields of interest such as drug abuse and drugs used in pregnancy and during lactation.
- Report when suspected ADRs are associated with drug withdrawals.
- Report ADRs occurring from overdose or medication error.
- Report when there is a lack of efficacy or when suspected pharmaceutical defects are observed.

Where and How to Report?

Patient should immediately report any type of adverse drug reaction due to the use of any medication to their primary doctor and help the doctor fill out the special ADR form. Doctor, nurses, pharmacist and health workers can fill out the ADR form in PDF format and send it back to the DGDA. Every hospitals and clinics must decide for itself how the reporting system should be operated and by whom. Generally, the physicians themselves act as reporters, completing the reporting form, keeping a record and sending them to the ADRM Cell, Directorate General of Drug Administration, Aushad Bhaban, Mohakhali, Dhaka-1212,Bangladesh. The hospital pharmacy in-charge may also report ADR by completion of the form after reporting physician consultation.[12] Adverse reactions can be also reported to pharmacology department of any medical college, civil surgeon office.

Current situation of pharmacovigilance in Bangladesh

In our county pharmacovigilance has been introduced and practiced, under the supervision of WHO-UMC (WHO-Uppsala Monitoring Committee). Adverse drug reaction monitoring (ADRM) cell was established in Directorate General of Drug Administration (DGDA), which is the drug regulatory authority of our country since 1996. Initially the cell circulated leaflets and posters bearing awareness slogans of drug use throughout the country. Also organized awareness meetings among the chemists (Retailers) of different area and published awareness instructions in the daily newspapers and broadcasted these awareness slogans on Radio Bangladesh. The cell has been trying from its inception to introduce a systematic mechanism for ADRs monitoring in Bangladesh through collection, analysis and compilation of ADRs, spontaneously reported by the medical and pharmaceutical professionals of all health services outlets of the country. For that reason, the Directorate General of Drug Administration has been organizing ADR Monitoring Workshops/meetings in the medical colleges and hospitals of the country and distributing printed ADR reporting forms to the doctors for spontaneous reporting of ADR cases since 2000 [13].

Recommendations and Suggestions for effective pharmacovigilance

Pharmacovigilance is a broad concept, and includes the re-evaluation of marketed drugs, risk management, communicating drug information, promoting rational drug use. It is becoming increasingly important to provide training in all of these activity areas and to carry out intensive monitoring of new drugs to evaluate the risk-benefit [14].

- There should be an involvement of all categories of healthcare professionals in ADR and pharmacovigilance planning to incorporate the sense of ownership.
- It should be ensured that the reporting forms are always available.
- An acknowledgment receipt should always be issued along with a reference number for all further correspondence to avoid any duplication of reports.
- There should be timely and easy feedback for all the cases reported.
- All ADRs should be published in journals, lay press, etc. to keep people as well as healthcare professionals informed.
- ADR monitoring and reporting issues should be introduced in undergraduate and post graduate curricula of medical education.
- Interaction with pharmacovigilance centers in other countries and with Uppsala monitoring center.
- Regulatory authorities should be encouraged to establish databases of clinical information suitable for epidemiological studies to examine and quantify signals of possible emerging risk.

- The regulatory authorities should investigate the feasibility and potential utility of creating a database of "recommendations for action" arising from evaluations and improve the usefulness of such information by making this generally available.

Conclusion:

It has become the responsibility of all the healthcare workers to develop strategies to report, monitor and prevent ADRs. The drug regulatory authority should take necessary steps to promote safe use of drugs in the country. The initial step can begin from a single hospital and later it can be expanded to the entire country. Post marketing surveillance studies must be made mandatory for new drug in the country. Teachers and students of higher secondary level and above should be educated on ADR through television program. Training regarding ADRs reporting should be mandatory during internship. A formal training program for the healthcare professionals is mandatory before starting the program in the medical college. Training and workshop regarding pharmacovigilance should be reviewed 1 or 2 times in a year. A well developed pharmacovigilance system can pay a lot to the healthcare system if nurtured well with dedicated, expertise people in the team. If properly developed, a Pharmacovigilance system will be of great value for the safety of patient and the community as a whole.

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Lead Poisoning: A Brief Review

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Abstract:

Lead poisoning is very important & its effects on the human body are devastating. There is almost all parts of the human body affected by lead poisoning.. It is a common environmental pollutant. It's levels rise in almost every country, posing serious threats. Lead is a metal which has been associated with human activities for the last 6000 years. In ancient civilization uses of lead included the manufacture of kitchen utensils, toys , and other decorative articles. However, lead is also toxic to humans, with the most deleterious effect on the heamopoietic, nervous, reproductive system, and urinary tract. The main sources of lead exposure are paint, water, food, dust, soil, kitchen utensil and leaded gasoline. The majority of cases of lead poisoning are due to oral ingestion and absorption through the gut. Lead poisoning in adult occurs more frequently during exposure in the work place and primarily involves the central nervous system. Symptoms of haemopoietic system involvement include microcytic, hypochromic anemia with basophilic stippling of the erythrocytes. Low intelligence quotient and poor school performance have been observed in children with high lead levels. Lead crosses the placenta during pregnancy and has been associated with intrauterine death, prematurity, and low birth weight . In 1991, the center for disease control and prevention in the USA redefined elevated blood lead levels as those greater than 10 microgram/ dl and recommended a new set of guidelines for the treatment of lead levels greater or equal 15 microgram/ dl.

Key Words: *Lead Poisoning , Encephalopathy , Hypochromic anemia , Chelation therapy.*

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Introduction:

Lead is a widely used metallic poison. Exposure to lead is harmful to physical development in young children. Metallic lead has constituted a part of the human environment for over 5000 years[1]. The characteristic features of lead toxicity including anaemia, colic, neuropathy, nephropathy, sterility, and coma, were noted both by Hippocrates and Nikander in ancient times. In 370 BC, Hippocrates first described abdominal colic in a man who mined metals[2]. The effects of lead toxicity on young children were first described in 1892 in Brisbane, Australia[3]. Even though two thousand years have passed since Vitruvius chronicled the dangers of lead in water supplies, this threat to public health still remains with us[4]. Besides drinking water, paint and leaded gasoline have also been identified as major sources of lead exposure. Lead in household paint was recognized as a danger early in the 20th century [5]. In 1923 a General Motors chemist, Thomas Miggely, found that tetraethyl lead was an effective anti-knocking agent and boosted engine power. When this company began to manufacture tetraethyl lead, workers started to display signs and symptoms of psychosis, and much fatal causality. In spite of this, leaded gasoline continued to be used for almost 70 years. The removal of lead from gasoline in 1990, regarded by many as one of the major public health triumphs of the 20th century[6,7].

Classification of Lead:[8]

It is a heavy steel-grey metal. Metallic lead and all its salts are poisonous. The principal salts which produce toxic effects are:

1) Lead acetate (sugar of lead): white crystals
2) Lead carbonate (safeda): white crystalline powder.
3) Lead chromate: bright yellow powder.
4) Lead monoxide (litharge)
5) Lead tetraoxide (red lead, vermilion, sindur)
6) Lead sulphide

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Absorption of Lead

Lead may enter the body by ingestion through the intestines, through the lungs by inhalation, through the skin, or by direct swallowing[9]. For adults with occupational exposure, the most significant route for absorption is through the respiratory tract[1,8]. The percentage of inhaled lead reaching the bloodstream is estimated to be 30–40%[1]. Rates of absorption through the gastrointestinal tract depend on the nutritional status and the age of the individual exposed. Therefore, while adults absorb an average of 10 to 15% of the ingested quantity, this amount can increase to 50% in infants, young children and pregnant women[1,8]. Absorption through the gut is the predominant route for children and increases when dietary intakes of iron, calcium, phosphorus, or zinc are low[1,8,10]. There is little transcutaneous absorption of lead when inorganic lead compounds, such as those found in paint, are applied to the skin. In contrast, organic (tetraethyl) lead, which is that found in gasoline, can be absorbed via the skin. This route may have contributed to the lead poisoning in chemical workers during the development of this gasoline additive in the 1920s[1,8,11].

Distribution of Lead after absorption

Once absorbed, lead accumulates in three compartments: blood, soft tissues, and bone. In blood, approximately 99% of the lead is found in the erythrocytes, leaving about 1% in the plasma and serum[12]. The concentration of lead in plasma is more significant than that in whole blood as the means of distribution to target organs, i.e. brain, lungs, spleen, renal cortex, aorta, teeth, and bones [1,13]. The kinetics of lead transfer from blood to soft tissues is low and takes approximately 4 to 6 weeks [1]. Lead in blood has an estimated half- life of 35 days [14], in soft tissue 40 days [15], and in bones 20 to 30 years [16]. The biological half-life of lead may be considerably longer in children than in adults [15]. More than 95% of lead is deposited in skeletal bone as insoluble phosphate [1].Autopsy studies have shown that 90 to 95% of the body's burden is present in cortical bone and teeth. In adults, some 80–95% of the total body burden of lead is found in the skeleton, compared with about 73% in children. Bone lead may be regarded as two physiologically distinct pools: an inert pool, with a half-life of decades, and a labile pool that readily exchanges with lead present in blood or soft tissues [1,12]

It has been determined that lead crosses the placental barrier, with fetal uptake, beginning at 12 weeks gestation and continuing throughout development up to birth. Concentrations of lead in umbilical cord blood were found to be 80–100% of the maternal blood lead level[1,17,18]

Several conditions known to increase bone turnover, such as pregnancy, lactation, chemotherapy, tumor infiltration of the bone, or postmenopausal osteoporosis, may be associated with the mobilization of lead in bone stores, leading to chronic lead toxicity [18-21].

Excretion of Lead

Inorganic lead is not metabolized; however, alkyl lead compounds are oxidized by the hepatic cytochrome P 450 system. Generally, lead excretion is low, with the most significant route being via the urinary tract. The use of chelating agents can enhance lead excretion in urine and this constitutes the basis of the therapeutic approach to lead poisoning. Lead may also be excreted with bile through the gastrointestinal tract. Although minute amounts of lead are excreted through the sweat and the nails. In general, lead is excreted extremely slowly from the body, with its biological half-life estimated at 10 years, thus facilitating accumulation in the body[1].

Epidemiology of Lead Poisoning

Lead is found in mineral deposits and is released into the environment from natural causes as well as through human industrial activity. Lead in dust becomes a long-term source of lead exposure. Worldwide, six categories of products account for most cases of lead exposure: gasoline additives, food-can soldering, lead-based paints, ceramic glazes, drinking water pipe systems, and folk remedies[8]. Inhalation of lead fumes or lead-containing dust is mainly a problem in occupational settings, such as smelting, recycling facilities, production of storage batteries, and lead-glazed ceramics. Swallowing of lead-containing particles, food or drinks is an important route for both occupational and environmental exposure to lead [22]. Airborne lead eventually settles on land, in water supplies, and on buildings, and thus can enter the food chain. Besides the settling of atmospheric lead, surface contamination also occurs from contact with industrial waste containing lead. Human beings are also exposed to lead from cigarette smoking[23].

Children are exposed to lead from a variety of sources and through various pathways, as well as via normal, repetitive hand-to-mouth activity, which is now recognized as a major contributor to the chronic lead poisoning in children. Moreover, many consumer products, including toys, have been made of, or painted with lead. Over the last 40 years, attempts have been made to remove lead from all these sources[1,9,24]. In infancy it comes from unusual sources, such as in-utero transmission of lead from women exposed to lead poisoning, or, in infants, through formula prepared with lead-contaminated water[25].

A locally used teething powder in Saudi Arabia known as "Saoott" and "Cebagin" prescribed by traditional healers[26,27]. Furthermore, "Kahal", a commonly used eye cosmetic in the Arabian Peninsula[27], involves a formula prepared with lead-contaminated water, or in a lead-soldered samovar[24].

Effect of Lead

Lead is a poison that affects virtually every system in the body. Children are more vulnerable to lead exposure than adults because of the frequency of pica, hand-to-mouth activity, and a higher rate of intestinal absorption and retention. The most deleterious effects of lead are on erythropoiesis, kidney function, and the central nervous system[28,29].

i. Hemopoietic system

The adverse effects of lead appear even with blood concentrations as low as 10 µg/dl. The best understood toxic effects of lead involve heme synthesis. It is suggested that the inhibition of delta aminolevulinic acid dehydrates starts at values as low as 5µg/dl. At higher lead concentrations this inhibition is very pronounced, reaching 50% inactivation at blood lead levels of 16 µg/dl and 90% inactivation at 55 µg/dl, resulting in the accumulation of delta aminolevulinic acid in plasma and its excretion in urine. Because this enzyme is normally present in great quantities, the inhibition of its activity may pass unnoticed[30,31]. Ferrochelatase is the enzyme that catalyzes the incorporation of iron into the porphyrin ring. If, as a result of lead toxicity, the enzyme is inhibited and its pathway is interrupted, or if adequate iron is not available, zinc is substituted for iron, and zinc protoporphyrin concentrations increase. The critical target, however, seems to be the enzyme's hemesynthesis, essential for the insertion of iron into the precursor, protoporphyrin IX[32,33]. The major consequences of this effect, which have been evaluated in both adults and children, are reduction of circulating levels of hemoglobin and the inhibition of cytochrome P 450-dependent phase I metabolism[32]. Lead clearly inhibits normal hemoprotein function in both respects, which results in basophilic stippling of erythrocytes related to clustering of ribosomes and microcytosis when blood lead levels are 20µg/dl. Thus microcytic hypochromic anemia is often diagnosed in victims of lead exposure.

ii. Nervous system

Headaches, poor attention span, irritability, loss of memory and dullness are the early symptoms of the effects of lead exposure on the central nervous system. The most serious manifestation of lead poisoning is acute encephalopathy, the symptoms of which include persistent vomiting, ataxia, seizures, pappiloedema, impaired consciousness, and coma. Lead encephalopathy rarely occurs at blood lead levels below 100µg/dl. Decreased play activity, low intelligence quotient and poor school performance are neurobehavioral abnormalities observed in affected children whose blood lead levels are approximately 35µg/dl. Results of more recent cross-sectional and prospective studies indicate that postnatal lead exposure resulting in blood levels as low as 25µg/dl, and probably lower, are also associated with deficits in intellectual attainment, achievement, and affect behavior. Impaired hearing has been observed at blood concentrations of 10 to 20µg/dl[29,33].

Peripheral neuropathy, on the other hand, is the most common manifestation among adults with occupational lead exposure. Typically, the peripheral neuropathy of lead toxicity is seen as involving the extensor muscles, with minimal sensory loss. Lead-induced neuropathy on the radial and peroneal nerve in adult lead toxicity results in the characteristic "wrist drop" and "foot drop". Gastrointestinal colic is caused by high lead exposure and may be associated with lead neuropathy[29,33,34].

There are few symptoms of chronic lead poisoning and they are mostly non-specific, involving abdominal and muscle pain, arthralgia, irritability, depression, altered sleep, memory disturbances, and hyperactivity in children[35]. The effects of chronic lead toxicity on psychological development were

first described by Byers and Lord in 20 children who suffered lead poisoning during the first two years of life from eating paint chips. These children were reassessed during the primary school period, and a high frequency of educational and behavioral problems was noted[36].

iii. Kidney

Abnormalities include aminoaciduria, glycosuria, and phosphaturia (Fanconi's syndrome). Characteristics of early or acute nephropathy include dysfunction of the proximal tubules (Fanconi's syndrome), manifesting as aminoaciduria, glycosuria, and phosphaturia with hypophosphatemia, and increased sodium and decreased uric acid excretion. Characteristics of chronic lead nephropathy include progressive interstitial fibrosis, a reduction in the glomerular filtration rate, and azothemia. Loghman-Adham evaluated the parameters of renal tubular function in 134 children and young adults 8–13 years after chelation therapy for severe lead poisoning and concluded that a partial Fanconi's syndrome can persist up to 13 years after lead poisoning[37].

iv. Other systems

Lead in low doses is associated with increased blood pressure in adults. Lead toxicity typically causes constipation and colic[26]. Reduced sperm counts and motility have also been associated with chronic lead exposure[33,38].

Effects on the fetus

Abortions, miscarriages, and stillbirths have all been reported among women working in lead-associated trades. Pre-natal exposure to lead has been associated with toxic effects on the fetus. These include reduced gestational age, birth weight, and adversely delayed cognitive development. Recent studies have suggested that a significant amount of bone lead is mobilized, enters the circulation during pregnancy and lactation, and crosses the placenta[17,18,29,38].

Acute and long-term exposure

Overt signs of acute toxicity include dullness, restlessness, irritability, poor attention span, headaches, muscle tremor, abdominal cramps, kidney damage, hallucinations, and loss of memory with encephalopathy, all occurring at blood lead levels of 100–120μg/dl in adults and 80–100 μg/dl in children. Signs of chronic lead toxicity, including tiredness, sleeplessness, irritability, headaches, joint pain, and gastrointestinal symptoms, may appear in adults at blood lead levels of 50– 80μg/dl. After 1–2 years of exposure, muscle weakness, gastrointestinal symptoms, lower scores on psychometric tests, mood disturbances, and symptoms of peripheral neuropathy were observed in occupationally exposed populations at blood lead levels of 40–60μg/dl. There is no safe level of blood lead below which children are not affected[15].

Laboratory Test for Lead

The most commonly used biological marker is the concentration of lead in blood. If either blood lead or free erythrocyte protoporphyrin is elevated, then other tests for lead effects on the kidneys (urea nitrogen, creatinine, and urinalysis) and blood (complete blood count with smear) should be performed. It is important to note that urea nitrogen and creatinine are not sensitive indicators of renal damage, since it is known that they do not rise until a large part of renal function is lost[33]

Nerve conduction velocity testing should be considered when there are persistent symptoms or clinical findings suggestive of the presence of peripheral neuropathy. Neurobehavioral testing is indicated in cases where there is persistent impairment of cognitive function and blood lead levels are usually above 80μg/dl. Sperm analysis is indicated in lead-exposed men with complaints of infertility.

Intervention and Treatment

The first step is to perform a confirmatory venous lead level assessment. Individualized case management, which includes a detailed medical history, nutritional assessment, physical examination, environmental investigation, and hazard reduction, begins at a blood lead levels of ≥20 μg/dl. Chelation therapy may be considered, but is not routinely recommended at blood lead levels of <45 μg/dl[39].

Chelating Agent

Dimercaprol (BAL)-Dimercaprol also known as British Anti-Lewisite (BAL) was developed in 1946 by the British to counteract German arsenic-based war gases. It increases the urinary excretion of heavy metals through the formation of stable, nontoxic,

soluble chelates. BAL lacks stability in water and is administered in an oil solution as a deep intramuscular injection. Despite the high incidence of side effects (fever, allergy), BAL has remained in use for more serious lead poisoning because of concerns that CaNa2EDTA therapy may translocate lead into the central nervous system and increase the potential for encephalopathy. Traditionally, pre-treatment with BAL has been recommended to avoid precipitation of encephalopathy[39].

Calcium Disodium EDTA (CaNa2EDTA)- In 1950, a second chelating agent, calcium disodium ethylenediaminetetraacetate, was found to be useful in the treatment of lead poisoning. It increases the urinary excretion of lead through the formation of a non-ionizing, soluble chelate. Because the use of CaNa2EDTA may cause increased lead concentration in the central nervous system, it should be administered after BAL is given. Very low bio-availability from oral intake necessitates parenteral administration. Treatment with CaNa2EDTA should usually be performed in a hospital setting by physicians experienced with chelation therapy on patients with normal renal function and with careful monitoring of renal parameters[39].

Succimer (2,3-meso-dimercaptosuccinic acid or DMSA)- This is an oral chelation agent that is approved by the United States Food and Drug Administration (FDA) for the treatment of lead poisoning in children and is also effective in adults. It is chemically similar to BAL, but has greater solubility in water, has a high therapeutic index, and is absorbed through the gastrointestinal tract. The recommended dose by the manufacturer is 10 mg/kg three times a day for five days, followed by 10 mg/kg twice a day for two weeks. This dose, which has been found to be acceptable in treating some adults, can be quite high for others, especially for heavier adults. Due to the lack of data on adult treatment with DMSA, an adult dose level of 500 mg twice a day for two weeks has also been given as a sensible maximum limit until additional clinical data become available for adults[39].

One study revealed that the serum ascorbic acid level was inversely related to the blood lead level in the adults and children involved. Given the benign nature of vitamin C, supplements in modest doses (100 to 1000 mg per day) may be an attractive adjunct to the management of patients with mild lead toxicity[40].

The BAL should be suspended as soon as blood lead levels fall below 60µg/dl. Repeated courses of treatment may be necessary for these children until blood lead levels return to a safe margin (≤20 µg/dl)[41].

Conclusion:

Identification of the various lead sources that surround us can help towards prevention of lead toxicity. We suggest that every case of encephalitis of unknown origin in children should undergo an X-ray of the knee, which can be rapidly performed and is easily available, because the presence of a dense metaphyseal band strongly supports a diagnosis of lead poisoning. Medical practitioners and parents need to be made more aware of the problem. They must fully understand that "the less lead in the developing brain, the better".

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A Case Report of Ovarian Torsion in the 3rd Trimester of Pregnancy- An Unusual Presentation

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Abstract:

Adnexal torsion is a very rare cause of acute abdominal pain during 3rd trimester of pregnancy though it is one of the most common gynaecologic surgical emergencies. It carries significant risk to a pregnant woman and fetus. Ovarian hyperstimulation in early pregnancy especially following infertility treatment is a major risk of ovarian torsion in 1st trimester of pregnancy. As the patient is likely to present with nonspecific symptoms like lower abdominal pain, nausea, vomiting and diagnostic accuracy of ultrasound is limited as ovaries are displaced by gravid uterus from their normal position, therefore treatment opportunity to preserve adnexa may be delayed. We report a case of ovarian torsion of a benign ovarian cyst during 3rd trimester of pregnancy, presented with acute abdominal pain, vomiting, subsequently developed high fever, vaginal bleeding and premature uterine contraction. She was known patient of placenta previa. She had history of pre pregnancy ovarian cyst but admission ultrasonogram unable to provide information about adnexal mass. On the basis of clinical presentation decision was taken for emergency caesarean section with keeping ovarian torsion in mind. Patient was managed by caesarean delivery followed by right sided salpingoophorectomy .Here we would like to emphasize that adnexal torsion should be kept in mind in case of lower abdominal pain in advanced gestation in spite of negative sonographic findings.

Key words: *Ovarian cyst, Pregnancy, Torsion, Ante Partum Hemorrhage (APH), In vitro fertilization (IVF).*

(MH Samorita Med Coll J 2020; 3(2): 77-79)

Introduction:

Torsion of ovary is total or partial rotation of the adnexa around the vascular axis or pedicle. Ovarian torsion accounts for 3% of gynecological emergencies[1]. Although the exact incidence during pregnancy is unknown , it has been reported to be 1 -5/10,000 in some studies[2]. It is unusual during 3rd trimester[2]. The clinical symptoms of adnexal torsion in advanced pregnancy are nonspecific and could be confused with other causes like acute appendicitis, ureteric colic, pyelonephritis and preterm labour[3]. The diagnostic accuracy of ultrasound in these weeks of pregnancy has limitations as the ovaries are displaced from normal position by enlarged gravid uterus[2,3]. It is generally diagnosed during surgery[3]. We report a case of torsion of benign ovarian cyst during 3rd trimester of pregnancy, which was diagnosed during caesarean section.

Case report:

A 24-year-old primigravid lady at her 34 completed weeks of gestation was admitted in Obstetrics & Gynaecology department of MH Samorita Hospital & Medical College on 25.10.2019 with 24 hours history of abrupt right lower quadrant abdominal

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pain, gradually increasing in intensity. Subsequently she started vomiting. There were no urinary complaints. She also gave history of vaginal bleeding for 6 hours prior to admission. She had history of recurrent painless, causeless vaginal bleeding at her 28 and 32 weeks of pregnancy. She had appendicectomy at her 12 years of age. On examination patient was anxious and a bit irritable, mildly anemic, with pulse100 beats/min, BP: 100/60 mm of Hg, temp 99 ^{0}F & oxygen saturation 98% in room air. There was mild uterine contraction. FHR was 120-160/min, regular. Moderate tenderness present in right lower quadrant. There was active vaginal bleeding in milder form. On admission transabdominal . ultrasonography (USG) visualized single fetus with gestational age of 32 weeks with placenta previa. This 3rd trimester ultrasound was unable to visualize adnexal mass.

Patient had one pre-pregnancy ultrasound commented on 4.4 cm right sided ovarian cyst suspected dermoid. Ultrasound in different period of pregnancy done but didn't put any comment about ovarian mass.

Urgent laboratory test was sent. Management started as per guideline of APH with preterm labour. Laboratory results showed elevated white cell count 16,700/mm^3, raised CRP with Hb% 9.5 gm/dl.

After 12 hours she developed high fever 102^0 F and vomiting. Right iliac fossa became severely tender and rigid. She had persisting uterine contraction not responding to tocolytic and also vaginal bleeding was persisting. On the basis of clinical presentation decision was made for emergency c-section with chance of ovarian torsion keeping in mind. Patient & guardian was counselled about suspected ovarian pathology and obstetric indication for surgery.

Operation was done under spinal anesthesia. On abdominal entry moderate amount of ascitic fluid was seen. Lower segment caesarean section was performed and a male baby weighing 2350 gm was delivered. Placenta was type III variety of placenta previa. Right ovary was found enlarged (10cm X 8cm), hemorrhagic, gangrenous and twisted twice at the infundibulo-pelvic ligament [Figure:1] Left ovary and tube were healthy looking. Right sided salpingo-oophorectomy was done. The post-operative course was uneventful. Histopathological examination revealed infarcted dermoid cyst.

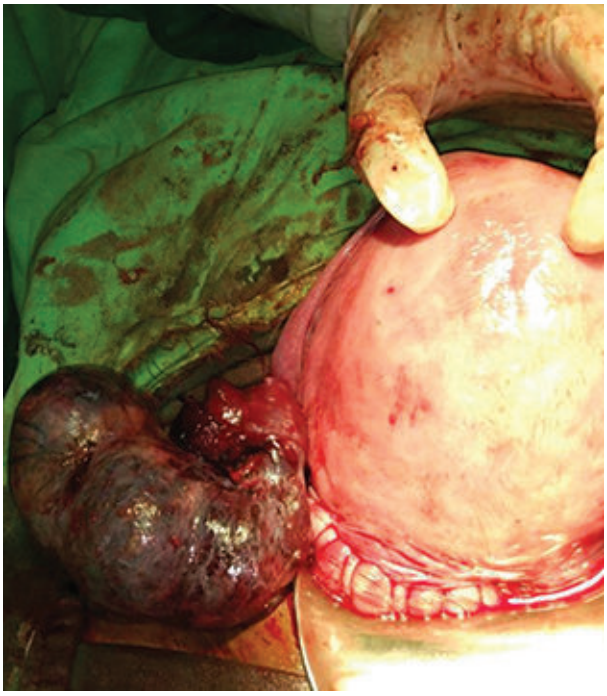

Fig. 1: *Hemorrhagic, gangrenous right ovary, twisted twice at the infundibulo-pelvic ligament.*

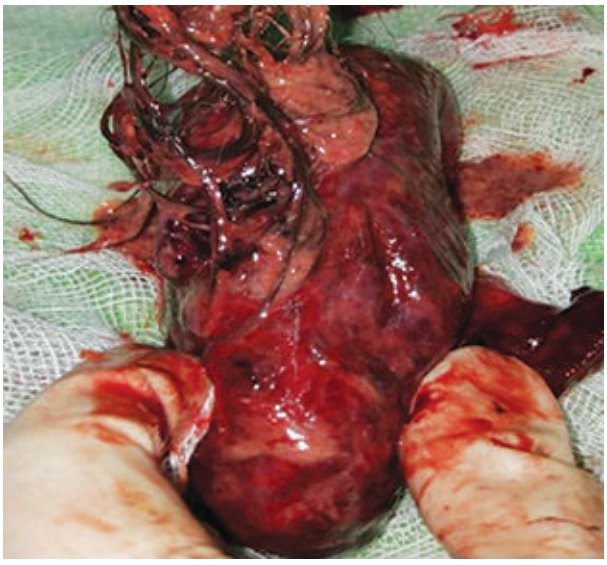

Fig. 2: *Cut section of right ovarian cyst showing hairs and sebum material.*

Discussion:

An ovarian cyst can be found up to 5% of pregnancy with 1 to 3% torsion rate[1,4]. The risk of torsion appears to decrease with gestation and unusual after 20 weeks[2,4,5,6]. Pregnancy following assisted reproductive technology (ART) is associated with an 11-fold increased risk of torsion [6,7]. In our case patient

conceived naturally and presented with adnexal torsion at 3rd trimester of gestation. Ovarian torsion results in circulatory stasis that is initially venous but it becomes arterial as the torsion and the resultant edema progress[8]. Therefore, clinical presentation is variable, ranging from nausea, vomiting and lower abdominal pain to circulatory collapse[8,9.] The diagnostic accuracy of 3rd trimester USG has limitation as ovaries are displaced[2,3]. So initial incorrect diagnosis has been reported in 15 to 35 % cases[8,9,10,11.] In our case we had suspicion of adnexal torsion on the basis of clinical findings and pre pregnancy USG but confirmed diagnosis was made per-operatively. The commonest type of ovarian tumor in pregnancy are serous cystadenoma, cystic teratoma, corpus luteal cyst etc[12,13.] In our case it was mature cystic teratoma.

Conclusion:

Torsion of the ovary in advanced gestation is rare as the compressive effect of the hugely enlarged gravid uterus restricts the mobility of the ovarian pedicle. However, this case clearly demonstrates that it can occur and needs to be considered as a differential diagnosis when pregnant patient present with acute abdomen irrespective of gestational age. Last of all it should not be forgotten that absence of radiological evidence suggestive of torsion does not necessarily exclude it and decision to operate should be considered on the basis of clinical background.

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Psoriasis with Multiple Comorbidities: A Case Report

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Abstract:

Psoriasis is a common, chronic, inflammatory and immune mediated dermatological disease of unknown etiology with systemic manifestation in many organ systems. Several epidemiological studies have shown that psoriasis is associated with psoriatic arthritis as well as cardiovascular and metabolic diseases. Furthermore, psychiatric disorders such as depressive and anxiety disorders are linked with psoriasis,require additional management. We report a case of 38-year-old female with psoriasis with multiple comorbidities.

Key Words: *Psoriasis, Comorbidities*

(MH Samorita Med Coll J 2020; 3(2): 80-82)

Introduction:

Psoriasis with a worldwide prevalence of 2-3% is now assumed as a systemic chronic inflammatory disease accompanied by comorbidities while it was accepted as a disease limited only to the skin in the past[1]. It is a chronic disorder with polygenic predisposition like environmental, genetic, immunological mediated inflammation and several modifying factors including obesity, trauma, infection and deficiency of the active forms of vitamin D3 [2,3].

Case Report:

A 38 year old female reported to the outpatient Department of M H Samorita Medical College and Hospital on 04th April, 2019 with the complaints of generalized scaling with redness of skin with occasional itching. Initially, there were multiple reddish, scaly lesions of different sizes and shapes present over scalp, front of knees, back of elbows and extensor surfaces of extremities. The scaly lesions were dry, white and thick without oozing or discharge.

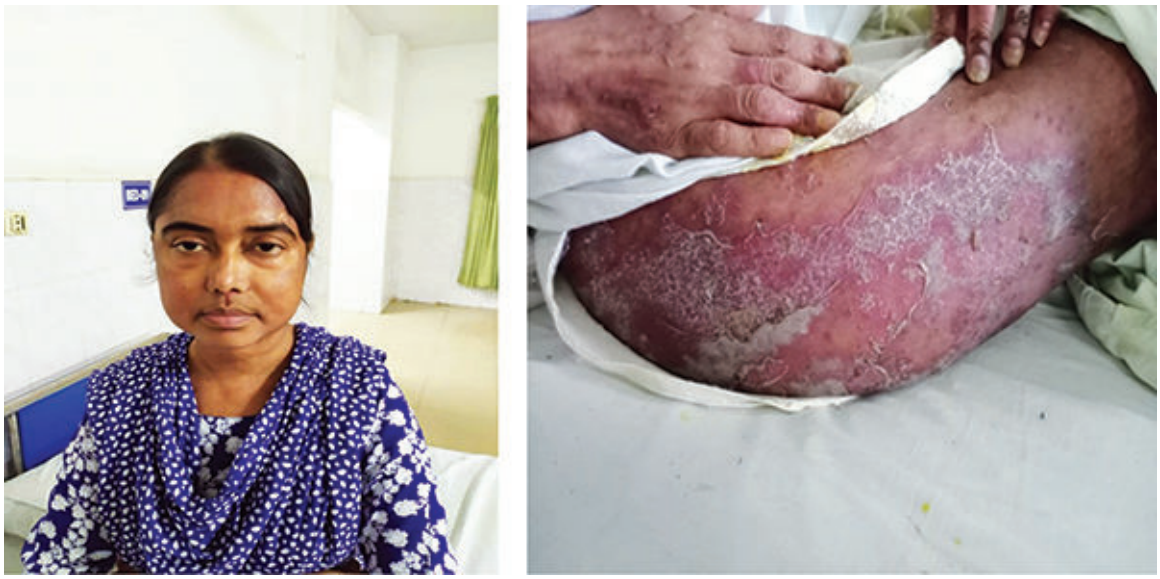

Fig. 1(a,b): *Zinia during treatment*

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She noticed bleeding upon scratching of the lesions and appearance of new lesion over scratch marks. In the scalp, lesions had caused hair loss. She also suffered from generalized bodyache for same duration. She also complained of pain and restricted movement of right hip joint and fracture neck of right femur due to accidental fall one and half months back. Her comorbidity was uncontrolled Hypertension with two antihypertensive drugs. On query she gave history of taking tablet Methotrexate 15 mg and Folic acid 5 mg weekly and also on non-steroidal anti-inflammatory drugs. On examination, she was ill looking with low body mass index (BMI) which was 16.89. She was moderately anaemic, orientation and alertness were normal but anxious. Her vital signs were within normal limit except blood pressure which was high on every follow up examination. Integumentary system revealed, generalized erythematous patches covered with silvery white scales over scalp, trunk and both upper & lower extremities. Auspitz Sign and Koebnerization were positive. Her Psoriasis Area and Severity Index (PASI) was >10. Nails showed nail pitting, onycholysis, subungual hyperkeratosis, onychomadesis involving several nails. Diffuse hair loss were observed over scalp. Mucous membrane appeared normal. Other systemic examination revealed no abnormality including cardiovascular, respiratory and alimentary system.

Laboratory Examination revealed grossly lower hemoglobin of 7.1 gm/dl along with very high erythrocyte sedimentation rate (ESR) of 140 mm in 1st hour, fasting lipid profile revealed high triglyceride (TG) level of 265 mg/dl. Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), renal function were normal. C reactive protein (CRP) was 42 mg/l. Urine analysis was also normal. Anti-nuclear antibody (ANA) and anti-double stranded DNA (Anti Ds DNA) were negative. Peripheral blood film showed dimorphic anaemia (normocytic normochromic with microcytic hypochromic cells). Serum iron profile was within normal range. Patient was advised to stop tablet methotrexate and transfuse two units of whole blood along with oral iron supplementation. At that time, she was only advised to continue topical corticosteroid and emollients for her condition. She was given amlodipine & olmesartan combination and fenofibrate for her uncontrolled hypertension and dyslipidaemia accordingly. After follow up, complete blood count (CBC) with Erythrocytic Sedimentation Rate (ESR) was done where hemoglobin was raised to 11.7 gm/dl & ESR decreased to 90 mm in 1st hour. For deterioration of her skin condition, later on tablet Acitretin, 25 mg daily was started. As the patient had long history of psoriasis and fracture neck of femur, we planned to do serum25 hydroxy vitamin D level,calcium, phosphate along with bone marrow density (BMD) to exclude osteoporosis due to decreased level of vitamin D in psoriasis. Though patient could not afford, we advised to take calcium along with low dose of vitamin D supplementation.

Discussion:

Comorbidities are more frequently seen in 15% of psoriasis patients who have moderate to severe psoriasis due to increased inflammatory impact and common pathogenesis [4]. The precise aetiology of this multimorbidity is uncertain and may include shared genetic susceptibility, direct effects of psoriasis per se, effects of psoriasis treatments and the consequences of behavioral responses to living with chronic disease.[5] Although comorbidities can be simply classified as classical, related to chronic systemic inflammation, lifestyle and treatment, they can be classified also as medical comorbidities, psychiatric/psychological comorbidities and conditions contributing to comorbidities.[6,7]

This patient suffered from severe anaemia with high ESR and Hypertension with Dyslipidemia. As a chronic disease psoriasis is sometimes associated with anaemia. In this patient anaemia could be due to anorexia, depletion of iron store with concomitant unmet cellular iron requirement, gastric erosion due to chronic stressful condition, drugs (NSAIDs, Methotrexate, Systemic steroids).[8]

In psoriatic patients without any risk factor, the prevalence of hypertension was found to be higher and increased prevalence of hypertension was observed as disease severity increased.[9] In pathophysiology, chronic inflammatory process in psoriasis increases angiotensin II, oxidative stress, endothelin-1, renin and angiotensin converting enzyme production from adipose tissue. Dyslipidemia is seen in studies where patient had severe psoriasis (skin involvement >10 %).[10] It plays a crucial role in the development of cardiovascular diseases. It may result from overproduction/lack of clearance of lipoprotein particles, or may be related

to other defects in the apolipoprotein /metabolic enzyme deficiencies. Cytokine, Tumor Necrosis Factor α(TNF) , Interleukin (IL) 6, Interleukin (IL) 17,Interleukin (IL) 20, Leptin and Vascular endothelial growth factors (VEGF) play a central role both in psoriasis and metabolic syndrome.

Recent studies suggest that 25-hydroxy vitamin D has important immune modulatory effect in psoriasis. Vitamin D has been shown to regulate keratinocyte differentiation, growth and protecting them from early apoptosis. Vitamin D deficiency can be explained by a fact that patients with psoriasis, except those undergoing phototherapy, tend to keep their affected areas covered. This attitude, prolonged during the years, could lead to decreased UV exposure with consequent reduced vitamin D levels. Reduced intake of vitamin D rich food due to lack of awareness among female in Bangladesh, along with lack of sun exposure, use of sunscreen due to cosmetic reason and a good number of female population usually cover their body for religious purpose.[11] This deficiency may lead to early osteoporosis and fracture.

Conclusion:

Because of the wide range of comorbid conditions are associated with psoriasis, the need for comprehensive screening and treatment must be recognized and addressed. The concept of psoriasis as a systemic inflammatory disorder provides the pathophysiologic link with many associated diseases. Therapeutic interventions for psoriasis may exacerbate comorbid conditions, and vice versa. Therefore, appropriate management of psoriasis must involve an integrated approach with comorbidities.

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Methotrexate-induced Pneumonitis

Mojumdar SK[1], Dhar D[2], Zaman KMU[3]

Abstract

A fifty-two-year-old lady being treated with methotrexate for rheumatoid arthritis for thirteen years were developed systemic and respiratory symptoms for last two weeks. These were improved on drug withdrawal, steroid treatment and supportive management.

Key words: *Methotrexate, Rheumatoid arthritis*

(MH Samorita Med Coll J 2020; 3(2): 83-86)

Introduction:

Methotrexate (MTX), a dihydrofolate reductase inhibitor, was developed in 1948 as an anti-metabolite that resembles folic acid. At present MTX is the most commonly prescribed disease modifying anti-rheumatic drug (DMARD) in rheumatoid arthritis (RA). At high doses it has antiproliferative properties, and is used in the treatment of cancer. Low dose MTX has immunosuppressive and anti-inflammatory properties. It is effective and well tolerated. One of the most serious although infrequent side effects of MTX is MTX induced pneumonitis .We discuss here a patient who developed methotrexate-induced pulmonary toxicity.

Case report:

A 52 year old woman with thirteen year history of rheumatoid arthritis was admitted with fever, cough and dyspnoea for 15 days. About 13 years ago she had been started on methotrexate 12.5 mg/week, and nine months ago the dose was gradually increased to 20 mg/week due to persistent disease activity with an excellent clinical response.While still on methotrexate she presented with gradually progressive exertional breathlessness and dry cough of two weeks duration. She had high grade, intermittent fever with chills along with anorexia and worsening breathlessness since seven days.On examination, she was tachypnoeic with a respiratory rate of 40/minute, SaO2 88% and had a temperature of 102°F. Pulse 104 bpm, BP 110/70 mm Hg.Respiratory system and other system examination was unremarkable. Her WBC count was 5200/mm^3 with P-70%, L-14%, E-16%. Serum creatinine, electrolytes and liver function test was normal. Chest x-ray (CXR) showed haziness in both lower zones (Fig 1). Sputum could not be examined, as she did not produce any. High resolution

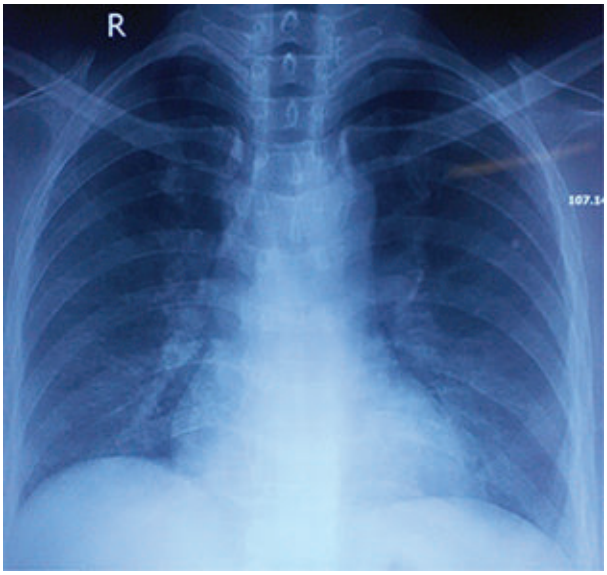

Fig.-1: *Chest x-ray showing basal opacities.*

computed tomograph (HRCT) of the chest showed diffuse hyper attenuated areas with interstitial fine septal thickening intermixed with ground glass opacities in all segments of both lung fields

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predominantly in basal segments suggestive of pneumonitis (Fig. 2). Bronchoscopy could not be done. Blood and urine cultures revealed no organism. ECG, Spirometry and DLCO test was normal. She had an ejection fraction of 60% on echocardiography; and pulmonary artery systolic pressure of 40 mm Hg. A diagnosis of methotrexate-induced pneumonitis was made. The drug was stopped, and she was started on prednisolone 50 mg daily which gradually tapered over 8 weeks. Her fever gradually settled down and she symptomatically started to improve with decrease cough and breathlessness. Her repeat WBC was 7300/mm^3 with normalization of eosinophilia and after four weeks HRCT of chest was normal (Fig. 3).

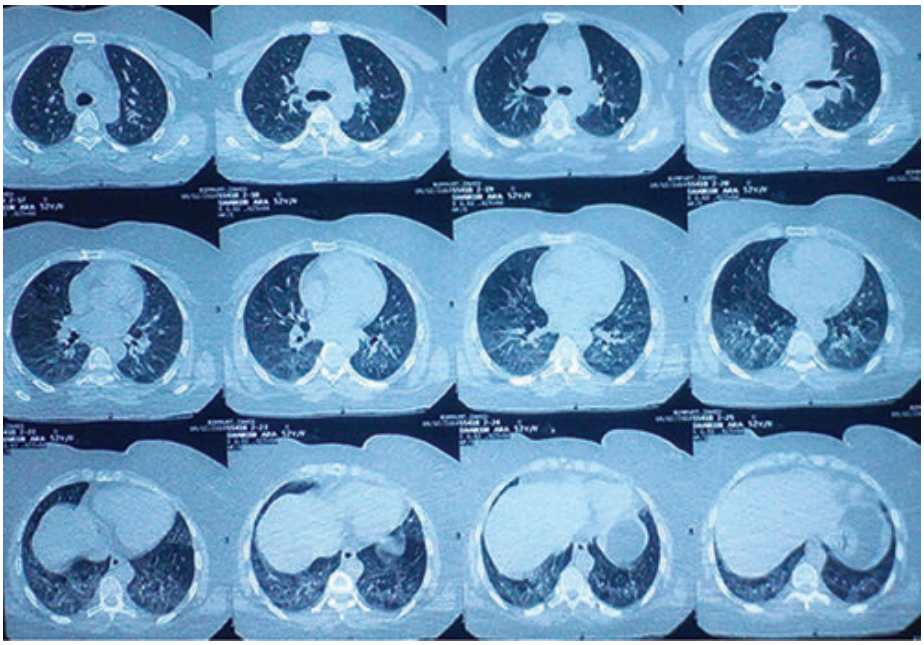

Fig.-2: *HRCT of chest before treatment*

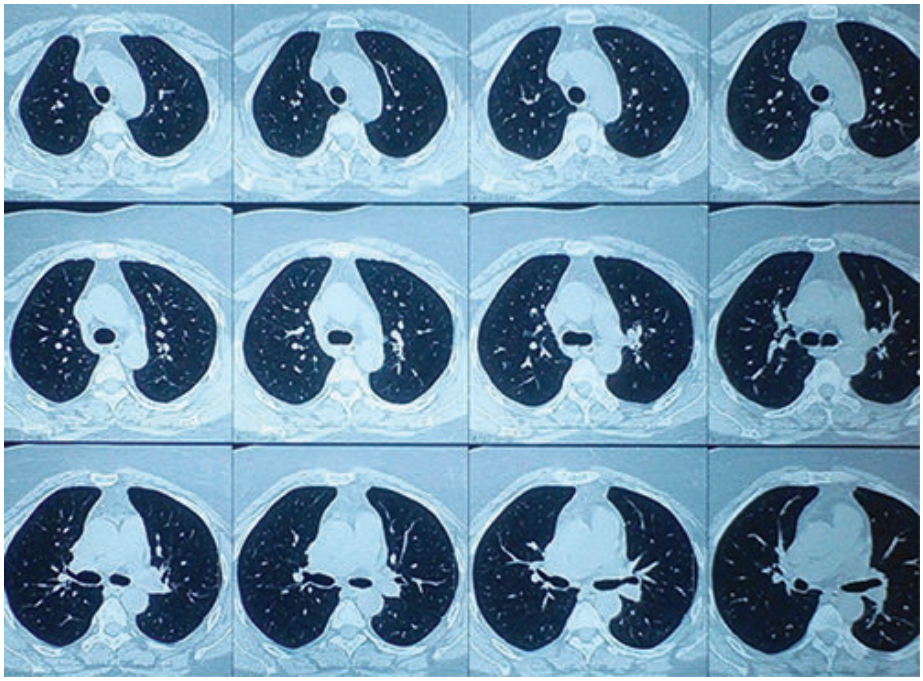

Fig.-3: *HRCT of chest after treatment*

Discussion:

Methotrexate is a folate antagonist used as a chemotherapeutic agent as well as for the treatment of non-neoplastic inflammatory diseases, rheumatoid arthritis (RA) being the commonest one. Methotrexate induced pulmonary toxicity occurs in 1 - 5% patients with RA[1]. The patient typically presents with fever, cough, dyspnoea, and inspiratory crepitations . Methotrexate pulmonary toxicity may present in an acute, subacute, or chronic form. Subacute presentations are most common. The majority of patients who develop methotrexate pulmonary toxicity during chronic oral low-dose therapy do so within the first year of treatment (mean nine months), although cases have been reported as early as 12 days and as late as 18 years after the drug was initiated [2] . Investigations reveal hypoxaemia with peripheral leukocytosis and eosinophilia in some patients. Patients on low-dose methotrexate are at increased risk for opportunistic infections [3]. These include *Pneumocystis carinii* pneumonia, disseminated histoplasmosis, and herpes zoster. Therefore, exclusion of opportunistic pathogens is important in the differential diagnosis of methotrexate pneumonitis. It is a diagnosis of exclusion [4]. A definite diagnosis of drug-induced pneumonitis is difficult, because the clinical and histological findings are nonspecific [5]. In addition, the frequent use of multiple drugs in combination and other therapies often confounds the chance of identifying the offending agent. The underlying disease may also complicate the identification of drug induced lung disease, as may opportunistic infections. Clinicopathological correlation is required for each individual case.

Radiologically, bilateral mixed interstitial-alveolar pulmonary shadows, pleural effusion, hilar lymphadenopathy may be present. Pulmonary function tests show a restrictive ventilatory defect with decreased diffusing capacity. The pathogenesis of this entity is not known. It probably has a hypersensitivity mechanism suggested by the frequent finding of peripheral eosinophilia and lymphocytosis on bronchoalveolar lavage. BAL lymphocyte CD4: CD8 may be increased, decreased, or normal. It may be an idiosyncratic immune reaction. Thus, different mechanisms may be operative in different subjects.

On histology, mononuclear cell infiltrates with type II pneumocyte hyperplasia in acute cases, and interstitial fibrosis in chronic cases, may be present. Isolated areas of bronchiolitis obliterans and non-caseating granulomas may be present. Factors that increase risk for methotrexate lung toxicity are[6]: Age greater than 60 years,rheumatoid pleuropulmonary involvement, previous use of disease-modifying antirheumatic drugs, hypoalbuminemia (either before or during therapy), diabetes mellitus,higher daily and cumulative doses, renal insufficiency, concomitant high-dose aspirin or non-steroidal anti-inflammatory drug therapy, and pre-existing lung disease. The treatment of methotrexate pneumonitis includes withdrawal of the drug and supportive care. Oral or intravenous pulse corticosteroid therapy[7] may be useful and is initiated after infection has been excluded. However, there are no clear guidelines for the optimal dose or duration of therapy. Patients with significant hypoxia will require oxygen therapy and intensive care with mechanical ventilation. Cyclophosphamide has been used successfully in significant pneumonitis[8]. Although there are instances of successful reintroduction of methotrexate after pneumonitis, there is not enough evidence to support this[9]. The prognosis with methotrexate-associated lung injury is generally favourable. The overall mortality is approximately ten per cent[10]. Our patient had a probable diagnosis of methotrexate induced pulmonary toxicity. She responded well to drug withdrawal and steroids, the latter having been tapered off in eight weeks time. A re-challenge of methotrexate was not attempted.

Conclusion:

RA patient treated with MTX may develop pneumonitis in any time regardless of disease severity, age, gender, total dose and duration of therapy. Attention should be given to early respiratory symptoms e.g cough, dyspnoea. RA patient need to be informed about these symptoms, once they are on MTX. High index of suspicion is crucial in early diagnosis and prompt treatment with steroid.

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Abstract From Current Literatures

(MH Samorita Med Coll J 2020; 3(2): 87-89)

LABORATORY DIAGNOSIS OF COVID-19: CURRENT ISSUES AND CHALLENGES

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The COVID-19 outbreak has had a major impact on clinical microbiology laboratories in the past several months. This commentary covers current issues and challenges for the laboratory diagnosis of infections caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In the preanalytical stage, collecting the proper respiratory tract specimen at the right time from the right anatomic site is essential for a prompt and accurate molecular diagnosis of COVID-19. Appropriate measures are required to keep laboratory staff safe while producing reliable test results. In the analytic stage, real-time reverse transcription-PCR (RT-PCR) assays remain the molecular test of choice for the etiologic diagnosis of SARS-CoV-2 infection while antibody-based techniques are being introduced as supplemental tools. In the postanalytical stage, testing results should be carefully interpreted using both molecular and serological findings. Finally, random-access, integrated devices available at the point of care with scalable capacities will facilitate the rapid and accurate diagnosis and monitoring of SARS-CoV-2 infections and greatly assist in the control of this outbreak.

Keywords: COVID-19, SARS-CoV-2, specimen type, molecular testing, serology, result interpretation

NUTRITION AND GENETICS IN NAFLD: THE PERFECT BINOMIUM

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Nonalcoholic fatty liver disease (NAFLD) represents a global healthcare burden since it is epidemiologically related to obesity, type 2 diabetes (T2D) and Metabolic Syndrome (MetS). It embraces a wide spectrum of hepatic injuries, which include simple steatosis, nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis and hepatocellular carcinoma (HCC). The susceptibility to develop NAFLD is highly variable and it is influenced by several cues including environmental (i.e., dietary habits and physical activity) and inherited (i.e., genetic/epigenetic) risk factors. Nonetheless, even intestinal microbiota and its by-products play a crucial role in NAFLD pathophysiology. The interaction of dietary exposure with the genome is referred to as 'nutritional genomics,' which encompasses both 'nutrigenetics' and 'nutriepigenomics.' It is focused on revealing the biological mechanisms that entail both the acute and persistent genome-nutrient interactions that influence health and it may represent a promising field of study to improve both clinical and health nutrition practices. Thus, the premise of this review is to discuss the relevance of personalized nutritional advices as a novel therapeutic approach in NAFLD tailored management.

Keywords: nonalcoholic fatty liver disease; nutrigenomics; nutrigenetics; nutriepigenomics; gene-diet interaction

CURRENT STATUS OF EPIDEMIOLOGY, DIAGNOSIS, THERAPEUTICS, AND VACCINES FOR NOVEL CORONAVIRUS DISEASE 2019 (COVID-19)

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Coronavirus disease 2019 (COVID-19), which causes serious respiratory illness such as pneumonia and lung failure, was first reported in Wuhan, the capital of Hubei, China. The etiological agent of COVID-19 has been confirmed as a novel coronavirus, now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is most likely originated from zoonotic coronaviruses, like SARS-CoV, which emerged in 2002. Within a few months of the first report, SARS-CoV-2 had spread across China and worldwide, reaching a pandemic level. As COVID-19 has triggered enormous human casualties and serious economic loss posing global threat, an understanding of the ongoing situation and the development of strategies to contain the virus's spread are urgently needed. Currently, various diagnostic kits to test for COVID-19 are available and several repurposing therapeutics for COVID-19 have shown to be clinically effective. In addition, global institutions and companies have begun to develop vaccines for the prevention of COVID-19. Here, we review the current status of epidemiology, diagnosis, treatment, and vaccine development for COVID-19.

Keywords: 2019-nCoV, COVID-19, SARS-CoV-2, coronavirus, outbreak

CONTRIBUTIONS OF EOSINOPHILS TO HUMAN HEALTH AND DISEASE

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The human eosinophil, which typically comprises about 1–5% of all circulating leukocytes, has long been felt to favorably impact innate mucosal immunity but at times has also been incriminated in disease pathophysiology. Research into eosinophil biology, especially with the use of murine models, has uncovered a number of interesting contributions of eosinophils to health and disease. However, it appears that not all eosinophils from all species are created equal. It remains unclear, for example, exactly how having eosinophils benefits the human host when helminth infections in the developed world have become scarce. This review will focus on our current state of knowledge as it relates to human eosinophils from birth to death, from circulation to tissue accumulation, in sickness and in health. When information on aspects of human eosinophil biology are lacking, lessons learned from relevant mouse studies will be discussed, with the understanding that such information may or may not directly apply to human biology and disease. The use of recently approved biologics that selectively target eosinophils, (i.e., precision pharmacology) is now providing the medical community with an exciting opportunity to directly test hypotheses in people by defining the contribution of this cell in eosinophil-associated diseases such as asthma and others. While it is an exciting time to be an "eosinophilosopher", there remain a number of important challenges and unmet needs in this field that provide opportunities for future studies and advancement as we explore the contributions of this enigmatic cell.

Keywords: Eosinophil; eosinophilia; hematopoiesis; cytokines; phenotype; adhesion; migration; function; eosinophil-related diseases; hypereosinophilic syndromes; biomarkers; biologics; treatments.

IMMUNOLOGIC EFFECTS OF VITAMIN D ON HUMAN HEALTH AND DISEASE

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Vitamin D is responsible for regulation of calcium and phosphate metabolism and maintaining a healthy mineralized skeleton. It is also known as an immunomodulatory hormone. Experimental studies have shown that 1,25-dihydroxyvitamin D, the active form of vitamin D, exerts immunologic activities on multiple components of the innate and adaptive immune system as well as endothelial membrane stability. Association between low levels of serum 25-hydroxyvitamin D and increased risk of developing several immune-related diseases and disorders, including psoriasis, type 1 diabetes, multiple sclerosis, rheumatoid arthritis, tuberculosis, sepsis, respiratory infection, and COVID-19, has been observed. Accordingly, a number of clinical trials aiming to determine the efficacy of administration of vitamin D and its metabolites for treatment of these diseases have been conducted with variable outcomes. Interestingly, recent evidence suggests that some individuals might benefit from vitamin D more or less than others as high inter-individual difference in broad gene expression in human peripheral blood mononuclear cells in response to vitamin D supplementation has been observed. Although it is still debatable what level of serum 25-hydroxyvitamin D is optimal, it is advisable to increase vitamin D intake and have sensible sunlight exposure to maintain serum 25-hydroxyvitamin D at least 30 ng/mL (75 nmol/L), and preferably at 40–60 ng/mL (100–150 nmol/L) to achieve the optimal overall health benefits of vitamin D.

Keywords: vitamin D; immune function; 25-hydroxyvitamin D; 1,25-dihydroxyvitamin D; immunomodulation; autoimmune disorders; infectious diseases; lymphocytes; monocytes; macrophages; multiple sclerosis; type 1 diabetes; inflammation; endothelial membrane stability.

Notes and News

(MH Samorita Med Coll J 2020; 3(2): 90)

CME presentations
(January-March 2020)

No.	Date	Department	Presenter	Topic
1	09.01.2020	Psychiatry	Prof. Dr.Md. Enayet Karim Professor & Head	Post –Partum mental disorders
2	23.01.2020	Pathology	Dr. Anika Tasnim Lecturer Dr. Farzana Mohsin Lecturer Dr. Fariana Saika Ruthmila Lecturer Dr. Meheronnesa Moutosi Lecturer	Leukaemia:Its types and lab diagnosis
3	20.02.2020	Orthopaedics	Dr. Shah Md. Samsul Hoque Associate Professor	Management of Avascular necrosis of femoral head
4	05.03.2020	Orthodontics	Dr. Umme Hafsa Lima Intern Doctor	Introduction and Prevention of malocclusion of teeth
5	12.03.2020	Medicine,Paediatrics & Microbiology	Dr. Dibya Jyoti Roy Intern doctor Dr. Shuvo Acharjia Intern doctor Dr. Shorme Rahman Intern doctor Bijoy Mehta 4th year MBBS student	Pandemic Corona Virus as global medical emergency
6	19.03.2020	Surgery	Dr. Riddita Mustica Assistant Registar	Updates on management of Hernia

Following students obtained honours in respective subjects against their name

Name	course	Type of Exam	Year of Exam	Exam.Roll No.	Subject
Farzana Tasnim	MBBS	First Professional	May, 2020	4556	Anatomy
Sumaiya Jahan Meem	MBBS	First Professional	May, 2020	4559	Anatomy
Mavilla Sreeja Charanya	MBBS	First Professional	May, 2020	4574	Anatomy

OBITUARY

Alhaj Mockbul Hossain

Alhaj Mockbul Hossain is the Founder Chairman of MH Samorita Hospital and Medical College, MH Samorita Dental unit and MH Samorita Nursing institute, Samorita Hospital Ltd. Spread of medical, dental and nursing education were his dream. He rendered immense support and inspiration for publication of our medical college journal.

He has established MH Samorita Hospital to provide low cost health care to the common people of the country and has established a Hospital in the name of his father and mother in his village home for free treatment of the poor people of the village.

He was born in 1950 in Bikrampur in an aristocratic Muslim family. He obtained his M.A and L.L.B. degree from Dhaka University. He is a successful politician, businessman, industrialist, journalist, lawyer and organizer. It is pertinent to point out that he was honorable Member of Parliament and CIP (Commercially Important Person) of our country.

He was one of the organizers of mass movement in the sixties.He was imprisoned for several times.He was the founder Head of the Sechhashebak League, affiliated to the Bangladesh Awami League and served as a member of the advisory council of the Bangladesh Awami league until his death.

He has played an important role in the development of the country's education.He has built a large number of educational institutions with his own hands other than MHSHMC, namely- City University, City Engineering Institute, Alhaj Mockbul Hossain University College, Dhaka International University, Mohammadpur Kendriyo College, Mohammadpur Law College. He has also established institution for the better Islamic education of the neglected and orphan children-Mohammadpur Jamia Madrasha Orphanage & Mosque Complex.

He also established many financial and industrial establishments like-Sandhani Life Insurance Co Ltd, Purabi General Insurance Co Ltd, Panna Textile Mills Ltd, Panna Spinning Mills Ltd, Amico Laboratories Ltd, Mona Group of Garments Ltd, Mona Financial Consultancy & Securities Ltd.

He has always engaged himself for the welfare of the people of the country and involved with the Abahoni Limited as director ,Member of Bikrampur Samity, Andho Kallayan Samity, Dhanmondi Club, Baridhara Club and Gulshan Club Limited.

Alhaj Mockbul Hossain passed away on May 24,2020 at CMH, Dhaka at the age of 70, after being infected with the global pandemic COVID-19, while providing financial and food assistance to the people. He has left behind his dearest wife Mrs. Golam Fatima Tahera Khanam, two sons- Mr. Ahsanul Islam Titu, Member of Parliament and Mr. Mojibul Islam Panna, renowned businessman, 8 grandchildren and a host of colleagues and relatives to mourn his death. He was laid to rest in Mohammadpur graveyard, Dhaka according to his last wish.

May Allah rest his soul in peace !

Prof. Dr. Sabbir Quadir
Professor & Head
Department of Ophthalmology
MH Samorita Hospital & Medical College