J

A

M

C

J

Journal of Army Medical College Jashore

BMDC
Approved

ISSN : 2780-1135 (Print)

JOURNAL OF ARMY MEDICAL COLLEGE JASHORE

Volume - 3
Number - 1
January 2022

An Official Organ of Army Medical College Jashore

Website: https://amcjbd.org

Journal of Army Medical College Jashore (JAMCJ)
January 2022 | Volume 3 | Number 1
ISSN: 2789-1135 (Print)

Name of the Reviewers

Back Cover Inner

Journal of Army Medical College Jashore (JAMCJ)
January 2022 | Volume 3 | Number 1
ISSN: 2789-1135 (Print)

Table of Contents

Front Cover Inner

JOURNAL OF ARMY MEDICAL COLLEGE JASHORE

January 2022 | Volume 3 | Number 1

ISSN: 2789-1135 (Print)

Journal of Army Medical College Jashore (JAMCJ) is leading, open access, peer-reviewed scientific journal on medical science for rapid publication of articles published Army Medical College Jashore, Jashore Cantonment, Bangladesh. This journal provides quick initial decisions followed by a high-quality medical editing service and an excellent publishing service to its authors. This journal has been launched since January 2020 and is continuing. **JAMCJ** is published 2 times per year. This journal aims to publish scientifically written, evidence-based articles from all disciplines of medical sciences and clinical practice, preventive medicine, epidemiology as well as healthcare research. It provides a great scope to publish different kinds of articles including original research papers, reviews of specific topics, case reports and short research communications. Submissions of basic and clinical research both are considered. Manuscripts should present novel findings addressing significant questions in clinical medicine research and practice, in the form of original research articles, editorial, review articles, short communications, case reports, letter to the editor, and others. In addition to that **JAMCJ** publishes studies performed by multi-center groups in the various disciplines of medicine, including clinical trials and cohort studies from large patient populations, specifically phase I, phase II, and phase III studies performed under the auspices of groups such as general clinical research centers, cooperative oncology groups, etc. Reports of patients with common presentations or diseases, especially studies that delineate the natural history and therapy of important conditions are also published. Reviews oriented to the practicing internist and diagnostic puzzles, complete with images from a variety of specialties are also published. Careful physiological or pharmacological studies that explain the normal function or the body's response to disease as well as analytic reviews such as meta-analyses and decision analyses using a formal structure to summarize an important field are acceptable to publish.

It is printed on acid free paper.

Please contact editorial office for further inquiry:

Brig Gen Mahbuba Sultana
Editor-in-Chief
Journal of Army Medical College Jashore
Jashore Cantonment Jashore, Bangladesh
ISSN: 2789-1135 (Print)
Email: amcj.journal.editorinchief@gmail.com
Website: https://amcjbd.org

Journal of Army Medical College Jashore (JAMCJ)
January 2022 | Volume 3 | Number 1
ISSN: 2789-1135 (Print)

Published By

Brig Gen Mahbuba Sultana
Principal
Professor & Head, Paediatrics
Army Medical College Jashore
Jashore Cantonment Jashore, Bangladesh

Correspondents

Dr. Omma Hafsa Any
Associate Professor & Head, Pharmacology & Therapeutics
Army Medical College Jashore
Jashore Cantonment Jashore, Bangladesh
Cell: +8801707543140
Email: omma.hafsa.anee@gmail.com

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 1-2
ISSN : 2789-1135 (Print)

Editorial ***Open Access***

Reemergence of Measles: Bangladesh Perspective

Mahbuba Sultana

Principal & Professor of Paediatrics, Army Medical College Jashore, Bangladesh

Measles is an acute highly contagious vaccine-preventable childhood disease caused by a single-stranded lipid-enveloped RNA virus in the family Paramyxoviridae and genus Morbillivirus. It is endemic virtually in all parts of the world. Measles tends to occur in epidemics when the proportion of susceptible children reaches about 40 percent[1]. When the disease introduced into a virgin community more than 90 percent of that community will be infected[1]. The Global measles and Rubella strategic plan 2012-20 period saw a significant reduction in the measles and rubella disease burden, a steep increase in the introduction of a second dose of measles-containing (MCV_2) and rubella vaccines, and improvements in surveillance. During 2018, approximately 346 million people received measles vaccination through 45 supplementary immunization activities (SIAs) in 37 countries. Estimated measles-related death declined by 73 percent and estimated cases by 76 percent from 2000 to 2018. It still accounted for an estimated 9.7 million cases and more than 140,000 measles related deaths worldwide during 2016[2]. Measles responsible for about 2 per cent of under-five mortality worldwide[3].

The incidents of devastating complications and sequelae of pre-vaccine era have been plummeted by the collaborative global vaccination initiatives. However, in spite of the availability of the safe, potent and cost-effective vaccine, the hard fought gains against measles are threatened now and the number of measles cases has soared in recent years. The causes of the outbreaks vary but the sub-optimal vaccine delivery is at the root of them in eliminating the last pockets of the unvaccinated residents is the hardest. Before implementation of the National Measles Vaccination program in 1963, approximately 500,000 persons in the United States were reported to have had measles every year, of whom 500 died, 48,000 were hospitalized, and another 1,000 had permanent brain damage[4]. Elimination of measles from a country means the absence of endemic measles cases for a period of ≥12 months in the presence of a high-quality epidemiological surveillance which is supported by a laboratory network. In 2019, member countries of WHO South-East Asia Region adopted a "Strategic Plan for Measles and Rubella Elimination 2020-2024" to prevent deaths and disabilities caused by these highly infectious childhood killer diseases[5]. In view of the resurgence of measles in many countries of the world, the cardinal question asked by many is whether it will be really possible to eliminate this disease globally by the year 2024. World health organization recommend that the first and second doses of measles containing vaccine should be given at ages 9 months and 15 to 18 months respectively in countries with high rates of measles transmission.

Bangladesh initiated the Expanded Program of Immunization on 7th April, 1979. Single dose measles vaccine for children aged 9 months was introduced in immunization program in 1989 and second dose was administered at 15 months of age since 2012. In 2015, estimated measles routine vaccine national coverage increased up to 92% for first dose of measles vaccine and 81% for the second dose[6]. Apart from high routine vaccine coverage nationwide, Bangladesh has implemented the strategy to provide a second opportunity for measles vaccination through supplementary immunization activities. Several other initiatives like strengthening the case-based surveillance system, developing and maintaining an accredited measles laboratory network to reach the goal of elimination of measles have been adopted. SIAs were carried out in 2005-2006, 2010, 2014 and 2019. After implementation of nationwide SIAs there was a drastic decline in the occurrence of the disease. In Bangladesh, incidence of measles cases decreased from 40 to 6 per million during 2000-2016 which constituted to a reduction up to 84%. In 2005-2006, confirmed measles cases dropped to 6 from 14,877 (2005). Unfortunately, the rate of occurrence of the disease was varying in the subsequent years. In 2016, measles cases increased to 972 confirmed cases in Bangladesh[7]. A program assessment was conducted using WHO Programmatic Risk Assessment Tool for measles in 2016 and it was found that 8 districts were at very high risk for measles transmission, 13 districts at high risk, 24 and 19 districts at medium risk and low risk respectively[8].

A multitude of factors pose challenges in achieving and maintaining the elimination of measles. It is primarily due to disinclination amongst parents to vaccinate their children, explosive outbreaks of measles in both developed and

Correspondence: Brig Gen Mahbuba Sultana, FCPS, DCH (Pediatrics) Principal, Professor & Head, Pediatrics, Army Medical College Jashore, Jashore Cantonment Jashore, Bangladesh;
email: amcj.journal.editorinchief@gmail.com
Cell no.: 01769555742

developing countries and international travelling especially to measles endemic areas[9]. The reason of disinclination amongst the parents to vaccinate their children is based on a conflicting vaccine-safety misinformation which arose by an article published in Lancet demonstrating a link between measles–mumps–rubella (MMR) vaccine and the development of autism in children. Although several studies have now thoroughly debunked that work, it gained attention on some social media networks and continues to be enforced by a small group of anti-vaccine activists[10]. Consequently, there has been a sharp fall in vaccination rates. Another cause behind the growing number of unvaccinated individuals accounts to be the unfamiliarity alongside lack of dread for the outcome of measles infection[11]. In addition, regarding inter-individual transmission dynamics, the fact that one measles virus infected person can be the source to infect 12-18 peoples which makes super spreader part of the picture.

The new challenge for measles elimination in Bangladesh is Rohingya refugees. Currently, there are more than 800,000 Rohingya refugees living in Bangladesh. About 480,000 have fled Rakhine since August 25, 2017 and thousands more are arriving every day. According to UNICEF, 60% of these new refugees are children below the age of 18. In the third week of September 2017, a vaccination campaign against measles, rubella and polio was conducted to immunize 150,000 Rohingya children below the age of 15 in 68 refugee settlements close to the border with Myanmar. The seven-day campaign is led by the Ministry of Health of the government of the people's republic of Bangladesh with support from UNICEF and WHO. With the growing number of Rohingya refugees, UNICEF and WHO are supporting the Ministry of Health to strengthen routine immunization program, assisting the Ministry to expand the number of doctors, nurses and lab technicians to reinforce maternal, newborn, child and adolescent health services, to strengthen other health support system to improve quality of life, strengthening health coordination for a better response at the field level, strengthening early warning system and surveillance for outbreak prone diseases and strengthening health data through supporting Health Management Information System.

Bangladesh has taken several initiatives like introduction of MCV_2 in the national immunization program, strengthening the case-based surveillance system to reach the goal of elimination of measles by 2024. But there are some issues that challenge the goal. Hence, Bangladesh will have to implement the following measures to overcome the challenges: carry out risk assessments on annual basis; prepare risk mitigation plans; carry out an immediate follow-up measles-rubella SIA all over the country so that current immunity gap among children aged 9-59 months could be addressed effectively; develop capacity to conduct epidemiologic investigations; and develop outbreak preparedness and capacity to prompt response in identifying and containing outbreaks. However, as the deadline for measles elimination from our country is knocking at the door, Bangladesh will have to implement these measures at a much quicker pace.

References

1. Park K. Epidemiology of communicable diseases. In: Park's Textbook of Prevention and Social medicine, 26th Edi. 2021, p.161.
2. Measles and Rubella Initiative (2020), Measles and Rubella Strategic Framework, 2021-2030.
3. WHO 2014, World Health Statistics 2014.
4. Odei MP. Measles is in the news yet again. J Family Med Prim Care. 2018; 7(6): 1166-1172.
5. World Health Organization. Outbreak news: measles outbreaks in Europe. Geneva: World Health Organization; 2011.
6. Khanal S, Bohara R, Chacko S, Sharifuzzaman M, Shamsuzzaman M, et al. Progress toward Measles Elimination-Bangladesh, 2000-2016. MMWR 2017;66(28): 753-757
7. Khanal S, Bohara R, Chacko S, Sharifuzzaman M, Shamsuzzaman M, Goodson JL, et al. Progress toward measles elimination Bangladesh, 2000–2016. Morb Mortal Wkly Rep. 2017;66(28):753-757
8. Lam E, Schluter WW, Masresha BG, Teleb N, Brav-Alcántara P, Shefer A, et al. Development of a district-level programmatic assessment tool for risk of measles virus transmission. Risk Anal. 2017; 37(6): 1052-1062.
9. Fiebelkorn AP, Redd SB, Gallagher K, Rota PA, Rota J, Bellini W, et al. Measles in the United States during the post-elimination era. J Infect Dis. 2010; 202(10):1520-1528
10. Taylor B, Miller E, Farrington C, Petropoulos MC, Favot-Mayaud I, Li J, et al. Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association. Lancet. 1999; 353(9169):2026-2029
11. McLaren Jr RA, Stein JL, Minkoff H. Measles: there is no vaccine against vaccine phobia. Am J Perinat. 2019;15(8): 201-203

[Journal of Army Medical College Jashore January 2022;3(1): 1-2]

JOURNAL OF ARMY MEDICAL COLLEGE JASHORE

INSTRUCTIONS TO AUTHOR(S)

ISSN: 2789-1135 (Print)

Aims and Scopes of the Journal

Journal of Army Medical College Jashore (JAMCJ) is an open access, peer-reviewed, scholarly, scientific medical journal. This journal aims to publish scientifically written, evidence-based articles from all disciplines of medical sciences, clinical practice, nursing, preventive medicine, epidemiology and healthcare research. Manuscripts should present novel findings addressing significant questions in clinical medicine research and practice, in the form of original articles, editorial, reviews, short communications, case reports, letter to the editor and others. In addition to that **JAMCJ** publishes studies performed by multi-center groups in the various disciplines of medicine, including clinical trials and cohort studies. Careful physiological or pharmacological studies that explain normal function or the body's response to disease as well as analytic reviews such as meta-analyses and decision analyses using a formal structure to summarize an important field are acceptable to publish.

Peer Review Process: This journal is committed to peer-review and upholding the highest standards of review. Once the submitted paper has been assessed for suitability by the editor, it will then be double blinded peer reviewed by independent, anonymous expert referees. The quality, validity, and relevance are assessed by independent peers within the relevant field.

Submission of Manuscript: Authors should submit electronic version (Microsoft word doc) of the manuscript to the editor via editor email (amcj.journal.editorinchief@gmail.com). Accepted papers will be acknowledged and will be processed further; if the papers are rejected, the decision will be informed the corresponding author. Acceptance or rejection of the manuscript for publication in journal will be decided after peer review or by the decision of editorial team and will be informed to corresponding author within 72 working hours from the time of submission.

Preparing a Manuscript: Authors should keep their manuscripts as short as they reasonably can (the total number of words should not exceed 3500 to 7500). Page number should appear in the upper right hand corner of each page, beginning with the title page. The language of manuscript must be simple and explicit. Author's and Co-author's name or any other identification should not appear anywhere in the body of the manuscript to facilitate blind review.

Types of Manuscript: The following categories of manuscripts are accepted for this journal like Original Research Articles, Systematic Review or Meta-Analysis, Review Articles, Short communications, Case reports and Letter to Editor.

Original Research Articles: It should be arranged into the following sections:

Title Page: It should be paginated as page 1 of the paper. It should carry the title, authors' names and their affiliations, running title, address for correspondence including Email address, mobile number and ORCID Id.

Title: Must be informative, specific and short and should not exceed 100 words.

Authors and Affiliations: The names of authors and their appropriate addresses should be given. It should be made clear which address relates to which author.

Running Title: It is a short title typed in the journal at the right top corner of right hand page of the article (except the lead page). A short running title of not more than 40 characters should be given.

Address of Correspondence: The corresponding author's contact address should be given in the title page. The fax number (if available) may be mentioned. The Email ID and mobile number of the corresponding author must also be provided.

Abstract and Keywords

Abstract: It must start on a new page carrying the following information: (a) Title (b) Abstract body (c) Key words (d) Running title. It should not exceed 350 words excluding the title and the keywords. The abstract must be concise, clear and informative rather than indicative. The abstract must be in a structured form consisting of background, objectives, methodology, result and conclusion.

Keywords: A list of 3-8 keywords should be provided. The words found in title may be given as keywords. All keywords should be provided according to MeSH terms at: http://www.nlm.nih.gov/mesh/MBrowser.html.

Introduction: This section should state the relevance and background to the study, its rationale and general objective. It should not exceed 450 to 500 words. Last sentence of this section will be the general objective of the study.

Methodology: This section should deal with how the work was carried out. The procedure adopted should be described in sufficient detail to allow the study to be interpreted and repeated by the readers, if necessary. The number of subjects, the number of groups studied, the study design, sources of drugs with dosage regimen or instruments used, statistical methods and ethical aspects must be mentioned under the section in text format not in structured format. The details of statistical analysis used and the level of significance should be stated.

Results: The results should be stated concisely without comments. It should be presented in logical sequence in the text with appropriate reference to tables and/or figures. The same data should not be presented in both tabular and graphic forms. Simple data may be given in the text itself instead of figures or tables. Avoid discussions and conclusions in the results section.

Discussion: This section should deal with the interpretation, rather than recapitulation of results. It is important to discuss the new and significant observations in the light of previous work. Discuss also the weaknesses or pitfalls in the study.

Conclusion: Conclusion must be drawn considering the strengths and weaknesses of the study.

Acknowledgements: Acknowledge only persons who have contributed to the scientific content or provided technical support. Sources of financial support should be mentioned.

References: Papers which have been submitted and accepted but not yet published may be included in the list of references with the name of the journal and indicated as "In press". The "unpublished observations" and "personal communications" may not be used as references but may be

inserted (in parentheses) in the text. References are to be cited in the text by superscripted number and should be in the order in which they appear. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. The references must be verified by the author(s) against the original documents. The list of references should be in the Modified Vancouver style.

Tables: The number of table should be 3 or 4 in number. Each table must be self-explanatory and presented in such a way that they are easily understandable. It should be typed with double spacing and numbered consecutively with Arabic numerals. Provide a short descriptive caption above each table with foot notes and/or explanations underneath. The number of observations, subjects and the units of numerical figures must be given.

Figures: Each figure must be numbered and a short descriptive caption must be provided. For graphs and flow charts, it is not necessary to submit the photographs. A manually prepared or computer drawn figure with good contrast on a good quality paper is acceptable. The approximate position of each figure should be marked on the margin of the text.

Systematic Review or Meta-Analysis: These should be critical assessments of current evidence covering a broad range of topics of concern to those working in the specific field of journal. Systematic reviews should be 4000-5000 words (abstracts to be structured as above). Authors should report systematic reviews and meta-analyses in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.

Meta-Analysis of RCT: A MOOSE checklist is required for meta-analysis of RCT.

Review Articles: These should contain title page, abstract (need not be structured) and key words. The text proper should be written under appropriate sub-headings. The total number of text words should not exceed 10000 and the total number of figures and tables should not be more than 7.

Short Communications

The manuscript should not be divided into sub-sections. It may have up to 1200 words (including a maximum of 5 references) and one figure or one table.

Case Reports

The case report should contain abstract (need not be structured), keywords, introduction, case presentation, discussion, conclusion & references (including a maximum of 20 references) in a sequential way. The number of case may be one or two, not more than three.

Letter to the Editor

A letter can have a maximum of 1000 words (including a maximum of 25 references) with one simple figure or table. The manuscript should not have sub-sections.

Address of Editorial Office
Dr. Omma Hafsa Any
Executive Editor, Journal of Army Medical College Jashore
Associate Professor of Pharmacology, Army Medical College Jashore
Jashore Cantonment Jashore, Bangladesh
ISSN: 2789-1135 (Print)
Email: amcj.journal.editorinchief@gmail.com
Website: https://amcj-bd.org

AUTHORSHIP/ WHO WILL BE THE AUTHORS OF THE ARTICLE?

Papers should only be submitted for consideration once the authorization of all contributing authors has been gathered. Those submitting papers should carefully check that all those whose work contributed to the paper are acknowledged as contributing authors.

Authorship credit should be based on

1. substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
2. drafting the article or revising it critically for important intellectual content; and
3. final approval of the version to be published.

Authors should meet conditions 1, 2, and 3.

When a large, multicenter group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship/contributorship defined above, and editors will ask these individuals to complete journal-specific author and conflict-of-interest disclosure forms.

When submitting a manuscript authored by a group, the corresponding author should clearly indicate the preferred citation and identify all individual authors as well as the group name. Journals generally list other members of the group in the Acknowledgments.

TYPES OF CONFLICT OF INTEREST

The followings are examples of possible conflicts of interest:

1. Source of funding
2. Paid consult to sponsor
3. Study investigator funded by sponsor
4. Employee of sponsor
5. Board membership with sponsor
6. Stock holder for mentioned product
7. Patent inventor for mentioned product
8. Any financial relationship to competitors of mentioned product

This information will be kept confidential. The Editor will discuss the method of disclosure of any potential conflict of interest with corresponding authors on an individual basis.

Author	No Conflict	Conflict (Please specify)
_____	_____	_____
_____	_____	_____
_____	_____	_____

RESEARCH ETHICS REGULATION

A. Researchers should be honest about their research. Researchers need to have a high ethical standard at all times during the research, in areas such as receiving funds for research, publishing research results, and fairly compensating participants. More specifically, research papers that are forged, altered, plagiarized, overlapped, and/or dishonest cannot be published either online or in journal and are not eligible for research funds.

1. Forgery, Alteration, Plagiarism

a. Forgery: making up data or research results that do not exist
b. Alteration: fabricating research materials, equipment, or processes, or changing/deleting research results intentionally to distort research contents or results.
c. Plagiarism: using other's ideas, research (process and contents), and/or results without proper authorization or citation.

2. Overlapped Publication and Dishonest Research

a. Publishing research papers that contain the same or similar contents to that which were/are published in other journals or books in the society's memoir, or publishing research papers that are/were published in the society's memoir in other journals or books.
b. Multiple or duplicate publication can be allowed after a review from the Publication Council, if it is qualified under the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org)
c. Wrongful Research Paper Author Indication: either refusing to grant a qualification to publish (without proper reasons) to a person who contributed science and/or technology with his/her research contents or results, or granting qualification to publish to a person who did not contribute to science and/or technology because of a wish to express appreciation or honor.

B. If a research object is human, researchers should follow the Declaration of Helsinki (http://www.wma.net). Details are as follows:

1. Researchers should fully explain the purpose and methods of research as well as possible mental and physical harm that could occur during research participation. If he/she is to publish the research results, he/she has to indicate that on the paper
2. Researchers cannot write down participants' names or initials. In case of possible disclosure of participants' identification through pictures face or anything similar, researchers should receive written informed consent from the participants or their guardians
3. Research should receive an approval from Institutional Review Board and indicate it on the paper if one wishes to publish the research results
4. Any research that deals with clinical trial should be registered to the primary national clinical trial registration site such as http://ncrc.cdc.go.kr/crics, or other sites accredited by WHO or International Committee of Medical Journal Editor.

C. If a research object is animal, researchers should follow these general rules.

1. Researchers should indicate what he/she did to minimize the pain or discomfort that experiment subjects went through.
2. Researchers should indicate that he/she did not violet NIH guideline (NIH Guide for the Care and Use of Laboratory Animals).
3. When necessary, the society can ask for a written consent and an approval letter issued by Animal Ethics Committee.

D. Conflicts of interest or financial support should be indicated on the paper.

Copyright Options: Copyright allows you to protect your original material, and stop others from using your work without your permission. This journal offers a number of different license and reuse options, including Creative Commons licenses preferably CC By-NC.

Copyright Assignment: You assign copyright in your article to the publisher or society. They manage the intellectual property rights (IPR) in your article, maintain your article as the Version of Record, and can represent your article in cases of copyright infringement.

Complying with Ethics of Experimentation: Please ensure that all research reported in submitted papers has been conducted in an ethical and responsible manner, and is in full compliance with all relevant codes of experimentation and legislation. All papers which report in vivo experiments or clinical trials on humans or animals must include a written statement in the Methods section. This should explain that all work was conducted with the formal approval of the local human subject or animal care committees (institutional and national), and that clinical trials have been registered as legislation requires. Authors who do not have formal ethics review committees should include a statement that their study follows the principles of the Declaration of Helsinki.

Consent: All authors are required to follow the ICMJE requirements on privacy and informed consent from patients and study participants. Please confirm that any patient, service user, or participant (or that person's parent or legal guardian) in any research, experiment, or clinical trial described in your paper has given written consent to the inclusion of material pertaining to themselves, that they acknowledge that they cannot be identified via the paper; and that you have fully anonymized them. Where someone is deceased, please ensure you have written consent from the family or estate. Authors may use Patient Consent Form, which should be completed, saved, and sent to the journal if requested.

Health and Safety: Please confirm that all mandatory laboratory health and safety procedures have been complied with in the course of conducting any experimental work reported in your paper. Please ensure your paper contains all appropriate warnings on any hazards that may be involved in carrying out the experiments or procedures you have described, or that may be involved in instructions, materials, or formulae. Please include all relevant safety precautions; and cite any accepted standard or code of practice. Authors working in animal science may find it useful to consult the International Association of Veterinary Editors' Consensus Author Guidelines on Animal Ethics and Welfare and Guidelines for the Treatment of Animals in Behavioural Research and Teaching. When a product has not yet been approved by an appropriate regulatory body for the use described in your paper, please specify this, or that the product is still investigational.

DECLARATION AND COPYRIGHT TRANSFER FORM
(To Be Signed By All Authors)

To
The Editor
Journal of Army Medical College Jashore

Subject: Declaration and Copyright Transfer Form

I/We, the undersigned author(s) of the manuscript entitled……..... hereby declare that the above manuscript which is submitted for publication in the **Journal of Army Medical College Jashore (JAMCJ)** is NOT under consideration elsewhere. The manuscript is NOT published already in part or whole (except in the form of abstract) in any journal or magazine for private or public circulation. No part of this manuscript (referenced or otherwise) has been copied verbatim from any source. Reproduced text, if any has been given in italics and within quotes.

I/we give consent for publication in any media (print, electronic or any other) and transfer copyright to the **Journal of Army Medical College Jashore (JAMCJ)**. I/we do not have any conflict of interest (financial or other) other than those declared*.

I/we have read the final version of the manuscript and am/are responsible for what is said in it. I/we are ready to take public responsibility for the content of the paper. The work described in the manuscript is my/our own and my/our individual contribution to this work is significant enough to qualify for authorship. No one who has contributed significantly to the work has been denied authorship and those who helped have been duly acknowledged. I/we also agree to the authorship of the article in the following sequence:

Author's name	**Signature**
1. _____	_____
2. _____	_____
3. _____	_____
4. _____	_____

Note: All authors are required to sign this form; No addition, deletion or change in the sequence of authors is allowed at a later stage without valid reasons; If the authorship is contested before publication the manuscript will be either returned or kept in abeyance till the issue is resolved; This form may be photocopied and used.

*Conflicts of interests if any, the details must be declared in a separate sheet.

JOURNAL OF ARMY MEDICAL COLLEGE JASHORE

INSTRUCTIONS TO AUTHOR(S)

ISSN: 2789-1135 (Print)

Aims and Scopes of the Journal

Journal of Army Medical College Jashore (JAMCJ) is an open access, peer-reviewed, scholarly, scientific medical journal. This journal aims to publish scientifically written, evidence-based articles from all disciplines of medical sciences, clinical practice, nursing, preventive medicine, epidemiology and healthcare research. Manuscripts should present novel findings addressing significant questions in clinical medicine research and practice, in the form of original articles, editorial, reviews, short communications, case reports, letter to the editor, and others. In addition to that **JAMCJ** publishes studies performed by multi-center groups in the various disciplines of medicine, including clinical trials and cohort studies. Careful physiological or pharmacological studies that explain normal function or the body's response to disease as well as analytic reviews such as meta-analyses and decision analyses using a formal structure to summarize an important field are acceptable to publish.

Peer Review Process: This journal is committed to peer-review and upholding the highest standards of review. Once the submitted paper has been assessed for suitability by the editor, it will then be double blinded peer reviewed by independent, anonymous expert referees. The quality, validity, and relevance are assessed by independent peers within the relevant field.

Submission of Manuscript: Authors should submit electronic version (Microsoft word doc) of the manuscript to the editor via editor email (amcj.journal.editorinchief@gmail.com). Accepted papers will be acknowledged and will be processed further; if the papers are rejected, the decision will be informed the corresponding author. Acceptance or rejection of the manuscript for publication in journal will be decided after peer review or by the decision of editorial team and will be informed to corresponding author within 72 working hours from the time of submission.

Preparing a Manuscript: Authors should keep their manuscripts as short as they reasonably can (the total number of words should not exceed 3500 to 7500). Page number should appear in the upper right hand corner of each page, beginning with the title page. The language of manuscript must be simple and explicit. Author's and Co-author's name or any other identification should not appear anywhere in the body of the manuscript to facilitate blind review.

Types of Manuscript: The following categories of manuscripts are accepted for this journal like Original Research Articles, Systematic Review or Meta-Analysis, Review Articles, Short communications, Case reports and Letter to Editor.

Reporting Guidelines: The guidelines listed below should be followed where appropriate. Please use these guidelines to structure your article.

- CONSORT Statement (http://www.consort-statement.org/) for reporting of randomised controlled trials
- STARD (www.stard-statement.org/) for reporting of diagnostic accuracy studies
- STROBE (http://www.strobe-statement.org/) for reporting of observational studies in epidemiology; Checklist for cohort, case-control, and cross-sectional studies (combined); Checklist for cohort studies; Checklist for case-control studies; Checklist for cross-sectional studies
- PRISMA (www.prisma-statement.org/index.htm) for reporting of systematic reviews
- MOOSE for reporting of meta-analyses of observational studies
- STREGA (www.medicine.uottawa.ca/public-health-genomics/web/eng/strega.html) for reporting of gene-disease association studies.
- The Equator Network (Enhancing the Quality and Transparency Of health Research) provides a comprehensive list of reporting guidelines. The web site of it is http://www.equator-network.org/resource-centre/library-of-health-research-reporting/library/

Original Research Articles: It should be arranged into the following sections:

Title Page: It should be paginated as page 1 of the paper. It should carry the title, authors' names and their affiliations, running title, address for correspondence including Email address, mobile number and ORCID Id.

Title: Must be informative, specific and short and should not exceed 100 words.

Authors and Affiliations: The names of authors and their appropriate addresses should be given. It should be made clear which address relates to which author.

Running Title: It is a short title typed in the journal at the right top corner of right hand page of the article (except the lead page). A short running title of not more than 40 characters should be given.

Address of Correspondence: The corresponding author's contact address should be given in the title page. The fax number (if available) may be mentioned. The Email ID and mobile number of the corresponding author must also be provided.

Abstract and Keywords

Abstract: It must start on a new page carrying the following information: (a) Title (b) Abstract body (c) Key words (d) Running title. It should not exceed 350 words excluding the title and the keywords. The abstract must be concise, clear and informative rather than indicative. The abstract must be in a structured form consisting of background, objectives, methodology, result and conclusion.

Keywords: A list of 3-8 keywords should be provided. The words found in title may be given as keywords. All keywords should be provided according to MeSH terms at: http://www.nlm.nih.gov/mesh/MBrowser.html.

Introduction: This section should state the relevance and background to the study, its rationale and general objective. It should not exceed 450 to 500 words. Last sentence of this section will be the general objective of the study.

Methodology: This section should deal with how the work was carried out. The procedure adopted should be described in sufficient detail to allow the study to be interpreted and repeated by the readers, if necessary. The number of subjects, the number of groups studied, the study design, sources of drugs with dosage regimen or instruments used, statistical methods and ethical aspects must be mentioned under the section in text format not in structured format. The details of statistical analysis used and the level of significance should be stated.

Results: The results should be stated concisely without comments. It should be presented in logical sequence in the text with appropriate reference to tables and/or figures. The same data should not be presented in both tabular and graphic forms. Simple data may be given in the text itself instead of figures or tables. Avoid discussions and conclusions in the results section.

Discussion: This section should deal with the interpretation, rather than recapitulation of results. It is important to discuss the new and significant observations in the light of previous work. Discuss also the weaknesses or pitfalls in the study.

Conclusion: Conclusion must be drawn considering the strengths and weaknesses of the study.

Acknowledgements: Acknowledge only persons who have contributed to the scientific content or provided technical support. Sources of financial support should be mentioned.

References: Papers which have been submitted and accepted but not yet published may be included in the list of references with the name of the journal and indicated as "In press". The "unpublished observations" and "personal communications" may not be used as references but may be inserted (in parentheses) in the text. References are to be cited in the text by superscripted number and should be in the order in which they appear. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. The references must be verified by the author(s) against the original documents. The list of references should be in the Modified Vancouver style.

Tables: The number of table should be 3 or 4 in number. Each table must be self-explanatory and presented in such a way that they are easily understandable. It should be typed with double spacing and numbered consecutively with Arabic numerals. Provide a short descriptive caption above each table with foot notes and/or explanations underneath. The number of observations, subjects and the units of numerical figures must be given.

Figures: Each figure must be numbered and a short descriptive caption must be provided. For graphs and flow charts, it is not necessary to submit the photographs. A manually prepared or computer drawn figure with good contrast on a good quality paper is acceptable. The approximate position of each figure should be marked on the margin of the text.

Systematic Review or Meta-Analysis: These should be critical assessments of current evidence covering a broad range of topics of concern to those working in the specific field of journal. Systematic reviews should be 4000-5000 words (abstracts to be structured as above). Authors should report systematic reviews and meta-analyses in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.

Meta-Analysis of RCT: A MOOSE checklist is required for meta-analysis of RCT.

Review Articles: These should contain title page, abstract (need not be structured) and key words. The text proper should be written under appropriate sub-headings. The total number of text words should not exceed 10000 and the total number of figures and tables should not be more than 7.

Short Communications

The manuscript should not be divided into sub-sections. It may have up to 1200 words (including a maximum of 5 references) and one figure or one table.

Case Reports

The case report should contain abstract (need not be structured), keywords, introduction, case presentation, discussion, conclusion & references (including a maximum of 20 references) in a sequential way. The number of case may be one or two, not more than three.

Letter to the Editor

A letter can have a maximum of 1000 words (including a maximum of 25 references) with one simple figure or table. The manuscript should not have sub-sections.

E**xamples of References – Modified Vancouver Style:** From Uniform Requirements for Manuscripts, www.icmje.org

1. Standard journal article: List the first six authors followed by et al.

Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreatobiliary disease. Ann Intern Med 1996;124(11):980-3

More than six authors: Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukaemia in Europe after Chernobyl: 5 year follow-up. Br J Cancer 1996;73:1006-12

2. Organization as author: The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 164: 282-4

3. Volume with supplement: Shen HM, Zhang QF. Risk assessment of nickel carcinogenicity and occupational lung cancer. Environ Health Perspect 1994;102 Suppl 1:275-82.

4. Issue with supplement: Payne DK, Sullivan MD, Massie MJ. Women's psychological reactions to breast cancer. Semin Oncol 1996; 23(1 Suppl 2):89-97.

5. Personal author(s): Ringsven MK, Bond D. Gerontology and leadership skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996.

6. Editor(s), compiler(s) as author: Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.

7. Chapter in a book: Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: Pathophysiology, diagnosis, and management. 2nd ed. New York: Raven Press; 1995. p. 465-78.

8. Conference paper: Bengtsson S, Solheim BG. Enforce-ment of data protection, privacy and security in medical informatics. In: Lun KC,

Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Infor-matics; 1992 Sep 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. p. 1561-5
9. Dissertation/Thesis: Kaplan SJ. Post-hospital home health care: the elderly's access and utilization [Dissertation/Thesis]. St. Louis (MO): Washington Univ.; 1995.
10. In press: (Note: NLM prefers "forthcoming" because not all items will be printed.) Leshner AI. Molecular mechanisms of cocaine addiction. N Engl J Med. In press 1996·

Address of Editorial Office
Dr. Omma Hafsa Any
Executive Editor, Journal of Army Medical College Jashore &
Associate Professor of Pharmacology, Army Medical College Jashore,
Jashore Cantonment, Jashore, Bangladesh
ISSN: 2789-1135 (Print)
Email: amcj.journal.editorinchief@gmail.com
Website: https://amcj-bd.org

AUTHORSHIP/ WHO WILL BE THE AUTHORS OF THE ARTICLE?

Papers should only be submitted for consideration once the authorization of all contributing authors has been gathered. Those submitting papers should carefully check that all those whose work contributed to the paper are acknowledged as contributing authors.

Authorship credit should be based on

1. substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
2. drafting the article or revising it critically for important intellectual content; and
3. final approval of the version to be published.

Authors should meet conditions 1, 2, and 3.

When a large, multicenter group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship/contributorship defined above, and editors will ask these individuals to complete journal-specific author and conflict-of-interest disclosure forms.

When submitting a manuscript authored by a group, the corresponding author should clearly indicate the preferred citation and identify all individual authors as well as the group name. Journals generally list other members of the group in the Acknowledgments.

The NLM indexes the group name and the names of individuals the group has identified as being directly responsible for the manuscript; it also lists the names of collaborators if they are listed in Acknowledgments.

- Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship.
- All persons designated as authors should qualify for authorship, and all those who qualify should be listed.
- Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.
- Please refer to the ICMJE Authorship guidelines at http://www.icmje.org/ethical_1author.html

DECLARATION AND COPYRIGHT TRANSFER FORM
(To Be Signed By All Authors)

To
The Editor
Journal of Army Medical College Jashore

Subject: Declaration and Copyright Transfer Form

I/We, the undersigned author(s) of the manuscript entitled……..... hereby declare that the above manuscript which is submitted for publication in the **Journal of Army Medical College Jashore (JAMCJ)** is NOT under consideration elsewhere. The manuscript is NOT published already in part or whole (except in the form of abstract) in any journal or magazine for private or public circulation. No part of this manuscript (referenced or otherwise) has been copied verbatim from any source. Reproduced text, if any has been given in italics and within quotes.

I/we give consent for publication in any media (print, electronic or any other) and transfer copyright to the **Journal of Army Medical College Jashore (JAMCJ)**. I/we do not have any conflict of interest (financial or other) other than those declared*.

I/we have read the final version of the manuscript and am/are responsible for what is said in it. I/we are ready to take public responsibility for the content of the paper. The work described in the manuscript is my/our own and my/our individual contribution to this work is significant enough to qualify for authorship. No one who has contributed significantly to the work has been denied authorship and those who helped have been duly acknowledged. I/we also agree to the authorship of the article in the following sequence:

Author's name	**Signature**
1. _____	_____
2. _____	_____
3. _____	_____
4. _____	_____

Note: All authors are required to sign this form; No addition, deletion or change in the sequence of authors is allowed at a later stage without valid reasons; If the authorship is contested before publication the manuscript will be either returned or kept in abeyance till the issue is resolved; This form may be photocopied and used.

*Conflicts of interests if any, the details must be declared in a separate sheet.

TYPES OF CONFLICT OF INTEREST

The followings are examples of possible conflicts of interest:

1. Source of funding
2. Paid consult to sponsor
3. Study investigator funded by sponsor
4. Employee of sponsor
5. Board membership with sponsor
6. Stock holder for mentioned product
7. Patent inventor for mentioned product
8. Any financial relationship to competitors of mentioned product

This information will be kept confidential. The Editor will discuss the method of disclosure of any potential conflict of interest with corresponding authors on an individual basis.

Author	No Conflict	Conflict (Please specify)
_____	_____	_____
_____	_____	_____
_____	_____	_____

RESEARCH ETHICS REGULATION

A. Researchers should be honest about their research. Researchers need to have a high ethical standard at all times during the research, in areas such as receiving funds for research, publishing research results, and fairly compensating participants. More specifically, research papers that are forged, altered, plagiarized, overlapped, and/or dishonest cannot be published either online or in journal and are not eligible for research funds.

1. Forgery, Alteration, Plagiarism

a. Forgery: making up data or research results that do not exist

b. Alteration: fabricating research materials, equipment, or processes, or changing/deleting research results intentionally to distort research contents or results.

c. Plagiarism: using other's ideas, research (process and contents), and/or results without proper authorization or citation.

2. Overlapped Publication and Dishonest Research

d. Publishing research papers that contain the same or similar contents to that which were/are published in other journals or books in the society's memoir, or publishing research papers that are/were published in the society's memoir in other journals or books.

e. Multiple or duplicate publication can be allowed after a review from the Publication Council, if it is qualified under the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org)

f. Wrongful Research Paper Author Indication: either refusing to grant a qualification to publish (without proper reasons) to a person who contributed science and/or technology with his/her research contents or results, or granting qualification to publish to a person who did not contribute to science and/or technology because of a wish to express appreciation or honor.

B. If a research object is human, researchers should follow the Declaration of Helsinki (http://www.wma.net). Details are as follows:

1. Researchers should fully explain the purpose and methods of research as well as possible mental and physical harm that could occur during research participation. If he/she is to publish the research results, he/she has to indicate that on the paper
2. Researchers cannot write down participants' names or initials. In case of possible disclosure of participants' identification through pictures face or anything similar, researchers should receive written informed consent from the participants or their guardians
3. Research should receive an approval from Institutional Review Board and indicate it on the paper if one wishes to publish the research results
4. Any research that deals with clinical trial should be registered to the primary national clinical trial registration site such as http://ncrc.cdc.go.kr/crics, or other sites accredited by WHO or International Committee of Medical Journal Editor.

C. If a research object is animal, researchers should follow these general rules.

1. Researchers should indicate what he/she did to minimize the pain or discomfort that experiment subjects went through.
2. Researchers should indicate that he/she did not violet NIH guideline (NIH Guide for the Care and Use of Laboratory Animals).
3. When necessary, the society can ask for a written consent and an approval letter issued by Animal Ethics Committee.

D. Conflicts of interest or financial support should be indicated on the paper.

Copyright Options: Copyright allows you to protect your original material, and stop others from using your work without your permission. This journal offers a number of different license and reuse options, including Creative Commons licenses preferably CC By-NC.

Copyright Assignment: You assign copyright in your article to the publisher or society. They manage the intellectual property rights (IPR) in your article, maintain your article as the Version of Record, and can represent your article in cases of copyright infringement.

Complying with Ethics of Experimentation: Please ensure that all research reported in submitted papers has been conducted in an ethical and responsible manner, and is in full compliance with all relevant codes of experimentation and legislation. All papers which report in vivo experiments or clinical trials on humans or animals must include a written statement in the Methods section. This should explain that all work was conducted with the formal approval of the local human subject or animal care committees (institutional and national), and that clinical trials have been registered as legislation requires. Authors who do not have formal ethics review committees should include a statement that their study follows the principles of the Declaration of Helsinki.

Consent: All authors are required to follow the ICMJE requirements on privacy and informed consent from patients and study participants. Please confirm that any patient, service user, or participant (or that person's parent or legal guardian) in any research, experiment, or clinical trial described in your paper has given written consent to the inclusion of material pertaining to themselves, that they acknowledge that they cannot be identified via the paper; and that you have fully anonymized them. Where someone is deceased, please ensure you have written consent from the family or estate. Authors may use Patient Consent Form, which should be completed, saved, and sent to the journal if requested.

Health and Safety: Please confirm that all mandatory laboratory health and safety procedures have been complied with in the course of conducting any experimental work reported in your paper. Please ensure your paper contains all appropriate warnings on any hazards that may be involved in carrying out the experiments or procedures you have described, or that may be involved in instructions, materials, or formulae. Please include all relevant safety precautions; and cite any accepted standard or code of practice. Authors working in animal science may find it useful to consult the International Association of Veterinary Editors' Consensus Author Guidelines on Animal Ethics and Welfare and Guidelines for the Treatment of Animals in Behavioural Research and Teaching. When a product has not yet been approved by an appropriate regulatory body for the use described in your paper, please specify this, or that the product is still investigational.

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 3-8
ISSN : 2789-1135 (Print)

Original Article ***Open Access***

Comparison of Infectious Complications between Internal Jugular and Subclavian Central Venous Access in Intensive Care Unit

Md. Enayet Karim[1], Arif Imtiaz Chowdhury[2], ASM Areef Ahsan[3], Reza Ershad[4], Manas Kanti Mazumder[5]

[1]Classified Specialist, Department of Anaesthesiology, Combined Military Hospital, Chattogram, Bangladesh; [2]Graded Specialist, Department of Anaesthesiology, Combined Military Hospital, Chattogram, Bangladesh; [3]Professor, Department of Critical Care Medicine, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh; [4]Professor, Department of Anaesthesiology, East-West Medical College, Dhaka. Bangladesh; [5]Assistant Professor, Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Abstract

Background: Central Venous Catheters (CVC) play an important role in treating critically ill patients in an Intensive Care Unit (ICU). **Objective:** The purpose of the present study was to compare the infectious complications between the Internal Jugular and Subclavian venous approaches so that clinicians may take advantage of that knowledge for insertion of a CVC in an individual patient. **Methodology:** This cross-sectional study was carried out prospectively in the Department of Critical Care Medicine at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh and Critical Care Centre at Combined Military Hospital (CMH), Dhaka, Bangladesh. The Catheters were inserted using Seldinger technique. During the study period, catheters that fulfilled the inclusion and exclusion criteria were taken. The catheters were inserted through Internal Jugular vein (IJV) and Subclavian venous access (SCV). The outcomes of all patients included in the study were noted at the end of ICU stay. **Results:** A total of 324 catheters were inserted of which 156 catheters were inserted through IJV and 168 catheters were inserted through SCV. About 46 patients developed infectious complications, which included exit site infections (16 patients), catheter tip colonization/infection (20 patients) and catheter-related blood stream infections (CRBSIs, 10 patients). Exit site infections, based on clinical signs of inflammation at the exit site, were suspected in 48 (14.20%) patients, but were microbiologically confirmed in only 16(4.94%) patients. Catheter tip colonization/infections were diagnosed in 20(6.17%) patients and CRBSIs in 10 (3.08%) patients. The overall incidence of catheter tip infections and CRBSIs were significantly higher in IJV route than SCV route ($p=0.02$). A significantly higher incidence of both CVC tip colonization/infection ($p<0.001$) and CRBSIs ($p=0.02$) were observed in patients with catheter in situ for more than 10 days in both IJV and SCV routes. Moreover, IJV cannulation with more than 10 days' duration had significantly higher incidence of catheter tip infection ($p=0.004$) and CRBSIs ($p=0.02$). The incidence of overall infectious complications was significantly more in IJV group than SCV group ($p=0.03$). **Conclusion:** Subclavian venousaccess was associated with a low rate of infectious complications in the Intensive Care Unit as compared with Internal Jugular access. *[Journal of Army Medical College Jashore January 2022;3(1):3-8]*

Keywords: Central venous access; Infectious complications; Intensive care unit

Introduction

Complications associated with central venous catheters (CVCs) have a major impact on the hospital course of patients admitted to the Intensive Care Unit (ICU) due to the morbidity, mortality and increased health care costs associated with them. Catheter related infections in the ICU are a cause of significant morbidity and add tremendously to the burden of health care costs[1]. A study among 55 ICUs in eight developing countries in the International Nosocomial Infection Control Consortium (INICC)

Correspondence: Colonel Md Enayet Karim, Classified Specialist in Anaesthesiology, Department of Anaesthesiology, Combined Military Hospital, Chattogram, Bangladesh; Email:enayet852@yahoo.com, Cell no.: +8801739988644;

revealed that CVC related blood stream infections accounted for 30% of all device associated infections, with an incidence density of 12.5 cases per 1000 catheter days, which was four times higher than that reported from American ICUs in the National Nosocomial Infectious Surveillance (NNIS) system. The occurrence of catheter infections is shown to increase the average length of ICU stay by 2.4 days, and hospital stay by 7.5 days[2].

Catheter-associated infections can be considered local or systemic. Local phenomena include simple colonization or true infection that may involve the exit site or tunnel. Micro-organisms may travel from the skin puncture wound along the external surface of the catheter or from the hub through the lumen of the catheter, to be shed into the circulation causing bacteraemia and sepsis[3,4].

In many institutions, the anatomical site of CVC insertion is chosen on the grounds of personal experience or local policies rather than on evidence based guidelines. If there was evidence for an increased risk of specific complications with one approach, then clinicians may take advantage of that knowledge for insertion of a CVC in an individual patient. This study was undertaken with a view to determine which approach is better in our hospital setup.

Methodology

This cross-sectional study was carried out prospectively in the Department of Critical Care Medicine BIRDEM General Hospital, Dhaka and Critical Care Centre, Combined Military Hospital (CMH), Dhaka during the period January 2019 to December 2020. The catheters used were not antimicrobial coated, but were multilumen radiopaque polyurethane catheters (Arrow, Reading, PA, USA). The catheters were inserted by physicians following sterile barrier precautions. The catheters were percutaneously inserted using land mark and Seldinger technique and fixed to the skin with 2-0 silk suture. After the line insertion, the area surrounding the catheter was cleaned with a sterile gauze soaked with povidone iodine and an occlusive gauze dressing applied over the site. No topical antimicrobial ointment was applied to insertion sites. If the patient had any intravenous (IV) line at other site, that was removed after insertion of CVC line. The inclusion criteria were; patients age >18 yrs, multi-lumen 16 cm polyurethane CVCs (Arrow, USA) inserted using Seldinger approach under maximum sterile barrier precautions, platelet count more than 50000/cumm and the prothrombin time international normalized ratio (INR) less than 1.5s. Exclusion criteria were CVCs inserted in other hospitals, patients having IV cannulation at more than one anatomical sites. The choice of the CVC insertion sites (either IJV or SCV) was left to the discretion of the performing doctor. The date, site and side of cannulation and the number of punctures required for successful cannulation as well as complications, if any, were noted for each insertion procedure. Chest radiograph was performed on all patients to verify the position of the tip of the CVC and to detect delayed complications like pneumothorax or haemothorax. CVCs were changed if required for more than 14 days or removed when no longer required or when suspected to be infected. The outcomes of all patients included in the study were noted at the end of ICU stay, i.e died or transferred to ward. Ethical approval was obtained from appropriate authority prior to the commencement of the study. The SPSS software for Windows, Version SPSS 16.0 (SPSS Inc, Chicago, IL, USA) and the EPI Info software (3.5.1) were used to process the data and generate the statistics. Mean and standard deviation (SD) was calculated as required for numerical variables. Univariate analysis was performed to compare the survivor with the non-survivor groups. Unpaired 't' test and Chi-square tests were performed where appropriate. P value less than 0.05 was considered statistically significant.

Results

During the study period, a total of 324 catheters fulfilled our inclusion and exclusion criteria. 156 catheters were inserted through IJV and 168 catheters were inserted through SCV (Table 1).

Table 1: Distribution of CVCs in study subjects

Variable	Frequency
IJV	156(48.15%)
SCV	168(51.85%)
Total CVCs	**324(100%)**

CVC : Central venous catheter; **IJV** : Internal jugular vein; **SCV**: Subclavian vein

There was no difference between the two groups in terms of age, gender distribution, presence of co-morbid illness (Table 2).

The total duration of CVC use in 324 patients was 3888 days, with a mean (standard deviation) duration of use of 11.51 (±1.32) days per catheter (Table III). In 132 patients, the CVCs were in situ less than 10 days. In the rest the CVC catheters were used for more than 10 days but it was changed when required for more than 14 days. It was noted that SCV catheters were used for significantly longer period of time than IJV catheters (p=0.004). 46 patients developed infectious complications, which included exit site infections (16 patients), catheter tip colonization/infection (20 patients), and catheter-related blood stream infections (CRBSIs, 10 patients) (Table 3).

All patients under study were followed up to study their outcomes from the ICU. 154 patients were transferred to ward (47.53%) and 170 patients expired (52.47%). There was no significant relation between occurrence of infectious complications and the overall crude morbidity rates of patients (Table 5 and Table 6).

Table 2: Univariate Analysis Comparing the Demographic Profile between the Patients in IJV and SCV Groups

Variables	IJV(n=156) (Mean±SD)	SCV(n=168) (Mean±SD)	Total	P value
Age	61.59±17.52	59.63±15.87		0.56
Gender				
• Male	82(52.56%)	108(64.28%)	190	
• Female	74(47.43%)	60(35.71%)	134	0.06
Co-morbid illnesses				
Diabetes mellitus	142(91.02%)	157(93.45%)	299	0.41
Hypertension	80(51.28%)	92(54.76%)	172	0.53
Coronary artery disease	66(42.30%)	77(45.83%)	143	0.52
Chronic Kidney Disease	74(47.43%)	82(48.80%)	156	0.77
Others	24(15.38%)	31(18.45%)	55	0.46
Medical cases	146(93.59%)	152(90.48%)	298	0.21
Surgical cases	10(6.41%)	16(9.52%)	26	0.30

Unpaired 't' test and X2 test were done; Values are number (percentage) unless otherwise indicated. n : Number of patients

Table 3: Characteristics of CVC usage and infectious complications in IJV and SCV groups

Variables	IJV(n=156)	SCV(n=168)	Total	P value
Total Catheter duration (days)	1872	2016	3888	
Average catheter duration (mean±SD)	11.39±1.52	12.01±1.87	11.51±1.32	0.48
Number of CVCs longer than 10 days	77(49.35%)	115(68.45%)	192(59.26%)	0.004
Overall infections	29(18.85%)	17(10.11%)	46(14.20%)	0.02
Exit site infections	10(6.41%)	6(3.57%)	16(4.94%)	0.23
Catheter tip infections	12(7.69%)	08(4.76%)	20(6.17%)	0.27
• CVCs <10 days	02	02	04(1.23%)	1.00
• CVCs >10 days	10	06	16(4.94%)	0.23
P value (comparing CVCs inserted for <10 days vs >10 days)	0.004	0.13	<0.001	
Incidence density of Catheter Tip Infections	6.41	3.95	5.13	0.01
CRBSIs	07(3.85%)	03(2.38%)	10(3.08%)	0.52
• CVCs <10 days	01	01	02	1.0
• CVCs >10 days	06	02	08	0.13
P value (comparing CVCs inserted for <10 days vs >10 days)	0.02	0.56	0.02	
Incidence density of CRBSIs	3.72	0.15	2.58	<0.001

Unpaired 't' test and X2 test were done; Values are number (percentage) unless otherwise indicated.

Table 4: Comparison of overall infectious complications between IJV and SCV groups

Infectious complications	IJV(n=156)	SCV(n=168)	Total(n=324)	P value
Present	29	17	46	0.03
Absent	127	151	278	

Values are number (percentage) unless otherwise indicated.

Table 5: Comparison of morbidity among patients who developed catheter- related immediate complications versus those who did not in IJV vs SCV groups

Morbidity	IJV (n=54)	SCV (n=52)	Total	P value
Catheter Tip Infection				
• Yes	6	3	9	0.66
• No	6	5	11	
Catheter Related Blood Stream Infection				
• Yes	4	2	6	1.0
• No	3	1	4	

Values are number (percentage) unless otherwise indicated.

Table 6: Comparison of Morbidity among Patients Who Developed Catheter-Related Immediate Complications Versus Those Who Did Not

Complications	Yes	No	P value
Catheter tip Infections	9/20(45.00%)	118/304(38.81%)	0.58
CRBSI	6/10(60.00%)	130/314(41.40%)	0.33

Values are number (percentage) unless otherwise indicated

Discussion

Central venous catheters (CVCs) are essential for the clinical management of many patients. Indications for a CVC are usually the intravenous administration of specific drugs (e.g. catecholamine), parenteral nutrition, haemodialysis, and haemodynamic monitoring. In many institutions, patients undergoing major surgery and patients with critical illness or cancer routinely receive a CVC. Thus percutaneous placement of a catheter into a central vein is a frequent procedure in many clinical settings[4-5].

Catheter associated infections can be considered local or systemic. Local phenomena include simple colonization or true infection that may involve the exit site or tunnel. Local inflammatory signs at the catheter's portal of entry or tunnel have a highly predictive value for infection but its absence has a very poor negative value[2]. Fever and signs of sepsis, such as chills, rigors, hypotension and hyperventilation should always be considered as catheter related infection (CRI) when there is no other identifiable source of infection is present. But clinical findings are unreliable for establishing a diagnosis of CRI[6]. Mortality of catheter related blood stream infection increases with old age, longer length of hospital stay, cancer, disease of the digestive tract and candida species detection[7]. Catheters placed under emergency situations, during which optimal aseptic conditions cannot always be fully respected, have been significantly associated with higher risk of catheter related infection[3]. Catheter tip colonization is a more objective estimate of CRBSI than insertion site inflammation[8].

In the latest 2002 Center for Disease Control and Prevention (CDC) guidelines the clinical definitions for catheter related infections are used as exit site infection, pocket infection, infusate related BSI and catheter related BSI. According to CDC criteria, catheter related infection was defined as catheter tip colonization significant growth of a micro-organism (>15 colony forming units) from the catheter tip and Catheter Related Local Infection (CRLI) any sign of local infection with induration, erythema, heat, pain, purulent drainage and catheter tip colonization. Catheter Related Blood Stream Infection (CRBSI) is defined as positive blood culture obtained from a peripheral vein and signs of systemic infection like fever, chills and /or hypotension with no apparent source of bacteraemia except the catheter and catheter tip colonization with the same organisms[8].

While the IJV route is implicated to be more commonly associated with greater infectious complication, Crnich and Maki[9] found both routes of CVC insertion showed similar incidences of all three infectious complications. However, when they sub analyzed the rates of infectious complications with the duration of CVC use, they found that CVCs that were used for greater than 7 days had a significantly greater association with infectious complications. This was more evident with IJV routes of insertions9. In a related study, when 2595 CVC insertions were studied, both CVC related infection as well as CRBSI related incidence densities were found to be significantly higher with IJV catheters as compared with the SCV catheters (7.65 versus 1.57 per 1000 catheters days and 2.99 versus 0.97 per 1000 catheter days, respectively)[10]. The risk of infectious complications with CVCs has also been reported to be more with increased duration of use[2]. Akmal et al6 found CVC related systemic infections in 10% with subclavian catheters and 4.3% with internal jugular catheters. Ruesch et al[11] found that blood stream infection happened more often with jugular catheters. Gowardman et al[12] have shown that in an environment of consistent CVC care, catheter tip colonization was significantly lower when the device was inserted via the subclavian route. For all CVCs no significant differences was detected in CRBSI rate among sites[12]. In this study, the overall infection rate was found more than neighbouring developing countries like India (14.20% vs 9.79%). On sub analysis, we found that the incidences of overall infection, exit site infection and catheter tip infection were more (although not statistically significant) with IJV access than SCV access, which supports the findings of Lorente et al[10] and Gowardman et al[12]. But it differs with Kaur et al[2], Akmal et al[6] and Deshpande et al[13] where there was no difference between the two sites or more with SCV route. Furthermore, although the incidence of CRBSIs was more with IJV access than SCV access, it was not statistically significant which was also found in studies by Gowardman et al[12] and Deshpande et al[13]. But it was also found that the incidence of catheter tip infections and CRBSIs was significantly more when catheter was left in place for more than 10 days than when it was removed in less than 10 days. This was found specially with IJV cannulation. These findings coincide with that of Kaur et al[2]. But we found that catheter related local infection incidence density and CRBSI incidence density between the IJV route and SCV route were statistically significant ($p=0.01$ and <0.001 respectively).

Indeed duration of catheterization has been suggested as an important risk factor in the development of CR-BSI in some studies[13-14]. However, other studies showed no relationship between prolonged catheterization and incidence of infection[12]. Tan et al[14] found a significant relationship between prolonged catheterization and incidence of infection. In this study, it was found that CVCs that were used for more than 10 days had a significantly greater association with catheter tip infection and CRBSIs ($p<0.001$ and $p=0.02$). It was evident especially with IJV access ($p=0.004$ and $p=0.02$ respectively).

A survey of 112 medical ICUs in the United States revealed the following microbial spectrum in primary hospital-acquired bacteremia mostly caused by indwelling catheters like coagulase negative *staphylococcus*, mostly *staphylococcus epidermidis* (36.0%), *enterococci* (16.0%), gram negative aerobic bacilli like *Pseudomonas aeruginosa*, *Klebsiella pneumonae, Escherichia coli* (16.0%), *Staphylococcus aureus* (13.0%), Candida species (11.0%) and other organisms (8.0%)[15]. A number of studies also reported coagulase negative *staphylococci* as the most common organism[10,15]. On the contrary, Tan et al showed that gram negative rods were more commonly the causative micro-organisms with *Klebsiella pneumoniae* (38.9%) being the commonest. It was also noted that 50.0% of these *Klebsiella pneumoniae* were ESBL inducers[14]. Sadoyama et al demonstrated that Coagulase negative *Staphylococci* (CoNS) and *Staphylococcus aureus* are associated with CVC infections (28% and 16% respectively) and they come from the skin. They also found that there was no quantitative difference in the numbers of the most frequent micro-organisms at the jugular versus the subclavian vein. However, qualitative analysis indicated a significantly higher presence ($p<0.05$) of gram negative bacilli (GNB) and yeasts in the jugular vein[15]. Kaur et al[2] found that microbiological yields from CVC tips predominantly grew Acinetobacter species. Data on CR-BSIs collected from other Indian hospitals revealed similar pattern of infections and include Enterobacteriaceae, Pseudomonas species, Acinetobacter and Candida species[16]. This is in contrast to Western literature, which mainly report coagulase-negative *Staphylococci* and S*taphylococci* aureus species[2]. Microbiological yields from exit site wound swab culture, catheter tip and blood culture showed predominantly growth of Acinetobacter species (40.58%) and *Klebsiella pneumonae* (23.19%) in this study population. Other organisms found included *Escherichia coli*, *Pseudomonas aeruginosa, Staphylococcus aureus* and Candida species.

Conclusion

This paper adds to our knowledge on the rates and some of the risk factors of infectious complications associated with landmark based techniques of CVC insertion. The rates of infectious complications associated with CVCs are higher in our ICUs in comparison to those of developed countries. We found that Subclavian access was associated with a low rate of infectious complications in the intensive care unit as compared with Internal Jugular access. CVCs need proper precaution during insertion and aftercare. Standard hand hygiene, proper technique and sterile precautions can lower the rate of CVC related infectious complications and the incidence of CRBSIs significantly. Routine changing of CVCs within 10 days may reduce the risk of infectious complications like catheter tip infections/colonization and CRBSIs.

Acknowledgements

We gratefully acknowledge the contributions of Commandant, CMH Dhaka, Director General, BIRDEM General hospital, Dhaka, for their encouragement and support in our research work.

Conflict of Interest

The authors have no conflicts of interest to disclose

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' Contributions

Md Enayet Karim conceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript.ASM Areef Ahsam contributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript. Reza Ershad, Mazumder MK involved in the manuscript review and editing. All authors read and approved the final manuscript.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board. The written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

How to cite this article: Karim ME, Chowdhury AI, Ahsan ASMA, Ershad R, Mazumder MK. Comparison of Infectious Complications between Internal Jugular and Subclavian Central Venous Access in Intensive Care Unit. J Army Med Coll Jashore, 2022;3(1):3-8

Publication History

Received on: 7 October 2021
Accepted on: 24 December 2021
Published on: 1 January 2022

References

1. Kusminsky RE. Complications of central venous catheterization. J Am Coll Surg. 2007; 204(4): 681-90.
2. Kaur R, Mathai AS, Abraham J. Mechanical and infectious complications of central venous catheterizations in a tertiary level intensive care unit in northern india. Indian Journal of Anaesthesia. 2012; 56(4): 376- 381.
3. Akaraborworn O. A review in emergency central venous catheterization. Chinese Journal of Traumatology. 2017; 20: 137-40.
4. Graham AS, Ozment C, Tegtmeyer K, Lai S, Braner DAV. Central venous catheterization. N Engl J Med. 2007; 356(21): 132-40.
5. Soni NJ, Reyes LF, Keyt H, Arango A, Gelfond JA, Peters J. Use of Ultrasound guidance for central venous catheterization: a national survey of Intensivists and Hospitalists. Journal of Critical Care. 2016; 36: 227-283.
6. Akmal A.H, Hasan M, Marium A. The incidence of complications of central venous catheters at an intensive care unit. Annals of Thoracic Medicine. 2007; 2(2): 61- 63.
7. Ruesch S, Walder B, Tramer MR. Complications of central venous catheters: Internal jugular versus subclavian access- A systematic review. Critical Care Medicine.2002; 30(2): 454- 460.

8. Lorente L, Villegas j, Martin MM, Jimenez A, Mora ML. Catheter related infection in critically ill patients. Intensive Care Medicine. 2004; 30: 1681-1684

9. Crnich CJ, Maki DG. In: APIC text of infection control and epidemiology. 2nd ed. Vol.1. Washington, DC: Association for professionals in infection control and epidemiology, Inc; Infections caused by intravascular devices: Epidemiology, pathogenesis, diagnosis, prevention and treatment. 2005; 24:21-24.

10. Lorente L, Henry C, Martin MM, Jimenez A, Mora LM. Central venous catheter-related infection in a prospective and observational study of 2,595 catheters. Critical Care. 2005; 9(6): 631- 635.

11. Ruesch S, Walder B, Tramer MR. Complications of central venous catheters: Internal jugular versus subclavian access- A systematic review. Critical Care Medicine. 2002; 30(2): 454- 460.

12. Gowardman JR, Robertson LK, Parkes S, Richard CM. Influence of insertion site on central venous catheter colonization and bloodstream infection rates. Intensive Care Medicine. 2008; 34: 1038- 1045.

13. Deshpande KS, Hatem C, Ulrich HL, Currie BP, Aldrich TK, Bryan-Brown CW, et al. The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. Critical Care Medicine. 2005; 33(1): 13- 20.

14. Tan CC, Zanariah Y, Lim KI, Balan S. Central venous catheter-related blood stream infections: incidence and an analysis of risk factors. Med J Malyasia. 2007; 62: 370-374

15. Sadoyama G, Gontijo Filho PP. Comparison between the jugular and subclavian vein as insertion site for central venous catheters: microbiological aspects and risk factors for colonization and infection. Braz J Infect Dis. 2003; 7(2): 142-148

16. Mehta A. Device associated nosocomial infection rates in intensive care units of seven Indian cities. Findings of the international nosocomial infection control consortium (INICC). J Hosp Infect. 2007; 67: 168-174

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 9-13
ISSN : 2789-1135 (Print)

Original Article ***Open Access***

Correlations of Epicardial Fat Thickness with Clinical, Anthropometric and Laboratory Biochemical Parameters among Metabolic Syndrome Patients

KAM Mahbub Hasan[1], Asraful Hoque[2], Naheed Fatema[3], AKM Mohiuddin Bhuiyan[4], SM Mainul Haque[5], Al-Mamun[6], Dewan Mohammad Karimul Islam[7]

[1]Medical Officer, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [2]Associate Professor, Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [3]Assistant Professor, Department of Obstetrics and Gynecology, Bangladesh Medical College, Dhaka, Bangladesh; [4]Associate Professor, Department of Cardiology, Ibn Sina Medical College & Hospital, Dhaka, Bangladesh; [5]Assistant Professor, Department of Respiratory Medicine, Khulna Medical College, Khulna, Bangladesh; [6]Junior Consultant Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh; [7]Junior Consultant, Department of Cardiology, National Institute of Neuroscience and Hospital, Dhaka, Bangladesh

Abstract

Background: Correlation of epicardial fat thickness with clinical, anthropometric and biochemical parameters indicate their association among metabolic syndrome patients. **Objective:** The purpose of the present study was to correlate the epicardial fat thickness with clinical, anthropometric and biochemical parameters variables among patients with metabolic syndrome. **Methodology:** This comparative cross-sectional study was conducted in the Department of Cardiology at National Institute of Cardiovascular Diseases, Dhaka, Bangladesh from April 2017 to March 2018 for a period of one year. The diagnosis of metabolic syndrome patients was selected for this study. The epicardial fat thickness was prospectively examined by echocardiography. Then the correlation of the epicardial fat thickness was done between the two groups. **Results:** A total of 65 patients were included in this study. The mean age of patients with metabolic syndrome was 44.4±9.8 years. Among the study population, the highest frequency was in the age group of 41 to 50 years (35.0%) followed by 31 to 40 years (31.0%), 51 to 60 years (20.0%) and ≤30 years (05.0%). A moderate positive correlation was found with body mass index (0.589; p<0.001), waist circumference (0.582; p <0.001), LDL (0.510; p<0.001) and triglyceride (0.463; p<0.001). A weak positive correlation was found with age (0.343; p<0.001) and total cholesterol (0.295; p=0.001). A weak negative correlation was also found with HDL (-0.350; p<0.001). **Conclusion:** In conclusion moderate positive correlation was found with body mass index, waist circumference, LDL and triglyceride. *[Journal of Army Medical College Jashore January 2022;3(1):9-13]*

Keywords: Correlations; epicardial fat thickness; clinical; anthropometric; biochemical parameters; metabolic syndrome patients

Introduction

Visceral adipose tissue (VAT) is difficult to obtain an accurate measurement and characterization; however, several methods are applied as surrogates for estimation of visceral adipose tissue[1]. Anthropometric measurements are the mostly used; however, these are frequently imprecise. Waist circumference is widely accepted as a good predictor of intra-abdominal fat mass[2]. Imaging techniques are certainly more precise and reliable than anthropometric measurements. Magnetic resonance imaging (MRI) is the gold standard technique and it estimates VAT accurately, but unfortunately it is costly and time consuming[3]. On this background, much attention has been focused on the measurement of intra-abdominal fat by a cheaper and non-invasive way. Recently many researchers have shown their interest in nontraditional visceral fat depots like epicardial fat. Many studies have found a close association between epicardial fat thickness and visceral adiposity[4-5]. Iacobellis et al[4] proposed and validated a new method to

Correspondence: Dr. KAM Mahbub Hasan, Medical Officer, Department of Cardiology, National Institute of Cardiovascular Diseases, Sher-E-Bangla Nagar, Dhaka, Bangladesh;
Email: kammahbub@yahoo.com; Cell No.: +8801711905240

estimate visceral adipose tissue by echocardiographic epicardial adipose tissue measurement. Epicardial adipose tissue is a true visceral fat deposited around the heart with characteristics of a high insulin-resistant tissue. Echocardiographically, it is generally identified as the relatively echo free space between the outer wall of the myocardium and the visceral layer of pericardium; its thickness is measured perpendicularly on the free wall of the right ventricle at the end of systole[6]. Several studies done among western population found significant association between epicardial fat thickness and metabolic syndrome (MetS)[7-9].

MetS is a combination of some anthropometric and biochemical abnormalities and has an increased predisposition to develop cardiovascular disease and type 2 diabetes[10]. Visceral adipose tissue is an important etiopathological factor of metabolic syndrome although the exact cause is not yet settled. Waist circumference is used as a surrogate marker of visceral adiposity though its sensitivity and specificity, as a measure of visceral adipose tissue, is poor[11]. Currently other reliable alternatives like estimation of epicardial fat is evolving as a measure of visceral adipose tissue.

Many studies have established a significant association between visceral adiposity and echocardiographic epicardial fat thickness[12]. As a marker of visceral adiposity, echocardiographic epicardial fat thickness may replace waist circumference due to its reliability and the easy estimation and wide availability of echocardiography as well. Therefore, the aim of this study was to find out the association of echocardiographic epicardial fat thickness with MetS.

Methodology

Study Settings and Population: This present study was designed as an analytic type of cross-sectional study which was carried out in the Department of Cardiology at National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh from April 2017 to March 2018 for a period of one (01) year. All patients ≥18-year-old of both sexes attended in the indoor and outdoor echocardiography department of NICVD for echocardiography during the specified period were selected as the study population. The samples were collected by purposive sampling method. Patients with moderate to severe valvular heart disease, congenital heart disease and cardiomyopathy, patients with acute coronary syndrome (ACS), patients who were on lipid lowering drugs, history of taking corticosteroid or other weight gaining drugs, patients with pericardial effusion, patients with ascites and or edema or patients with poor echo window were excluded from this study. The study protocol was approved by Ethical Review Committee of NICVD. Informed written consent was a mandatory prerequisite for every patient.

Study Procedure: Blood pressure and anthropometric parameters were measured according to standard protocol. Echocardiography was done with the help of Siemens Acuson X 700 and epicardial fat thickness was measured by 2-D echocardiography in two different views which were in parasternal long axis (PLAX) view and in parasternal short axis (PSAX) view at mid-ventricular level. Two cardiologist experts in echocardiography were measured the fat thickness and would be unaware about the clinical and laboratory parameters of the patients. Data were collected by using a preformed data collection sheet. MetS was diagnosed on the basis of modified NCEP ATP III definition. Depending on the diagnosis of MetS, patients were divided into two groups designated as group I and group II. Group I included patients with MetS and group II included patients without MetS. The epicardial fat thickness among the groups were compared and analyzed.

Statistical Analysis: The numerical data obtained from the study was analyzed and significance of differences was estimated by using statistical methods. Continuous variables were expressed as mean values with standard deviation and compared using Student's t-test. Categorical variables were expressed as frequencies with percentages and compared using Chi-square test or Fisher's exact test when & where appropriate. Correlation analyses were done by Pearson's correlation coefficient test. Logistic regression analysis was performed to adjust for the potential confounders in predicting the association. Statistical significance was assumed if p value was less than 0.05. Statistical analyses were carried out by using SPSS 23.0 (Statistical Package for the Social Sciences by SPSS Inc., Chicago, IL, USA, 2015).

Results

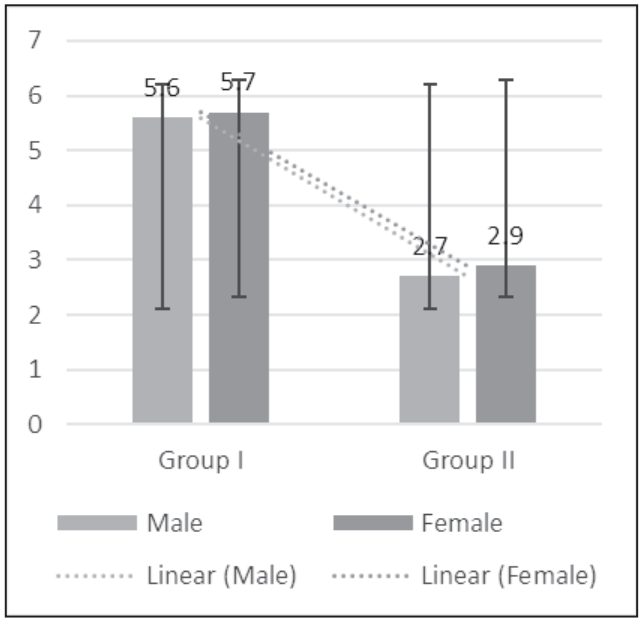
A total of 65 patients were included in this study. The mean age of patients with metabolic syndrome was 44.4±9.8 years. Among the study population, the highest frequency was in the age group of 41 to 50 years (35.0%) followed by 31 to 40 years (31.0%), 51 to 60 years (20.0%) and ≤30 years (05.0%) (Table 1).

Table 1: Comparison of the study groups according to their age (n=130)

Age Group	Frequency	Percent
≥30 Years	6	9.0
31 to 40 Years	20	31.0
41 to 50 Years	24	35.0
51 to 60 Years	13	20.0
More than 60 Years	3	5.0
Total	**65**	**100.0**
Mean ± SD (Years)	44.4±9.8	

MetS = Metabolic syndrome; ns = Not significant (p >0.05); p value of mean age reached from unpaired t-test.

The mean epicardial fat thickness (mm) was found significantly higher in both male and female metabolic syndrome patients in comparison to non-metabolic syndrome patients which was 5.6±0.9 vs. 2.7±0.8 and 5.7±0.9 vs. 2.9±1.0 respectively (Figure II).



The univariate correlations of echocardiographic epicardial fat thickness with clinical, anthropometric and biochemical parameters were measured. A moderate positive correlation was found with body mass index (0.589; p = <0.001), waist circumference (0.582; p <0.001), LDL (0.510; p = <0.001) and triglyceride (0.463; p = <0.001). A weak positive correlation was found with age (0.343; p = <0.001) and total cholesterol (0.295; p = 0.001). A weak negative correlation was also found with HDL (-0.350; p = <0.001).

Table 2: The univariate correlations of epicardial fat thickness with clinical, anthropometric and biochemical parameters

Variables	*r*	P value
Age	0.343	<0.001
Body mass index	0.589	<0.001
Waist Circumference	0.582	<0.001
Triglyceride	0.463	<0.001
Total Cholesterol	0.295	0.001
LDL	0.510	<0.001
HDL	-0.350	<0.001

Pearson's correlation coefficient test was done; LDL: Low density lipoprotein; r = Correlation coefficient; HDL: High density lipoprotein

Discussion

MetS and cardiovascular risk in Bangladeshi population are also heightened by their relative increase in body fat mass, truncal subcutaneous fat mass, intra-abdominal fat mass, and also in ectopic fat deposition10. Among the different types of adipose tissue, visceral adipose tissue (VAT) plays a key role in the etiopathology of MetS. Waist circumference is considered as a surrogate marker of visceral adiposity. However, as a measure of visceral adipose tissue, its sensitivity and specificity are not so high. Therefore, other new reliable markers are evolving. In this respect epicardial adipose tissue estimation might be a suitable alternative. Many studies have found a significant association between echocardiographic epicardial fat thickness and visceral adiposity. So epicardial fat thickness being a marker of visceral adiposity is gaining more attention worldwide. Several studies done in different populations have proven relationship between epicardial fat thickness and MetS.

This observational analytic (cross sectional) study was undertaken at the National Institute of Cardiovascular Diseases (NICVD), Dhaka, during the period of April 2017 to March 2018. This study was performed with an aim to find out the association of echocardiographic epicardial fat thickness with MetS. A total of 130 patients who agreed to do echocardiography and relevant investigations were included in the study. Anthropometric parameters and blood pressure were measured and relevant investigations were sent. On the basis of the diagnosis of MetS, the study subjects were divided into two groups. 65 patients who fulfilled the diagnosis of MetS were assigned in group I and another 65 patients who did not fulfill the diagnosis of MetS were assigned in group II.

The mean age of the whole study population was 44.1±9.9 and the mean age of metabolic and non-metabolic syndrome groups were 44.4±9.8 and 43.7±10.2 respectively. The difference of age in between the groups was not significant statistically (p = 0.77). In some of the studies done at NICVD supports the mean age of this study[13-14]. In an Indian study undertaken by Prasad et al[15] found the mean age was 45.9 ± 13.9 which was very close to our study population. However, they found a significant difference in mean age between metabolic and non-metabolic syndrome groups. The reason behind this significant difference is that the mentioned study was an epidemiological study undertaken to measure the prevalence of metabolic syndrome.

The epicardial fat thickness was studied among metabolic and non-metabolic syndrome patients. The mean epicardial fat thickness (mm) was found significantly higher in patients with MetS than in patients without MetS like 5.7 ± 0.83 vs. 2.7 ± 0.86; p = 0.00. Faroque[16] found the mean epicardial fat thickness 7.14 ± 1.81 in patients with significant CAD at DMCH. The mean was relatively higher in this study probably because the study population had established CAD and other risk factors of cardiovascular disease. Another study done by Okyay et al[7] found the mean epicardial fat thickness 5.1 ± 1.7 in metabolic syndrome patients which is consistent with our study. In another study conducted by Iacobellis et al8 found the median epicardial fat thickness in MetS group was 9.5 mm and in non- MetS group was 4.5 mm. In this western population-based study, the mean BMI was 32 Kg/M2 that explain the relative higher value of epicardial fat thickness.

Epicardial fat thickness was studied in metabolic and non-metabolic syndrome patients according to the age grouping. The mean epicardial fat thickness (mm) was

found significantly higher in MetS patients of 31 to 40, 41 to 50, 51 to 60 and more than 60 years age groups in comparison to non-metabolic syndrome patients of similar age group i.e., 5.7 ± 0.7 vs. 3.1 ± 1.1, 5.5 ± 1.0 vs. 2.6 ± 0.8, 5.7 ± 0.9 vs. 2.5 ± 0.4 and 6.3 ± 0.5 vs. 2.7 ± 0.3 respectively. A systematic review done by Rabkin1[7] also found significantly higher epicardial fat thickness in MetS patients irrespective of the age of the studied patients. In this study, there was no significant difference of epicardial fat thickness in metabolic and non- MetS patients of less than 30 years age i.e., 4.0 ± 0.0 vs. 2.8 ± 1.0 (p = 0.302). The reason behind this was very small sample size in this age group.

Comparison of Epicardial Fat thickness in metabolic and non- MetS patients according to the gender was studied. The mean epicardial fat thickness (mm) was found significantly higher in both male and female MetS patients in comparison to non- MetS patients. A study done by Iacobellis and Willens6 found significantly higher epicardial fat thickness in male and female MetS patients over non- MetS patients i.e., 9.5 and 7.5 vs. 4.8 and 4.3. Comparison of Epicardial Fat thickness of study groups according to smoking status was also studied. The mean epicardial fat thickness (mm) was found significantly higher in both smoker and non-smoker MetS patients than non- MetS patients i.e., 5.7±1.0 vs. 2.9±0.8 and 5.6±0.9 vs. 2.7±0.9 respectively. This finding was also consistent with the same above-mentioned study done by Iacobellis and Willens[6].

The univariate correlations of echocardiographic epicardial fat thickness with blood pressure, anthropometric and biochemical parameters were measured. A moderate positive correlation was found with body mass index (0.589; p = <0.001), waist circumference (0.582; p <0.001), LDL (0.510; p = <0.001) and triglyceride (0.463; p = <0.001). A weak positive correlation was found with age (0.343; p = <0.001) and total cholesterol (0.295; p = 0.001). A weak negative correlation was also found with HDL (-0.350; p<0.001). These findings were also supported by a study done by Okyay et al[7] where they found moderate positive correlation of epicardial fat thickness with waist circumference r = 0.592 p<0.001 and body mass index r = <0.505; p<0.001 and a weak positive correlation with triglyceride level r = 0.371, p<0.001.

Conclusion

From this study it may be concluded that a moderate positive correlation of epicardial fat thickness is found with body mass index, waist circumference, LDL and triglyceride level. A weak negative correlation of epicardial fat thickness was found with HDL and a weak positive correlation was also found with age and total cholesterol level. From this study, it may be recommended that the epicardial fat thickness can be considered as an easy tool for the evaluation of visceral adiposity and it can be used as a diagnostic criterion of metabolic syndrome.

Acknowledgements

None

Conflict Of Interest

The authors have no conflicts of interest to disclose

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' Contributions

Hasan KAMM, Hoque A, Fatema N conceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript. Hasan KAMM contributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript. Bhuiyan AKMM, Haque SMM, Mamun A, Islam DMK involved in the manuscript review and editing. All authors read and approved the final manuscript.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board. The written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

How to cite this article: Hasan KAMM, Hoque A, Fatema N, Bhuiyan AKMM, Haque SMM, Mamun A, Islam DMK. Correlations of Epicardial Fat Thickness with Clinical, Anthropometric and Laboratory Biochemical Parameters among Metabolic Syndrome Patients. J Army Med Coll Jashore, 2022;3(1):9-13

Publication History

Received on: 7 October 2021

Accepted on: 24 December 2021

Published on: 1 January 2022

References

1. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith Jr SC, Spertus JA. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation. 2005;112(17):2735-52

2. Boden G, Shulman GI. Free fatty acids in obesity and type 2 diabetes: defining their role in the development of insulin resistance and β-cell dysfunction. European journal of clinical investigation. 2002; 32:14-23

3. Baber U, Holmes D, Halperin J, Fuster V. Definitions of Acute Coronary Syndromes. In: V Fuster, RA Harrington, J Narula, ZJ Eapen, eds. 2017. Hurst's the heart. New York: McGraw-Hill Education, pp. 946–976

4. Iacobellis G, Corradi D, Sharma AM. Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with the heart. Nature clinical practice Cardiovascular medicine. 2005;2(10):536-43

5. Jeong JW, Jeong MH, Yun KH, Oh SK, Park EM, Kim YK, Rhee SJ, Lee EM, Lee J, Yoo NJ, Kim NH. Echocardiographic epicardial fat thickness and coronary artery disease. Circulation Journal. 2007;71(4):536-9

6. Iacobellis G, Willens HJ. Echocardiographic epicardial fat: a review of

research and clinical applications. Journal of the American Society of Echocardiography. 2009;22(12):1311-9

7. Okyay K, Balcioglu AS, Tavil Y, Tacoy G, Turkoglu S, Abacı A. A relationship between echocardiographic subepicardial adipose tissue and metabolic syndrome. The International Journal of Cardiovascular Imaging. 2008;24(6):577-83

8. Iacobellis G, Willens HJ, Barbaro G, Sharma AM. Threshold values of high-risk echocardiographic epicardial fat thickness. Obesity. 2008;16(4):887-92

9. Conroy RM, Pyörälä K, Fitzgerald AE, Sans S, Menotti A, De Backer G, De Bacquer D, Ducimetiere P, Jousilahti P, Keil U, Njølstad I. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. European heart journal. 2003;24(11):987-1003

10. Bhowmik B, Afsana F, Siddiquee T, Munir SB, Sheikh F, Wright E, et al. Comparison of the prevalence of metabolic syndrome and its association with diabetes and cardiovascular disease in the rural population of Bangladesh using the modified National Cholesterol Education Program Expert Panel Adult Treatment Panel III and International Diabetes Federation definitions. J Diabetes Investig. 2015;6(3):280-8

11. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the international diabetes federation. Diabetic medicine. 2006;23(5):469-80

12. Bhuiyan GR, Roy GC, Siddique MA, Rahman M, Ahmed K, Nahar F. Relationship between echocardiographic epicardial adipose tissue (EAT) thickness and angiographically detected coronary artery disease. Mymensingh medical journal: MMJ. 2017;26(3):498-504

13. Rafiquzzaman K. Association of body mass index with angiographic severity of coronary artery disease in patients acute ST segment elevation myocardial infarction. Master's dissertation. Dhaka, Bangladesh, 2015

14. Chayan S. Correlation of Visceral adiposity index score with the angiographic severity of coronary artery disease in patients with ischemic heart disease. Master's dissertation. Dhaka, Bangladesh, 2016

15. Prasad DS, Kabir Z, Dash AK, Das BC. Prevalence and risk factors for metabolic syndrome in Asian Indians: A community study from urban Eastern India. Journal of cardiovascular disease research. 2012;3(3):204-11

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 14-17
ISSN : 2789-1135 (Print)

Original Article ***Open Access***

Antimicrobial Resistance Patterns of Gram Negative Bacteria from Blood Stream Infection Patients in a Tertiary Care Hospital, Bangladesh

Md. Badrul Islam[1], Md. Abdullah Yusuf[2], Tarana Jahan[3], Md. Sabur Khan[4], Shafiqul Islam[5], Khandaker Md. Tasnim Sajid[6], Jaba Roy[7]

[1]Associate Professor, Department of Microbiology, Dhaka National Medical College, Dhaka, Bangladesh; [2]Associate Professor, Department of Microbiology, National Institute of Neurosciences & Hospital, Dhaka, Bangladesh; [3]Assistant Professor, Department of Microbiology, Monno Medical College, Manikganj, Bangladesh; [4]Senior Medical Technologist (Lab), IBN Sina D. Lab and Consultation Centre, Doyagonj, Dhaka, Bangladesh; [5]Senior Medical Technologist, Dhaka National Medical College & Hospital, Dhaka, Bangladesh; [6]Assistant Professor, Department of Microbiology, Bangabandhu Sheikh Mujib Medical College, Faridpur, Bangladesh; [7]Associate Professor, Department of Microbiology, Dhaka National Medical College, Dhaka, Bangladesh

Abstract

Background: There is an emerging trend of BSI caused by Gram-negative organisms and an increased incidence of drug-resistant strains. **Objective:** The purpose of this study was to evaluate the antimicrobial resistance pattern of predominant isolated bacterial in blood culture. **Methodology:** This cross-sectional study was conducted in the department of Microbiology at Dhaka National Medical College, Bangladesh from January 2020 to December 2020 for duration of one year. The blood was collected according to blood collection guidelines and inoculated into BacT/ALERT FA plus aerobic blood culture bottles. After collection these bottles were immediately incubated in BacT/ALERT 3D (manufactured by bioMerieoux, France) a fully automated blood culture system. Antimicrobial susceptibility test was done for all isolated bacteria by disc diffusion method. **Result:** A total number of 3220 patients were recruited, among them 372 (12%) yielded growth of different bacteria. The most frequently identified Gram-negative bacteria were Salmonella typhi 276(74.2%) followed by Salmonella paratyphi A, Escherichia coli and Pseudomonas which were 52(14%), 30(8%) & 14(3.8%) respectively. All isolated Gram negative bacteria are highly resistance to Azithromycin and Cefradine which was 86.96% and 66.38% in Salmonella typhi, 80.77% and 78.85% in Salmonella paratyphi A, 90.48% and 85.71% in Escherichia coli and 92.86% and 100% in case of Pseudomonas Spp respectively. **Conclusion:** There were a high percentage of GNB resistant to several antibiotics. Antibiotic susceptibility testing is a prerequisite guide for the selection of appropriate antibiotic therapy for bacterial infections. *[Journal of Army Medical College Jashore January 2022;3(1):14-17]*

Keywords: Blood stream infection; Blood culture; Gram negative rods; Antibiotic resistance; BacT/ALERT

Introduction

Bloodstream infections pose a significant health problem worldwide and are a major cause of morbidity and mortality in many countries. Bloodstream infections (BSI) are defined broadly as the presence of viable microorganisms in the blood, which can lead to inflammation in the host and alter the clinical and hemodynamic properties and lead to morbid consequences[1]. Bloodstream infections are a major public health problem worldwide, and it has been associated with significant morbidity and mortality[2]. Although it is still common in developed nations, the burden is high in the least developed and developing countries[3].

This is a considerable variation in epidemiology and pathogen profile of microorganisms, which cause BSI[4]. The estimated fatality rate associated with blood stream infection (BSI) is 15- 20% but reaches 35-50% in ICU patients. Approximately 200,000 cases of bloodstream infections occur every year, causing 20-50% mortality worldwide[5]. Respiratory tract, uroge-nital tract, and

Correspondence: Dr. Md. Badrul Islam, Associate Professor, Department of Microbiology, Dhaka National Medical College, Dhaka, Bangladesh; Email: badrulislam19@gmail.com;
Cell No.: +8801670738692

intra-abdominal infections are com-monly identifiable primary foci of BSIs[6]. The impact of BSI has a tremendous impact on health care facilities by prolonging patient stay in the hospital and there-fore in the intensive care unit, leading to increased health care costs[7].

There is a considerable variation in epidemiology and pathogen profile of microorganisms, which cause BSI[4]. Population-based studies originating in countries such as Australia, Canada, Denmark, Finland, Iceland, New Zealand, Sweden, and USA show the etiologies of BSI to be mainly from the organisms *Escherichia coli, Staphylococcus aureus,* and *Streptococcus pneumoniae*[8]. In contrast to this, the pathogen profiles vary in Africa and Asia. Salmonella enterica has been implicated as one of the major pathogens causing BSI in both African and Asian nations[9]. The most common include gram-negative bacteria such as *Escherichia coli, Pseudomonas aeroginosa, Klebsiella species,* Enterobacter, Serratia, Citrobacter, Salmonella and Acinetobacter[10]. China antimicrobial surveillance network (CHINET) in 2018 recently reported that the frequency of gram-negative bacilli among clinical isolates was over twice higher than that of gram-positive cocci[11,12].

The timely diagnosis and rationale use of appropriate antibiotics remains the cornerstone in treating and managing patients with BSI. However, frequent and irrational use of broad-spectrum antibiotics in critically ill patients who stay in the ICU for more pro-longed periods has increased bacterial resistance over time[13]. Potential outcomes of BSI and the delays in performing and receiving culture results often lead to empirical treatment. In developing countries, this may also be due to the lack of treatment guidelines and unavailability of susceptibility patterns for local isolates[2]. Antibiotics resistance is becoming an alarming problem in developing countries, including Bangladesh. Increasing antimicrobial resistance has become a global concern with economic and social implications worldwide[14]. The purpose of this study was to evaluate the antimicrobial resistance pattern of predominant isolated bacterial in blood culture.

Methodology

This cross-sectional study was conducted in the department of Microbiology at Dhaka National Medical College, Bangladesh. This study was carried out during the period from January 2020 to December 2020 for duration of one year. A total number of 3220 patients were selected both outdoor & indoor patient irrespective of age, sex, growth positivity and antibiotic susceptibility. Patients who were taking antibiotics within last 14 days those were excluded in this study. Informed written consent was taken from all patients or their legal guardians before specimen collection. About 20ml blood was collected from patient using strict aseptic precautions and inoculated immediately into BacT/ALERT FA plus aerobic blood culture bottles with 0.025% of sodium polyanethol sulfonate (SPS) as anticoagulant. After collection these bottles were immediately incubated in BacT/ALERT 3D (manufactured by bioMerieoux, France) a fully automated blood culture system for detection of growth in blood culture. In case of a positive growth, the BacT/ALERT automatically gives an alert. The positive bottles were then subculture on Blood Agar, Chocolate Agar and MacConkey Agar (HI Media Laboratories Pvt. Limited, India) and then incubated aerobically at 37°C for 24 h. Standard microbiological methods were applied for the identification of the bacterial species[10]. All the isolated organisms were identified by their colony morphology, staining characters pigment production, motility, oxidase, catalase, TSI and MIV, citrate tests and further confirmed by relevant biochemical tests. Susceptibility to antimicrobial agents of all isolates was done by Kirby Bauer modified disc diffusion technique using Mueller Hinton agar plates and zones of inhibition were interpreted according to CLSI guidelines[11]. All data were processed and analyzed with the help of IBM SPSS (Statistical package for Social Sciences) Version 22.0. Quantitative data were expressed as mean and standard deviation and qualitative data as frequency and percentage.

Results

A total number of 3220 blood samples were recruited after fulfilling the inclusion and exclusion criteria. Among them 372 (12%) yielded growth of different Gram negative bacteria (Figure I).

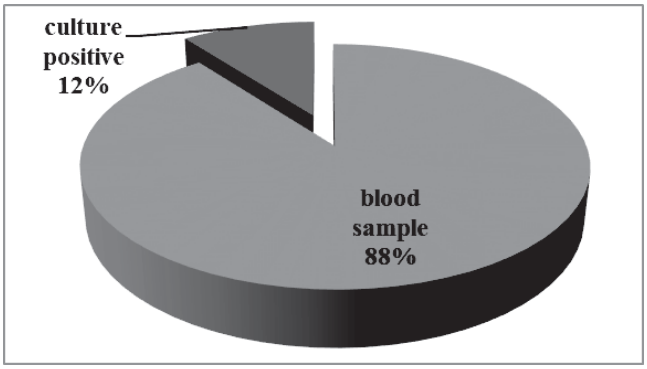


Figure I: Pie chart showing distribution of culture positive cases.

The most frequently identified Gram-negative bacteria were Salmonella typhi 276(74.2%) followed by Salmonella paratyphi A, Escherichia coli and Pseudomonas which were 52(14%), 30(8%) & 14(3.8%) respectively (Figure II)

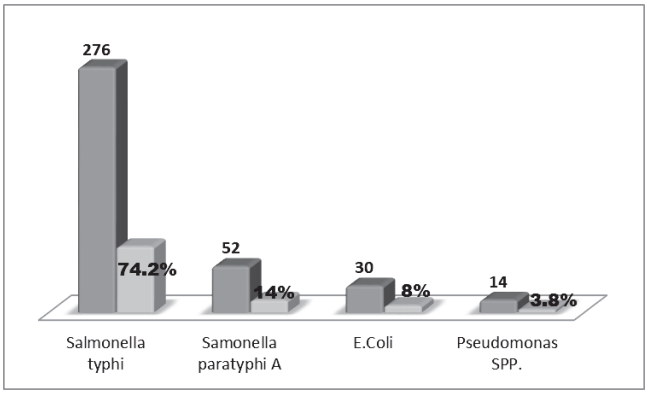


Figure II: Bar Diagram Showing Distribution of Gram Negative Isolates

Table 1: Showing Antibiotic Resistance Pattern of the Isolated Gram Negative Bacteria

Antimicrobial drugs	*Salmonella typhi*	*Salmonella paratyphi A*	*Escherichia coli*	*Pseudomonas*
Amikacin	64 (23.19%)	6 (11.54%)	16 (76.19%)	11 (78.5%)
Azithromycin	36 (86.96%)	42 (80.77%)	19 (90.48%)	13 (92.86%)
Ceftazidime	128 (46.38%)	30 (57.69%)	17 (80.95%)	8 (57.14%)
Ceftriaxone	13 (4.7%)	21 (40.38%)	16 (76.19%)	10 (71.43%)
Cefradine	183 (66.38%)	41 (78.85%)	18 (85.71%)	14 (100%)
Cefixime	78 (28.26%)	31 (59.62%)	19 (90.48%)	10 (71.43%)
Cefuroxime	99 (35.87%)	40 (76.92%)	17 (80.95%)	14 (100%)
Ciprofloxacin	140 (50.72%)	30 (57.69%)	15 (71.42%)	6 (42.86%)
Colistin	32 (11.59%)	10 (19.23%)	6 (28.58%)	8 (57.14%)
Doxycycline	-	-	10 (47.62%)	6 (42.86%)
Cotrimoxazole	141 (51.08%)	30 (57.69%)	12 (57.14%)	8 (57.14%)
Gentamycin	86 (31.16%)	18 (34.62%)	14 (66.67%)	11 (78.57%)
Impinenam	6 (2.17%)	5 (9.62%)	8 (38.10%)	4 (28.57%)
Nalidixic acid	237 (85.87%)	40 (76.92%)	12 (57.14%)	7 (50%)
Tozabactum Piperacillin	40 (14.49%)	25 (48.08%)	10 (47.62%)	4 (28.57%)
Amoxycillin Clavalanic acid	34 (12.32%)	12 (23.08%)	12 (57.14%)	6 (42.86%)

All isolated Gram negative bacteria are highly resistance to Azithromycin and Cefradine which was 86.96% and 66.38% in *Salmonella typhi*, 80.77% and 78.85% in *Salmonella paratyphi A*, 90.48% and 85.71% in *Escherichia coli* and 92.86% and 100% in case of *Pseudomonas species* respectively. Most of the antibiotics were highly resistance to *Escherichia coli* which were amikacin (76.19%), azithromycin (90.48%), ceftazidime (80.95%), ceftriaxone (76.19%), cefradine (85.71%), cefixime (90.48%), cefuroxime (80.95%), ciprofloxacin (71.42%) and gentamycin (66.67%).(Table:1)

Discussion

To study the profile of Gram negative bacteria that causing blood stream infections and evaluate antibiotic resistance patterns 3220 blood samples has been selected after fulfilling the inclusion and exclusion criteria. Blood culture positivity has been seen in 372(12%) cases which is quite similar to Gohel et al[15] (9.2%), Mehta et al[16] (9.94%) and Wang et al[17] (12.9%).

In this present study the most frequently identified Gram-negative bacteria were *Salmonella typhi* 276(74.2%) followed by *Salmonella paratyphi A, Escherichia coli* and *Pseudomonas species* which were 52(14%) cases, 30(8%) cases and 14(3.8%) cases respectively. The study of Jain S and Chugh[18] has been recorded that *Salmonella typhi* and *S. Paratyphi A* were isolated in a proportion of about 4:1. A study has been conducted among blood stream infection patients has been recorded that about 44.6% isolates are Gram-negative bacilli and frequently identified species were *Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas*[17]. Another study was conducted among septic pediatrics patient has been recorded that predominant isolated bacteria was *Klebsiella pneumonia followed by Salmonella typhi, Pseudomonas aeruginosa, Acinetobacter species, Escherichia coli* and *Proteus mirabilis*[19].

In this study all isolated Gram negative bacteria are highly resistance to Azithromycin and Cefradine which was 86.96% and 66.38% in *Salmonella typhi*, 80.77% and 78.85% in *Salmonella paratyphi A*, 90.48% and 85.71% in Escherichia coli and 92.86% and 100.0% in case of *Pseudomonas species* respectively. The most eminent isolated bacteria were *Salmonella typhi* that has been highly resistant to azithromycin, cefradine, ciprofloxacin, cotrimoxazole and nalidixic acid. Such increasing rates of resistance to azithromycin, ciprofloxacin, cephalosporin, nalidixic acid were detected[18]. Regarding *Salmonella paratyphi A,* highly resistance antibiotics were azithromycin, ceftazidime, cefradine, cefixime, cefuroxime and ciprofloxacin. Such increasing isolation rates of *Salmonella paratyphi A* have been reported across India[20]. In this study most of the antibiotics were highly resistance to *Escherichia coli* which were amikacin (76.19%), azithromycin (90.48%), ceftazidime (80.95%), ceftriaxone (76.19%), cefradine (85.71%), cefixime (90.48%), cefuroxime (80.95%), ciprofloxacin (71.42%) and gentamycin (66.67%). A retrospective study has been recorded that *Escherichia coli* were highly resistance to third-generation of Cephalosporin[21]. This present study reveals that *Pseudomonas species* has been showed highly resistance to most of the antibiotics namely amikacin (78.5%), azithromycin (92.86%), ceftazidime (57.14%), ceftriaxone (71.43%), cefradine (100%), cefixime (71.43%), cefuroxime (100%), colistin (57.14%).

Conclusion

The study of bacteriological profiles with antibiotic resistance patterns plays a pivotal role in the effective management of blood stream infection cases. Early detection of causative pathogen and initiation of targeted

therapy is the mainstay of treatment. This study anticipated that gram-negative bacteria are predominant isolates responsible for BSI. Among them, *Salmonella typhi* followed by *Salmonella paratyphi A, Escherichia coli* and P*seudomonas species* were the most common. The rising trends in antibiotic resistance emphasized the importance of hospital infection control policies and implementation of rational prescription of antimicrobial practices with continued surveillance to prevent the emergence and further spread of resistant bacterial pathogens.

Acknowledgements

None

Conflict Of Interest

The authors have no conflicts of interest to disclose

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' Contributions

Islam MB, Yusuf MA, Jahan T conceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript. Islam MB contributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript. Khan MS, Islam S, Sajid KMT, Roy J involved in the manuscript review and editing. All authors read and approved the final manuscript.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board. The written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

How to cite this article: Islam MB, Yusuf MA, Jahan T, Khan MS, Islam S, Sajid KMT, Roy J. Antimicrobial Resistance Patterns of Gram Negative Bacteria from Blood Stream Infection Patients in a Tertiary Care Hospital, Bangladesh. J Army Med Coll Jashore, 2022;3(1):14-17

Publication History

Received on: 7 October 2021

Accepted on: 24 November 2021

Published on: 1 January 2022

References

1. C. Viscoli, "Bloodstream infections: the peak of the iceberg Virulence, vol. 7, no. 3, pp. 248–251, 2016.

2. K. B. Laupland, "Incidence of bloodstream infection: a review of population-based studies," Clinical Microbiology and Infection, vol. 19, no. 6, pp. 492–500, 2013.

3. H. Lochan, V. Pillay, C. Bamford, J. Nuttall, and B. Eley,"Bloodstream infections at a tertiary level paediatric hospital in South Africa," BMC Infectious Diseases, vol. 17, no. 1, pp. 1–9, 2017.

4. R. A. Balk, "Severe sepsis and septic shock: definitions, epidemiology, and clinical manifestations," Critical Care Clinics,vol. 16, no. 2, pp. 179–192, 2000.

5. Malmir J, Bolvardi E, Afzal Aghaee M. Serum lactate is a useful predictor of death in severe sepsis and septic shock. Rev Clin Med 2014; 1(3): 97-104.

6. Gupta S, Kashyap B. Bacteriological profile and antibiogram of blood culture isolates from a tertiary care hospital of North India. Trop J Med Res 2016; 19(2): 94.

7. Dagnew M, Anagaw B, Motbaynor E. Bacterial Profile and Antimicrobial susceptibility pattern of bacterial meningitis among neonates and children at Gondar University hospital. Northwest Ethiopia. Infect Drug Resist 2021; 14(1): 1703–1711

8. J. Deen, L. von Seidlein, F. Andersen, N. Elle, N. J. White, and Y. Lubell, "Community-acquired bacterial bloodstream infections in developing countries in south and southeast Asia: a systematic review," _e Lancet Infectious Diseases, vol. 12, no. 6, pp. 480–487, 2012.

9. Maldive??(do search)International Journal of MicrobiologyVolume 2021, Article ID 3088202, 10 pages https://doi.org/10.1155/2021/3088202

10. Ramachandran G. Gram-positive and gram-negative bacterial toxins in sepsis: a brief review. Virulence 2014; 5 (1): 213–218.

11. F. Hu, D. Zhu, F. Wang, and M. Wang, "Current status and trends of antibacterial resistance in China," Clinical Infectious Diseases, vol. 67, no. suppl_2, pp. S128–S134, 2018.

12. F. Hu, Y. Guo, Y. Yang et al., "Resistance reported from China antimicrobial surveillance network (CHINET) in 2018," European Journal of Clinical Microbiology & Infectious Diseases, vol. 38, no. 12, pp. 2275–2281, 2019

13. Mahendra AD, Tirtodiharjo MK, Kusuma IT. the pattern of bacteria and its resistance on adult sepsis patient at dr. moewardi general hospital, Indonesia. BioRxiv 2016; 1(1): 044032.

14. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. Phar Therap 2015; 40(4): 277.

15. Gohel K, Jojera A, Soni S, Gang S, Sabnis R, Desai M. Bacteriological profile and drug resistance patterns of blood culture isolates in a tertiary care nephrourology teaching institute. BioMed research international. 2014 Jan 1;2014.

16. M. Mehta, P. Dutta, and V. Gupta, "Antimicrobial susceptibilitypattern of blood isolates from a teaching hospital in NorthIndia," Japanese Journal of Infectious Diseases, vol. 58, no. 3, pp. 174–176, 2005.

17. Wang C, Li W, Gao J, Zhang D, Li Y, Li F, Lei J. Microbial Predominance and Antimicrobial Resistance in a Tertiary Hospital: A Six-year Retrospective study from Outpatients and Patients Visiting the Emergency Department.

18. Jain S, Chugh TD. Antimicrobial resistance among blood culture isolates of Salmonella enterica in New Delhi. The Journal of Infection in Developing Countries. 2013 Nov 15;7(11):788-95

19. Prabhu K, Bhat S, Rao S. Bacteriologic profile and antibiogram of blood culture isolates in a pediatric care unit. Journal of laboratory physicians. 2010 Jul;2(02):085-8.

20. Gupta V, Kaur J, Chander J (2009) An increase in enteric fever cases due to Salmonella Paratyphi A in & around Chandigarh. Indian J Med Res 129: 95-98.

21. Wang, C., Li, W., Gao, J., Zhang, D., Li, Y., Li, F. and Lei, J., 2020. Microbial Predominance and Antimicrobial Resistance in a Tertiary Hospital in Northwest China: A Six-Year Retrospective Study of Outpatients and Patients Visiting the Emergency Department. Canadian Journal of Infectious Diseases and Medical Microbiology, 2020.

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 18-21
ISSN : 2789-1135 (Print)

Original Article ***Open Access***

Prevalence of Risk Factors among Eclampsia Patients attending a Tertiary Hospital in Dhaka City of Bangladesh

Jesmin Ara[1], Kamil Ara Khanom[2], Joysree Saha[3], Shahin Fariya Shetu[4], Priyanka Podder[5], Iffat Ara[6]

[1]Assistant Professor, Department of Gynaecology & Obstetrics, Popular Medical College Hospital, Dhaka, Bangladesh; [2]Associate Professor, Department of Gynaecology & Obstetrics, Popular Medical College Hospital, Dhaka, Bangladesh; [3]Associate Professor, Department of Gynaecology & Obstetrics, Popular Medical College Hospital, Dhaka, Bangladesh; [4]Registrar, Department of Gynaecology & Obstetrics, Popular Medical College Hospital, Dhaka, Bangladesh; [5]Resident Surgeon, Department of Gynaecology & Obstetrics, Popular Medical College Hospital, Dhaka, Bangladesh; [6]Professor, Department of Gynaecology & Obstetrics, Popular Medical College Hospital, Dhaka, Bangladesh

Abstract

Background: Eclampsia is potentially fatal disorder of pregnant women that has been prevalent and important cause of maternal mortality throughout the world. **Objective:** The purpose of the present study was to find out the risk factors among pregnant woman with complications with eclampsia. **Methodology:** This was a prospective cross-sectional study of 245 study population at the Department of Obstetrics & Gynaecology (Eclampsia unit) in Dhaka Medical College & Hospital, Dhaka, Bangladesh from July, 2010 to December, 2010. All the admitted patient having eclampsia (ante-partum, intra-partum, post-partum) with associated complication. Study population included as all the admitted patient having eclampsia (ante-partum, intra-partum, post-partum) with associated complication.Patients excluded from study who having pre-existing medical disorder. Data collection done with pretested questionnaire. Data collection done after thorough evaluation of the cases by history taking from the patient & patient's attendance, physical examination & investigations, necessary information were collected in a preformed data collection sheet. **Results:** The study group showed that three forth of them belonged to 20 to 30 years of age group and most (61.0%) of the patients were nulliparous.Nearly half of (47.7%) of the patients had received irregular ANC and 32.5% had no ante-natal care. Almost the three forth of them presented with antepartum & intrapartum eclampsia with severe hypertension with unconscious, lung congestion, oliguric and attended delayed at hospital after convulsion. **Conclusion:** The risk factor was identified in young age with irregular anti natal care to develop eclampsia which can be prevented to reduce mortality and morbidity and can ensure safe motherhood. *[Journal of Army Medical College Jashore, January 2022;3(1):18-21]*

Keywords: Eclampsia; risk factors; pregnancy; ANC

Introduction

More than half a million women in the world every year meet an untimely end of their lives from complications of pregnancy and child birth, 99% of these unfortunate women are in developing countries1. Besides those who die, there are many more who during the process of child bearing suffer temporary, sometimes long term or even permanent damage or injuries. Eclampsia is potentially fatal disorder of pregnant women that has been prevalent since the time of Hippocrates; it remains an important cause of maternal mortality throughout the world, accounting for about 50,000 deaths worldwide[1]. ln developed countries, eclampsia complicates about 1 in 2000 deliveries[2]. In developing countries the prevalence of eclampsia varies widely, from 1 in 100 to 1 in 1700[3-5].

The incidence of eclampsia is exceptionally high in Bangladesh which is 7.9% cases, according to the results of a house-to-house survey,[6] and account for 16% of maternal death[7]. Eclampsia is the 3rd major cause of maternal death

Correspondence: Dr. Jesmin Ara, Assistant Professor, Department of Gynaecology and Obstetrics, Popular Medical College Hospital, Dhaka, Bangladesh; Email: jesminara0907@gmail.com; Cell no: +8801677718469

in Bangladesh which is also the major cause of mortality in hospital settings because PPH and sepsis can be managed efficiently in the hospitals if patients admit there; that is death from this condition usually occur outside the hospital settings. Patients with eclampsia however develop complications gradually in the form of system failure by the time they reach the hospital; complications have become so severe that they cannot be reversed easily[8]. Case fatality in eclampsia had been found to range from 11.0% to 46.4% in hospitals in Bangladesh[9-12]. Eclampsia can occur in ante partum period (38.0%), intra partum period (18%) and post-partum period (44%) involvement; however, death associated with eclampsia is more difficult to prevent. In different studies it has been found that intracranial bleeding (cerebrovascular accident) is the most common cause of death in eclampsia. Others are cardiac failure, pulmonary edema, HELLP (hemolysis, elevated liver enzyme, low platelet count) syndrome, Disseminated Intravascular Coagulation (DIC), Renal failure, hepatic failure, post-partum shock and so one[13-15]. These complications develop as a result of a delayed decision for treatment. There occurrence indicate gross inaptitude and incompetence of antenatal services. Unfortunately, in Bangladesh, the antenatal services are at infantile stage.

In Bangladesh only 2.3% women and their pregnancy under medical supervision whether it be abortion or delivery[16] the rest have no access to obstetric care. As a result, most pre-eclampsia cases remain unrecognized until severe complications, such as eclampsia occurs. Illiteracy, lack of health awareness and education, poor socio-economic conditions, various superstitions and social taboos prevent women from seeking medical advices during pregnancy. Bad communications and absence of nearby hospital facilities are also adding into the problems[17]. Late referral of cases which delay the control of convulsion by appropriate anticonvulsants and delay the interventions from 1st fit to delivery increases the maternal and perinatal loss. Substandard health care facilities & services are also responsible for poor out come in developing countries. Paradoxically, although it is a disease of young women having their 1st babies, those who die tend to be older and parous[18]. The aim of this study is to find out the risk factors associated with eclampsia developing complications.

Methodology

Study Population and Setting: This was a cross-sectional study in the Department of Obstetrics & Gynaecology at Dhaka Medical College & Hospital, Dhaka in Eclampsia unit for a period of 6 months from July 2010 to December 2010. Study population included all the admitted patient who had eclampsia (ante-partum, intra-partum, post-partum) with associated complication. Eclampsia patient having pre-existing medical disorder was excluded from the study. Ethical clearance permitted from the ethical committee of the DMCH.

Study Procedure: Data collection done with pretested questionnaire. Data collection done after thorough evaluation of the cases by history taking from the patient or patient's attendance, physical examination & investigations, necessary information were collected in a preformed data collection sheet.

Statistical Analysis of Data: All the relevant collected data was compiled on master chart first and Statistical analyses was done by computer software devised as the statistical package for social science (SPSS windows ver4sion14). The value will express as frequencies, percentage, the results were presents in tables.

Results

In this study maximum (44.0%) patients belonged to less than 20 years of age followed by 20.5% patients were belonged to 31 to 35 years, 15.5% patients belonged to 20 to 25 years, 14.0% patients belonged to 26 to 30 years and 6.0% patients were belonged to 36 to 40 years. So, majority of the patients who developed complication were less than 20 years' age group (Table1).

Table 1: Age Distribution of Patients (n=200)

Age Group	Frequency	Percent
Less Than 20 Years	88	44.0
20 to 25 Years	31	15.5
26 to 30 Years	28	14.0
31 to 35 Years	41	20.5
36 to 40 Years	12	6.0
Total	**200**	**100.0**
Mean ± SD	25.19±7.01	

Maximum 47.7% patients had irregular antenatal checkup followed by 32.5% had no antenatal checkup and 20.5% had regular antenatal checkup. About 61.0% of patients were nulliparous, 32.5% were para 1 to 3 and only 6.5% were para more than 4. About 58.0% patients were more than 34 weeks of gestational age; 32.5% cases were between 28 to 33 weeks and 9.5% were more than 28 weeks of gestational age (Table 2).

Table 2: Distribution of Patients by ante-natal checkup (n=200)

Antenatal Checkup	Frequency	Percent
• Regular	41	20.5
• Irregular	94	47.0
• None	65	32.5
Parity		
• Nulliparous	122	61.0
• 1 to 3	65	32.5
• More than 4	13	6.5
Gestational Age		
• Less Than 28 Weeks	19	9.5
• 28 to 33	65	32.5
• More Than or Equal to 34 Weeks	116	58.0

Table 3: Distribution of Patients by Physical Findings on Admission (n=200)

Findings	Frequency	Percent
Level of Consciousness		
• Conscious (GCS >13)	54	27
• Semi-conscious (GCS 9-12)	58	29
• Unconscious (GCS <8)	88	44
Respiratory Rate		
• 17 to 20/m	45	22.5
• More than 20/m	155	77.5
Diastolic Blood Pressure		
• 90 to 100 mmHg	40	20
• 101 to 110 mmHg	65	32.5
• More Than 110 mmHg	95	47.5
Lungs		
• Clear	9	28.5
• Congested	22	71.5
Urine volume		
• Normal	6	20
• Oliguria	20	64
Anuria	5	16
Knee jerks		
• Normal	23	16.5
• Clonus	27	13.5
• Exaggerated	95	47.5
• Absent	45	22.5

Considering the risk factor of the patients, 70.5% cases were more than 20 years of age or 35 years; 61% cases were nulliparous, 58% cases had gestational age more than 34 weeks; 79.5% cases had either more irregular pattern of ANC; 82% cases had antepartum & intrapartum eclampsia; 47.5% cases were severe hypertension (DBP >110); 73.0% cases had unconscious; 11.0% cases had lung congestion; 12.5% cases had oliguric; 73.16% cases had time interval between developments of convulsion to hospitalization >8 hours (Table4).

Table 4: Risk Factors of the Eclamptic Patients Developed Complications

Risk Factors	Frequency	Percent
Age (<20 years &>35 years)	141	70.5
Nulliparous	122	61.0
Gestational age >34 weeks	116	58.0
Pattern of ANC (irregular to none)	159	79.5
Antepartum & intrapartum eclampsia	164	82.0
Severe hypertension (DBP >110)	95	47.5
Unconscious	146	73.0
Lung congestion	22	11.0
Oliguria	25	12.5
Time interval between developments of convulsion to hospitalization (>8 hours)	30	73.16

Discussion

This prospective cross-sectional study was conducted in Dhaka Medical College Hospital, Dhaka during this study period total 200 eclamptic patients who developed grave complications were included in this study. This study found most of the patients who developed complications belonged to < 20 years of age group (44.0%). This has also similarities with the study conducted by Chesley et al[19] where 43.0% patients were in this age group.

This study shows most (61.0%) of the patients were nulliparous. Suman[20] showed 77.24% patients were primigravida, which also had similarities with the present study. It can be concluded that eclampsia is now occurring in nulliparous patients in a severe form. This study found 58.0% of the patients had gestational age 34 weeks and above. A study conducted by Naznin[21] showed 62.9% of the patients were at term which also correlated more or less with the present study.

In this study shows 47.7% of the patients had received irregular ANC and 32.5% had no ante-natal care. Other study, Miguil and Chekairi[22] observed that most (62.0%) of the patients had no or irregular ANC. As eclampsia is largely a preventable disease regular and proper ANC may prevent the severe form of preeclampsia leading to eclampsia.

On analyzing the presentation of the patients, the majority of the patients (47.5%) had severe HTN (diastolic BP >110 mm of Hg). Most of the patients were unconscious and had pulmonary edema (70.0%). About 64% patients were oliguric and knee Jerks were absent in 22.5% cases, which correlate with other study of Naznin[21]. So complications developed before arrival at hospital. As eclampsia is a multi-system disorder early initiation of treatment would prevent systemic failure and complications.

This study analyzed various risk factors for developing complications. About 70.5% were less than 20 years of age or 35 years, 61.0% were nulliparous, 58.0% had gestational age more than 34 weeks, 79.5% had either more irregular pattern of ANC, 82.0% antepartum and intrapartum eclampsia, 47.5% were severe hypertension (DBP >110), 73.0% cases had unconscious, 11.0% cases had lung congestion, 12.5% cases oliguric, 73.16% cases had time interval between developments of convulsion to hospitalization more than 8 hours.

Conclusion

In conclusion different risk factor for developing complications in eclampsia are age that is young pregnant woman mostly nulliparous, gestational age more than 34 weeks, irregular pattern of ANC, severe hypertension, delayed hospitalization and delay in initiation of treatment. So to avoid complication these risk factors should be follow up regularly for safe motherhood.

Acknowledgements

None

Conflict Of Interest

The authors have no conflicts of interest to disclose

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' Contributions

Jesmin A, Kamil A, Joysree Sconceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript. Jesmin Acontributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript. Shahin FS, Priyanka P, Iffat Ainvolved in the manuscript review and editing. All authors read and approved the final manuscript.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board. The written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

How to cite this article: Jesmin A, Kamil A, Joysree S, Shahin FS, Priyanka P, Iffat A. Prevalence of Risk Factors among Eclampsia Patients attending a Tertiary Hospital in Dhaka City of Bangladesh. J Army Med Coll Jashore, 2022;3(1):18-21

Publication History

Received on: 7 October 2021

Accepted on: 24 November 2021

Published on: 1 January 2022

References

1. Deley I. Maternal mortality associated with the hypertensive disorder of pregnancy in Africa, Asia, Latin America and Caribbean. Br JObstetGycecol1992;99:547-53

2. World health organization. The world health report 1998:Iife in the 21st century;a vision for all.Geneva:W1-lO 1998,p.97

3. Ghosh MK.Maternalmortality:a global perspective.J Report Med 2001;46:427-33

4. World health organization.The hypertensive disorder of pregnancy Report of a WHO study group. WHO technical report serious 758.Geneva:WHO 1987;.63-9

5. Mahmoudi N, .Graves, SW Solomon CG,etal. Eclampsia: 13-year experiences at a United States tertiary care center.J Women's health Gend-Based Med 1999;8:495-500

6. EkholamE,SalmiMM, Erkkola R. Eclampsia in Finland in 1990-94.Acta ObstetGynecoiScand 1999,78:877-82

7. Kenneth H. Adult female mortality level and cause in Bangladesh maternal health service and maternal survey. Dhaka Nipport, 2001

8. Begum MR. Begum A, Quadir E, Shamsuddin L. Eclampsia; still a problem in Bangladesh. Medscape General Medicine. 2006;8(10):68

9. Jahan S. A Study on obstetrical cases Admitted in Khulna Sadar Hospital in the year 1981 Paper presented at the 7th annual contributors conference of Bangladesh Fertility Research Programme (BFRP) held on 8-9 December 1982 at Dhaka

10. Chowdhury TA. Profile of 17,751 Institutional Deliveries for the period 1975-80 in Bangladesh, Paper presented at the Annual Contributors Conference of the Bangladesh Fertility ResearchProgramme held on 4th December 1981 at Dhaka

11. Chowdhury TA. Report on obstetrics Deliveries at Institute of Post¬graduate Medicine, Paper presented at International Fertility Research programme at North Carolina, USA. 1982

12. MDU (1992) Report of eclampsia study at Manikgonj Hospital Management Development unit (MDU), MOHFW, Dhaka 1992;3-27

13. Dutta DC. Safe motherhood epidemiology of obstetrics. in: Konar H, editor. Textbook of obstetrics including perinatology and contraception, 6th revised ed. Calcutta: Central Book Agency (P) limited, 2008: 599

14. Begum MR, Begum A, Quadir E, Akter S, Shamsuddin L, et al. 'Eclampsia: Still a problem in Bangladesh' MedGenMed. ob/Gyn and Women's Health 2004; 6(4):52

15. Kenneth H. Adult female mortality level and causes, In: Bangladesh maternal health services and maternal survey. Dhaka: NIPPORT, 2001

16. Kenneth H, Caria AZ, Tessa W. Estimates of maternal mortality for 1995, Bull WHO 2001; 79:182-93

17. Benoit S, Marie HBC, Noelle V, Sophie A, Alison M. Classification differences and maternal mortality: a European study. Int. J Epidemiol 1999; 28: 64-9

18. Lars H, Jakob S, Peter A Maternal Mortality in Guinea-Bissau: the use of verbal autopsy in multi-ethnic population. Int J Epiderniol 1988;28: 70-6

19. Chesley LC. Hypertensive disorders in pregnancy. New York; Appleton century-crofts, 1978

20. Suman G. Somegowda. Maternal and perinatal outcome in a district hospital. J ObstetGynecol India 2007; 57(4): 324-326

21. Naznin S. 'clinical evaluation of causes of eclampsia in a tertiary care hospital.' A Study in COMCH, Comilla(Dissertation). Bangladesh colleges of Physicians and Surgeon. 2008

22. Miguil M, Chekairi A eclampsia study of 342 cases. Hypertension in pregnancy 2008;27:103-111

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 22-27
ISSN : 2789-1135 (Print)

Original Article ***Open Access***

Contemporary Role of Janus Kinase Inhibitor (Tofacitinib) in the Management of Dermatological Lesions: A Randomized Control Trial

Quazi Salim Yazdi[1], S M Khalid Shams[2], Jannatun Nayeem[3]

[1]Head, Department of Dermatology & Venereology, Combined Military Hospital, Bogura and Army Medical College, Bogura, Bangladesh; [2]Medical Officer, Combined Military Hospital, Bogura, Bangladesh; [3]Head, Department of Dermatology & Venereology, Combined Military Hospital, Jashore and Army Medical College, Jashore

Abstract

Background: Tofacitinib is an oral Janus kinase inhibitor (jakinib), a new treatment option for systemic inflammatory diseases that is well-established in its efficacy, is now being actively investigated for skin diseases that are unresponsive to classical immunosuppressants or persist intolerable side effects and other targeted therapies including psoriasis, alopecia areata, vitiligo, and atopic dermatitis. **Objective:** This article was aimed to describe the therapeutic role of tofacitinib in dysimmune diseases of the skin, most common dermatoses for which oral and topical jakinibs such as tofacitinib had been evaluated and used, albeit as an off-label indication, including psoriasis, alopecia areata, vitiligo, and atopic dermatitis. **Methodology:** From June 2021 to June 2022, an outdoor randomized control trial was conducted at the Department of Dermatology and Venereology of the Combined Military Hospital in Bogura where 50 patients with psoriasis, psoriatic arthritis, alopecia areata, vitiligo and atopic dermatitis were included and classified according to the inclusion and exclusion criteria. Selected patients were treated with oral tofacitinib for their skin disorders. **Results:** Tofacitinib appears to show strong efficacy for a number of dermatologic conditions. The results showed that the mean age of the patients was average 35 years with male predominance (58%). Features of psoriasis, alopecia areata, vitiligo and atopic dermatitis were found among 14%, 44%, 28%, and 14% of patients respectively. Available data for oral tofacitinib administration shows more efficacy for vitiligo than alopecia areata. **Conclusion:** Although tofacitinib exhibits a broad spectrum of immunoregulatory properties, making it a potential candidate for the treatment of many dermatological conditions unresponsive to other therapies, more evidence is needed to assess its efficacy and usefulness in the future. *[Journal of Army Medical College Jashore January 2022;3(1):22-27]*

Keywords: Alopecia areata; atopic dermatitis; Janus kinase inhibitors; psoriasis; tofacitinib; vitiligo

Introduction

Tofacitinib is an immunomodulator and it is a Janus kinase inhibitor (Jakinib), a new treatment option for systemic inflammatory diseases that is well-established in its efficacy, is now being actively investigated for skin diseases (due to patient's dysimmune responses) that are unresponsive to classical immunosuppressants or persist intolerable side effects and other targeted therapies.[1] It blocks non receptor tyrosine kinases. Janus kinase (JAK) activate signal transducer and activator of transcription (STAT) pathways, the effect of which is the production of multiple proinflammatory cytokines including IFN-γ, IL-12, and IL-23, and the maturation of dendritic cells. The most common dermatoses for which oral and topical jakinibs such as tofacitinib have been evaluated and used, albeit as an off-label indication, include psoriasis, alopecia areata, vitiligo, and atopic dermatitis.[2] The well-established efficacy of jakinibs by blocking this signaling pathway,

Correspondence: Colonel (Dr.) Quazi Salim Yazdi, MBBS, DDV, MCPS, FCPS, Head, Department of Dermatology & Venereology, Combined Military Hospital (CMH) Bogura, Bogura Cantonment, Bogura and Army Medical College, Bogura, Bangladesh; Email: yazdi886@hotmail.com, Cell No.: +8801711119371,

particularly in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ulcerative colitis (UC), suggests the potential in a variety of inflammatory dermatoses[3].

Jakinibs are preferred options for biologics-directed therapy due to their inhibition of multiple cytokines signaling pathways, unreported potential to generate neutralizing antibodies, and ease of oral and topical administration. Tofacitinib may be used in combination with other non-biologic disease-modifying antirheumatic drugs (DMARD). The recommended dosing is 5 mg twice daily or 11 mg once daily as an extended-release tablet[4-5].

The major skin and associated disorders that have shown the most promising results with tofacitinib and other jakinibs include psoriasis and alopecia areata (AA), and variants including AA totalis (AT) and AA universalis (AU), atopic dermatitis (AD), and vitiligo. Anecdotal reports also suggest its efficacy in cutaneous lupus erythematosus, dermatomyositis, chronic actinic dermatitis, erythema multiforme, hyper eosinophilic syndrome, skin graft-versus-host disease, pyoderma gangrenosum (PG), lichen planus, and Sjogren's syndrome, among others[6].

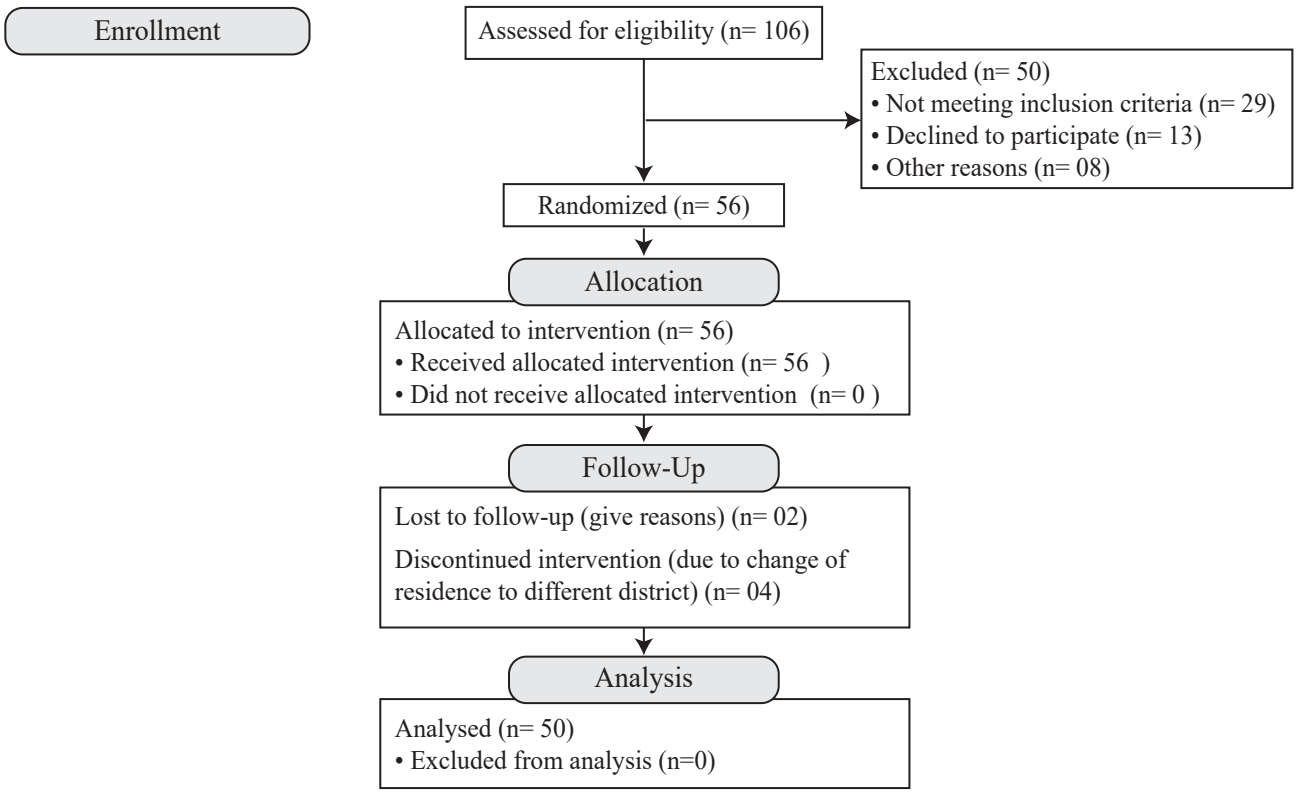
Isoforms of JAK are known as JAK1, JAK2, JAK3 and TYK2. Among four isoforms, JAK1, JAK2, and TYK2 bind to many cytokine receptors; JAK3 only binds to one subunit, the common gamma chain. This common receptor subunit is used by a small family of cytokines that include interleukin (IL) 2, IL 4, IL 7, IL 9, IL 15, and IL 21. While the first generation jakinibs (tofacitinib, ruxolitinib, baricitinib) block several JAKs, the second generation (decernotinib) targets a specific JAK. Specific jakinibs are associated with fewer adverse events (AEs), particularly serious infections and cytopenias[7].

Tofacitinib, a JAK 1/3 inhibitor, is the most well-studied jakinib in skin diseases. Because it only weakly inhibits JAK2, it has fewer hematological side effects than other JAK2 inhibitors[8]. The aim of this article was to evaluate the therapeutic role of tofacitinib and further assessment for its implication in different dermatological diseases.

Methodology

Study Settings and Population: This was a randomized control study conducted at Combined Military Hospital, Bogura, Bangladesh from June 2021 to May 2022 for a period of one year. For this purpose, patients of both genders were drawn as an appropriate sample in Inclusion and Exclusion Criteria. A face-to-face interview was used to collect data in a pre-tested questionnaire containing personal and socio-demographic information as well as medication feedback. For this study purpose, ethical approval was obtained from the Ethical Committee of CMH, Bogura, Bangladesh and no intervention or invasive procedure was performed. Informed consent was taken from each of the study subjects before enrolling them in the study. Inclusion and exclusion criteria were followed in data collection, in which patients treating for rheumatoid arthritis, ulcerative colitis, psoriatic arthritis, myasthenia gravis, known cases of heart disease, hypertension, obesity, thyroid disorders and pregnancy were excluded, and patients treating for psoriasis, alopecia areata, vitiligo, and atopic dermatitis were included.

Flow Diagram



Randomization and Blinding: Simple random sampling technique was used.

Allocation: They were recommended to take tofacitinib 5-10 mg twice daily on an empty stomach and for the same duration. The study instruments are selected and developed according to the requirements of the study objectives.

Follow-up and Outcomes Measures: Laboratory investigations like complete blood counts, liver function tests, thyroid function tests, serum creatinine, random blood sugar levels and serum cholesterol and triglyceride levels were carried out for the purpose of exclusion and monitoring of side effects.

Statistical Analysis: Pretests, data interpretation, and statistical analysis were performed using the Statistical Package for Social Sciences (SPSS v.25)[9]. After the data extraction, the information corresponding to the different diseases have been processed and reorganized in the form of a narrative review with an attempt to objectify the article by summarizing the content in tables and pie charts.

Results

This randomized control trials (RCTs) of tofacitinib had been conducted among 25 to 50 years aged outdoor patients for five off-label dermatologic conditions like psoriasis, alopecia areata, vitiligo and atopic dermatitis. Among the respondents, the results showed that the mean age of the patient was 35 years with male predominance (58%) (Table 1).

Table 1: Gender Distribution of Patients (n=50)

Variables	Frequency	Percent
Male	29	58.0
Female	21	42.0
Total	**50**	**100.0**

Here, Figure I shows the gender distribution of patients where 42% patients were female and 58% patients were male.

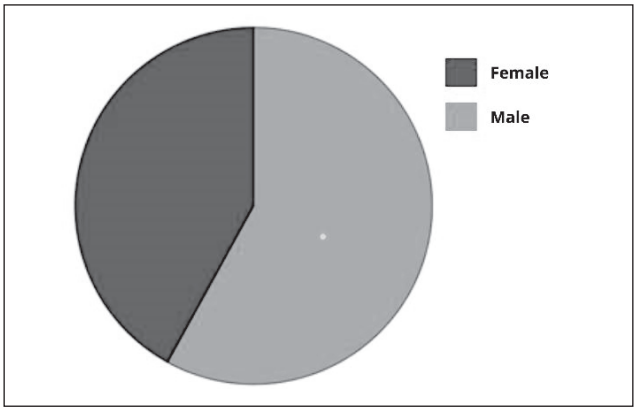


Figure I: Gender distribution of patients (n=50)

Among the samples (n=50), the majority of the frequency of dermatological diseases concerns alopecia areata (44.0%) and then vitiligo (28.0%). Patients with psoriasis and atopic dermatitis are 14.0% cases in each (Table 2).

Table 2: Dermatological conditions' distribution of patients (n=50)

Variables	Frequency	Percent
Psoriasis	7	14.0
Alopecia areata	22	44.0
Vitiligo	14	28.0
Atopic dermatitis	7	14.0
Total	**50**	**100.0**

The efficacy of oral tofacitinib in patients with psoriasis can be seen in (Table 3). It shows similar effectiveness as alternative medications for moderate to severe plaque psoriasis. However, doubling the dose shows better efficacy in moderate to severe chronic cases.

Table 3: Prognosis after oral tofacitinib administration among patients with psoriasis (n=7)

Variables	Frequency	Efficacy
Moderate to severe chronic plaque psoriasis	5	10 mg BD > 5 mg BD
Moderate to severe psoriasis	2	Similar to alternative medications
Total	**7**	

The prognosis among patients with Alopecia Areata (AA) including Alopecia totalis (AT), Alopecia universalis (AU), after 3 months administration of oral tofacitinib were assessed. About 44.0% showed improvement in Moderate to severe cases. Around 44.0%, 58.0%, 32.0% improvement is observed in case of >30%, >40%, >50% scalp hair loss respectively (Table 4).

In (Table 5), almost complete repigmentation of the forehead and hands and partial repigmentation of other areas were found in 54.0% of patients after 3 months oral administration of tofacitinib for progressive vitiligo with 10% BSA and sustained progression with NB-UVB phototherapy. Rapid and almost complete facial repigmentation was observed in 31% of long-standing cases.

Table 6 showed the clinical response to oral tofacitinib in moderate-to-severe, lifelong and moderate-to-severe atopic dermatitis (AD) in which common treatment has failed.

Table 4: Prognosis after Oral Tofacitinib Administration among Patients with Alopecia Areata (AA) (n=22)

Variables	Frequency (n=22)	Improvement of>50% in SALT scores at 3 months
AA with>50% scalp hair loss, AT and AU	7	32% of patients
AA with >40% scalp hair loss, AT, and AU	2	58% of patients
AA with>30% scalp hair loss, AT and AU	11	44.4% of patients
Moderate to severe AA, AT, and AU	2	44.4% of patients
Total	**22**	

Here, SALT score=Severity of Alopecia Tool

Table 5: Prognosis after oral tofacitinib administration among patients with Vitiligo (n=14)

Variables	Frequency (n=14)	Clinical response at 3 months
Progressive vitiligo involving 10% BSA Continued progression with NB UVB phototherapy	7	almost complete repigmentation of the forehead and hands and partial repigmentation of other areas
Generalized vitiligo/acral vitiligo of 4—33 years duration	3	A mean decrease of 5.4% BSA involvement with vitiligo, only in sun exposed or NB UVB phototherapy treated areas
Longstanding vitiligo with significant facial involvement	4	Rapid and nearly complete repigmentation of face after 3-6 month
Total	**14**	

Here, BSA= Body surface are, NB UVB= Narrow band ultraviolet

Table 6: Prognosis after oral tofacitinib administration among patients with Atopic dermatitis (AD) (n=7)

Variables	Frequency (n=7)	Results
Moderate to severe AD that had failed all common treatments, including systemic agents	2	Reduction in SCORAD 66.6%, Reduction in pruritus and sleep loss scores 69.9%
Lifelong history of AD	3	Partial remission of AD in 3 months
Moderately severe AD	2	Reduction in itch score from 8 to 3.
Total	**7**	

Here, AD=Atopic dermatitis, SCORAD=Scoring of Atopic Dermatitis

Discussion

Tofacitinib has already been approved by US FDA for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ulcerative colitis (UC). Studies of tofacitinib in patients with plaque psoriasis have shown a dose dependent improvement in moderate to severe chronic plaque psoriasis. The result shows that it is similarly effective as alternative medications for moderate to severe plaque psoriasis. However, doubling the dose shows better efficacy in moderate to severe chronic cases[10]. It has also shown improvement in health-related life expectancy across multiple qualitative end points. In other studies, tofacitinib 2% ointment formulations have also shown beneficial effects in psoriasis after 8 weeks of daily or twice daily dosing.

In alopecia areata, the JAKSTAT-dependent cytokines, interferon (IFN)γ and IL15 induced activation of autoreactive CD8 T cells, which are critical for AA pathogenesis[11]. This retrospective evidence suggests that tofacitinib may be effective in regenerating hair in alopecia areata and its variants, alopecia totalis and alopecia universalis. Several prospective studies have confirmed these results[12-15]. Patients with alopecia areata who received tofacitinib achieved at least a 50% change in Severity of Alopecia Tool (SALT) score starting at 5 mg twice daily in these studies and increasing to 10 mg twice daily in patients not responsding to above dose. Patients receiving treatment tofacitinib 10 mg daily along with combination drugs for 3 months showing better result. Side effects were not reported. Efficacy varies with disease severity, drug dose, and adjuvant treatments. Better overall outcomes were reported for AA patch (vs. AT/AU), 10 mg bid (vs. 5 mg bid), and with concomitant oral steroids. However, relapses were common to systemic corticosteroids. Hence, concomitant use of local immune suppressor or modulator (avoiding systemic steroids) showed less relapsing incidence. Tofacitinib has been reported to offer similar efficacy to oral ruxolitinib, greater efficacy than contact immunotherapy alone, and better tolerability than traditional immunosuppressive therapies (corticosteroids ± cyclosporine) in AA. The longest reported duration of treatment with tofacitinib in AA/AT/AU is 18 months[16-17].

In vitiligo, tofacitinib inhibits IFN-γ signaling, which drives CD8 T cell-mediated destruction of melanocytes. There are no robust clinical studies showing the effectiveness of tofacitinib in vitiligo, but there is successful repigmentation

has been reported with 5 to 10 mg twice daily, with better results on sun-exposed areas and concomitant narrow-band ultraviolet B (UVB NB) therapy[18-21].

In atopic dermatitis, tofacitinib reduces IL-4, IL-5 and IL-13 signaling involved in the pathogenesis of AD. In addition, it reduces AD-associated pruritus since JAK signaling in the nerves is crucial in regulating AD-associated pruritus. Moderate to severe AD that had failed all common treatments, including systemic agents shows reduction in SCORAD scale after tofacitinib administration. Patients with lifelong history of AD received a significant permanent improvement from AD in 3 months under tofacitinib administration[22-25].

Side effects associated with oral jakinibs, such as opportunistic infections, Lymphocytopenia, neutropenia, lipid abnormalities, rarely GI perforation and malignancies can be offset by their topical formulations. Topical tofacitinib (TT), most commonly used as a 2.0% ointment with or without a penetration enhancer, has shown modest improvement in psoriasis and AA[26].

However, tofacitinib does not cause significant inhibition or induction of major drugs that metabolize human cytochrome P450 (CYP), but its pharmacokinetics and effects/side effects may be altered by drugs that affect CYP isoforms[27]. Interestingly, the clinically observed toxicity is limited, probably due to the rapid kinetics of action. The risk of disseminated disease and serious infections is greater with higher doses (10 mg twice daily) and with concomitant use of immunomodulators like methotrexate or corticosteroids and requires more careful monitoring. The most commonly reported adverse events with oral tofacitinib include upper respiratory tract infection, headache, diarrhea, and reactivation of viral infections particularly herpes zoster[28].

Conclusion

Although tofacitinib exhibits a broad spectrum of immunoregulatory properties, creating it a possible candidate for the treatment of psoriasis, alopecia areata, vitiligo and atopic dermatitis less/unresponsive to regular therapies, more proof is required to assess its efficaciousness and quality within the future.

Acknowledgements

The authors would like to forward special thanks to Brigadier General Md Sharif Ahmed, Commandant, CMH Bogura for his sincere guidance. We thank all of the respondents who kindly contributed to this study.

Conflict Of Interest

The authors have no conflicts of interest to disclose

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' Contributions

Yazdi QS, Shams SMK, Nayeem J conceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript. Yazdi QS, contributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript. Shams SMK, Nayeem J involved in the manuscript review and editing. All authors read and approved the final manuscript.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board. The written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

How to cite this article: Yazdi QS, Shams SMK, Nayeem J. Contemporary Role of Janus Kinase Inhibitor (Tofacitinib) in the Management of Dermatological Lesions: A Randomized Control Trial. J Army Med Coll Jashore, 2022;3(1): 22-27

Publication History

Received on: 7 October 2021

Accepted on: 24 November 2021

Published on: 1 January 2022

References

1. Shreberk Hassidim R, Ramot Y, Zlotogorski A. Janus kinase inhibitors in dermatology: A systematic review. J Am Acad Dermatol 2017; 76:745 53

2. Stephen E. Wolverton, Comprehensive Dermatologic Drug Therapy, 14th edition, chapter 18, 203-204

3. Samadi A, Ahmad Nasrollahi S, Hashemi A, Nassiri Kashani M, Firooz A. Janus kinase (JAK) inhibitors for the treatment of skin and hair disorders: a review of literature. J Dermatol Treat 2017; 28:476 83

4. Kochar B, Herfarth N, Mamie C, Navarini AA, Scharl M, Herfarth HH. Tofacitinib for the treatment of pyoderma gangrenosum. Clin Gastroenterol Hepatol Epub 2018; pii: S1542 3565

5. Kim SR, Charos A, Damsky W, Heald P, Girardi M, King BA. Treatment of generalized deep morphea and eosinophilic fasciitis with the Janus kinase inhibitor tofacitinib. JAAD Case Rep 2018; 4:443 5

6. Welsch K, Holstein J, Laurence A, Ghoreschi K. Targeting JAK/STAT signalling in inflammatory skin diseases with small molecule inhibitors. Eur J Immunol 2017; 47:1096 107.

7. Mahajan S, Hogan JK, Shlyakhter D, Oh L, Salituro FG, Farmer L, et al. VX 509 (decernotinib) is a potent and selective Janus kinase 3 inhibitor that attenuates inflammation in animal models of autoimmune disease. J Pharmacol Exp Ther 201; 353:405 14

8. US Food and Drug Administration. Xeljanz prescribing information. Available from: https://www.accessdata.fda.gov/ drugsatfda_docs/label/2018/203214s018lbl.pdf. [Last cited on 2018 Nov 22]

9. en.wikipedia.org/wiki/SPSS

10. Bissonnette R, Iversen L, Sofen H, Griffiths CE, Foley P, Romiti R, et al. Tofacitinib withdrawal and retreatment in moderate to severe chronic plaque psoriasis: A randomized controlled trial. Br J Dermatol 2015; 172:1395 406

11. Lee JS, Huh CH, Kwon O, Yoon HS, Cho S, Park HS. Nail involvement in patients with moderate to severe alopecia areata treated with oral tofacitinib. J Dermatol Treat 2018; 29:819 22

12. Kennedy Crispin M, Ko JM, Craiglow BG, Li S, Shankar G, Urban JR, et al. Safety and efficacy of the JAK inhibitor tofacitinib citrate in patients with alopecia areata. JCI Insight 2016;1: e89776
13. Liu LY, Craiglow BG, Dai F, King BA. Tofacitinib for the treatment of severe alopecia areata and variants: A study of 90 patients. J Am Acad Dermatol 2017; 76:22 8
14. Chiang A, Ortenzio F, Juhasz MLW, Yu V, Mesinkovska NA. Balance of tofacitinib efficacy and disease flare in the treatment of alopecia universalis: A case report and review of the literature. JAAD Case Rep 2018; 4:733 6
15. Jabbari A, Sansaricq F, Cerise J, Chen JC, Biterman A, Ulerio G, et al. An open label pilot study to evaluate the efficacy of tofacitinib in moderate to severe patch type alopecia areata, totalis, and universalis. J Invest Dermatol 2018; 138:1539 45
16. K.W. Wyrwich, H. Kitchen, S. Knight, N.V.J. Aldhouse, J. Macey, et al The Alopecia Areata Investigator Global Assessment scale: a measure for evaluating clinically meaningful success in clinical trials
17. Jabbari A, Sansaricq F, Cerise J, Chen JC, Bitterman A, Ulerio G, et al. An open label pilot study to evaluate the efficacy of tofacitinib in moderate to severe patch type alopecia areata, totalis, and universalis. J Invest Dermatol 2018; 138:1539 45
18. Craiglow BG, King BA. Tofacitinib citrate for the treatment of vitiligo: A pathogenesis directed therapy. JAMA Dermatol 2015; 151:1110
19. Liu LY, Strassner JP, Refat MA, Harris JE, King BA. Repigmentation in vitiligo using the Janus kinase inhibitor tofacitinib may require concomitant light exposure. J Am Acad Dermatol 2017; 77:675 82
20. Kim SR, Heaton H, Liu LY, King BA. Rapid repigmentation of vitiligo using tofacitinib plus low dose, narrowband UV B phototherapy. JAMA Dermatol 2018; 154:370
21. Grace D Bandow , John Y M Koo Narrow-band ultraviolet B radiation: a review of the current literature
22. Levy LL, Urban J, King BA. Treatment of recalcitrant atopic dermatitis with the oral Janus kinase inhibitor tofacitinib citrate. J Am Acad Dermatol 2015; 73:395 9
23. Vu M, Heyes C, Robertson SJ, Varigos GA, Ross G. Oral tofacitinib: A promising treatment in atopic dermatitis, alopecia areata and vitiligo. Clin Exp Dermatol 2017; 42:942 4
24. Morris GM, Nahmias ZP, Kim BS. Simultaneous improvement of alopecia universalis and atopic dermatitis in a patient treated with a JAK inhibitor. JAAD Case Rep 2018; 4:515 7
25. Ports WC, Feldman SR, Gupta P, Tan H, Johnson TR, Bissonnette R. Randomized pilot clinical trial of tofacitinib solution for plaque psoriasis: Challenges of the intra subject study design. J Drugs Dermatol 2015; 14:777 84
26. Craiglow BG. Topical tofacitinib solution for the treatment of alopecia areata affecting eyelashes. JAAD Case Rep 2018; 4:988 9
27. Schwartz DM, et al. JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. Nat Rev Drug Discov. 2017. PMID: 29282366
28. Damsky W, King BA. JAK inhibitors in dermatology: The promise of a new drug class. J Am Acad Dermatol 2017; 76:736 44

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 28-32
ISSN : 2789-1135 (Print)

Original Article ***Open Access***

Serum Gamma-Glutamyl Transferase Enzyme Status in Patients with Different Stages of Chronic Kidney Disease with or without Undergoing Hemodialysis

Sabrina Afrin Chowdhury[1], Sadia Chowdhury[2], Mohammed Asif[3], Farhana Afroz[4]

[1]Assistant Professor, Department of Biochemistry, Northern International Medical College, Dhaka, Bangladesh; [2]Assistant Professor, Department of Biochemistry, Army Medical College, Jashore, Bangladesh; [3]Indoor Medical Officer, Department of Orthopaedics, Kurmitola General Hospital, Dhaka, Bangladesh; [4]Assistant Professor, Department of Biochemistry, Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka, Bangladesh

Abstract

Background: Chronic kidney disease (CKD) refers to progressive loss of renal function over a period of months and even years. High blood pressure and diabetes are two primary causes of CKD. Liver function tests particularly serum liver enzymes play an important role to assess the hepatic dysfunction in these CKD patient. **Objectives:** The present study is designed to analyze the serum gamma-glutamyltransferase in patients with different stages of chronic kidney disease with and without undergoing hemodialysis. **Methodology:** This cross sectional comparative study was conducted in the department of Biochemistry, Dhaka Medical College, Dhaka from July 2015 to June 2016 for duration of one year. 50 CKD patients with hemodialysis attending the Department of Nephrology, DMCH were included in group A, 50 CKD patients without hemodialysis (stage 1-5) were included in group B according to selection criteria, age 40-65 years, both male and female and 50 healthy individual were selected as group C from same hospital premises by personal contact. All study subjects were subjected to detailed history and physical examination. Blood samples was collected from each subject. e-GFR was calculated by MDRD equation and serum GGT and serum creatinine were assayed on a semi-automated biochemical analyzer. Correlation of eGFR with serum GGT was done. **Results:** The study shows that serum GGT was significantly higher in CKD with hemodialysis than, CKD without hemodialysis and serum GGT was significantly lower in early stages (stage 1,2,3) of CKD than the later stages (stage 4& 5). Serum GGT was significantly increased with the increment of the duration of hemodialysis. There was negative correlation between eGFR with serum GGT in both CKD with and without hemodialysis. **Conclusion:** Routine screening for serum GGT level in CKD patients with and without undergoing hemodialysis might help in early diagnosis of liver disease, to prevent the aggression of hepatic disease, and might help in monitoring, treatment of liver disease and adjustment of their targeted therapy to reduce the risk of hepatic disease in these patients.
[Journal of Army Medical College Jashore, January2022;3(1):28-32]

Keywords: Chronic kidney disease; hemodialysis; Serum GGT; eGFR

Introduction

Chronic kidney disease (CKD) refers to progressive loss of renal function over a period of months and even years. According to National Kidney Foundation, Chronic kidney disease is either permanent kidney damage for ≥3 months (structural or functional abnormalities), with or without decreased glomerular filtration rate (GFR) or GFR<60 ml/min/1.73 m^2 for ≥3 months, with or without kidney damage[1]. Various conditions such as high blood pressure and diabetes are the most important two causes of CKD[2]. According to the 1998 to 2004 National Health and Nutritional Survey (NHANES), the prevalence of CKD in the US population is 15.3% cases[3]. The overall prevalence of CKD in Bangladesh is 19.0% cases[4]. It has been found that, in Bangladesh there are about 20 million people suffering from CKD. Among them, 20,000 people died of

Correspondence: Dr. Sabrina Afrin Chowdhury, Assistant Professor, Department of Biochemistry, Northern International Medical College, Dhaka, Bangladesh; email: sabrina_afrin@ymail.com,
Cell no.: 01727336973

end-stage renal disease (ESRD) in each year[4]. CKD is classified into 5 stages based on estimated GFR (eGFR). Stage 1 refers to e-GFR 90 ml/min/1.73 m^2 along with demonstrable kidney damage. Next Stage 2,3 and 4 correspond to e-GFR of 60-89 ml/min/1.73 m^2, 30-59 ml/min/1.73 m^2 and 15-29 ml/min/1.73 m^2 respectvely[1]. Stage 5 is known as end-stage renal disease correspond to eGFR of less than 15 mL/min/1.73 m^2 which is treated by hemodialysis or renal replacement therapy. A patient with CKD leads to many complications over a period of time such as cardiovascular, cerebrovascular and peripheral vascular disease. Hepatic disease is also common co-morbid condition in CKD patients with and without hemodialysis. Studies have revealed that there is alteration of liver enzymes (gamma-glutamyltransferase) occurs in patients with CKD with and without hemodialysis. Gamma-glutamyltransferase (GGT) is primarily present in kidney, liver, and pancreatic cells. Small amounts are present in other tissues.

Even though renal tissue has the highest level of GGT, the enzyme present in the serum appears to originate primarily from the hepatobiliary system, and GGT activity is elevated in any and all forms of liver disease. In patients with CKD on hemodialysis gamma-glutamyltransferase level exceed. The high GGT levels in patients who were undergoing dialysis may have been induced by the use of medication or been related to the origins of CKD, such as diabetes mellitus, which can cause steatohepatitis[5]. In addition, high GGT serum levels could be related to malnutrition-inflammation-atherosclerosis (MIA syndrome), which has been observed in patients with CKD who were undergoing dialysis because of systemic arterial hypertension or diabetes mellitus[6]. There are only a few articles, however, that describe the GGT levels in patients with CKD[7-9] and further studies are needed to assess the possibility of other mechanisms that may be involved in the changes of this liver enzyme. The present study was designed to analyze the serum gamma-glutamyltransferase in patients with different stages of chronic kidney disease with and without undergoing hemodialysis.

Methodology

This cross-sectional study was carried out in the Department of Biochemistry, Dhaka Medical College, Dhaka, Bangladesh during the period of July 2015 to June 2016. This period included the time for selection of study places, seeking permission from the appropriate authority, development of research instrument, its pre-testing and printing, interviewing, physical examination and measurement of serum GGT, serum creatinine for both patients of CKD with and without hemodialysis and Healthy individuals. A total number of 150 subjects were selected according to selection criteria. Among them, 50 CKD patients with hemodialysis were included in group A, 50 CKD patients without hemodialysis (stage 1-5) were included in group B and 50 healthy subjects were included in group C. Patients were selected from the Nephrology department of Dhaka Medical College Hospital, Dhaka and control was selected from same hospital premises by personal contact. Written informed consent was taken from each subject. After all aseptic precaution 5 ml of venous blood sample drawn from antecubital vein of each study subject and 30 minutes after dialysis in case of CKD with hemodialysis in a disposable plastic syringe. The collected blood transferred immediately to a dry clean test tube after removing the needle touching the inside wall of the test tube with all precursors to avoid hemodialysis. Then serum was separated after centrifuging at 3000 rpm for 10 minutes and collected in eppendorf tube and labeled appropriately and then separated serum was used for measurement of serum GGT and serum creatinine on a semi-automated biochemical analyzer. Continuous variables were expressed as mean ± SD and were compared between groups of patients by Student's 't' test. Categorical variables were compared using a Chi-square test and was presented as absolute frequencies with percentages. Correlation was done by Pearson correlation coefficient test and ANOVA test. All analysis was done using the SPSS 20.0 package for window.

Results

The serum GGT level in study subjects were assessed. Mean±SD serum GGT was 39.6±10.3, 34.8±9.2 and 18.3±4.1 in CKD with hemodialysis, CKD without hemodialysis and healthy subjects respectively. Serum GGT was significantly higher in CKD with hemodialysis 39.6±10.3 than healthy subjects 18.3±4.1. Serum GGT was significantly higher in CKD without hemodialysis 34.8±9.2 than healthy subjects 18.3±4.1. Serum GGT was significantly higher in CKD with hemodialysis 39.6±10.3 than CKD without hemodialysis 34.8±9.2 (Table 1 & Figure I).

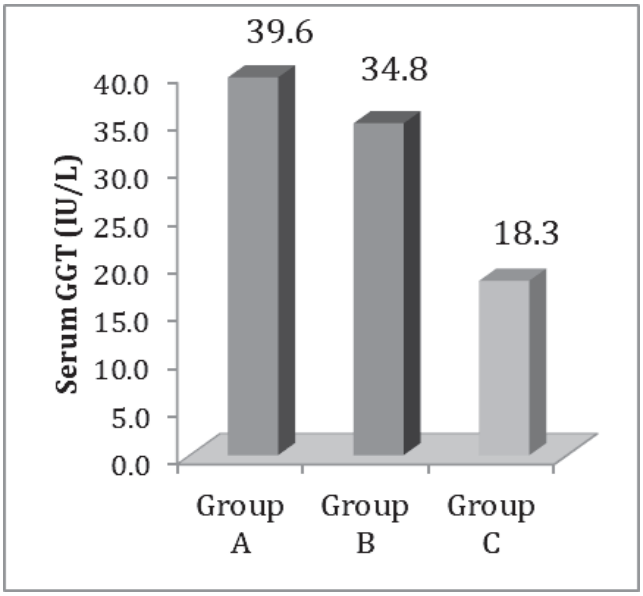


Figure I: Bar diagram of Mean serum GGT in different groups (Group A: CKD with hemodialysis; Group B: CKD without hemodialysis; Group C: Healthy)

Table 1: Serum Gamma-Glutamyl Transferase of Study Subjects in Different Groups (n=150)

Parameter	(A) Mean ± SD (Min –max)	(B) Mean ± SD (Min –max)	(C) Mean ± SD (Min –max)	P value
Serum gamma-glutamyl transferase (U/L)	39.6 ± 10.3 (20.0 - 60.0)	34.8 ± 9.2 (17.0 - 54.0)	18.3 ± 4.1 (14.0 - 42.0)	<0.001
	39.6 ± 10.3 (20.0 - 60.0)		18.3 ± 4.1 (14.0 - 42.0)	<0.001
		34.8 ± 9.2 (17.0 - 54.0)		<0.001

Group A: CKD with hemodialysis; Group B: CKD without hemodialysis; Group C: Healthy individuals; Level of significance –P<0.05,Un paired t test was done to measure the level of significance.

Table 2: Serum GGT in different stages of CKD without hemodialysis (n=50)

CKD Stages	GGT (IU/L)	Serum creatinine (gm/dl)	eGFR (ml/min/1.73m²)
Stage 2	30.38 ± 9.21	1.25 ± 0.05	63.19 ± 2.94
Stage 3	32.92 ± 8.09	1.80 ± 0.28	39.23 ± 7.19
Stage 4	38.27 ± 8.62	2.70 ± 0.54	22.09 ± 4.47
Stage 5	51.00 ± 4.24	3.95 ± 0.78	14.27 ± 0.18
P value	0.007	<0.001	<0.001

ANOVA test was done to measure the level of significance

Table 2 showed pattern of GGT level in different stages of CKD patients and their relation with serum creatinine and eGFR. Serum GGT was significantly higher in stage 5 (51.00 ± 4.24). Serum GGT was gradually increased as per increment of serum creatinine and it was statistically significant but increment of serum GGT was inversely related with eGFR and it was significant.

Table 3: Serum GGT Status in Different Duration of HD (n=50)

Enzymes	Duration of H/D			P value
	≤1	1 – 3 years	>3 years	
Serum GGT	27.5 ± 15.3 (2.0 - 56.0)	43.5 ± 3.4 (40.0 - 48.0)	45.2 ± 5.1 (38.0 - 54.0)	<0.001

ANOVA test was done to measure the level of significance

Table 3 showed serum GGT status at different duration of hemodialysis. Mean (SD) of serum GGT was gradually increased as per increment of duration of hemodialysis and it was statistically significant.

Table 4 showed Pearson's correlation test of eGFR with serum GGT in different groups. There was a negative correlation between e-GFR and serum GGT (r=-0.575, p=<0.001) in Group A. Negative correlation was seen between eGFR and serum GGT (r=-0.354; p=0.012) in Group B. In Group C there was also negative correlation between eGFR with serum GGT (r=-0.590, p=<0.001).

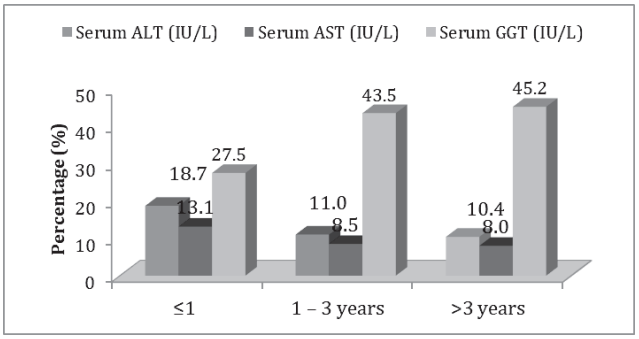


Figure II: Bar chart of Enzymes Status in Different Duration of HD

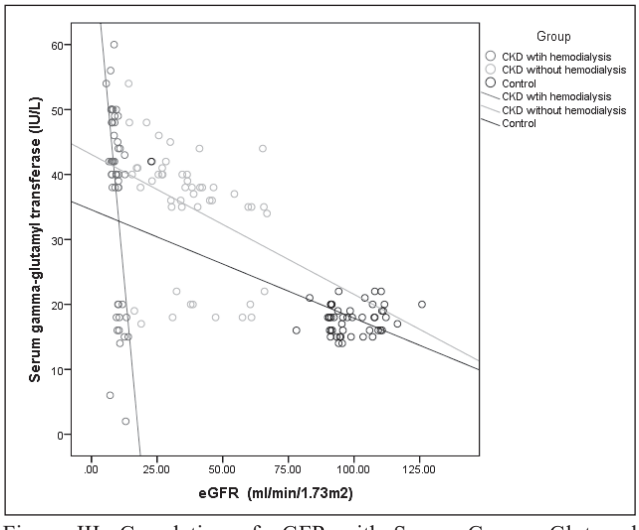


Figure III: Correlation of eGFR with Serum Gamma-Glutamyl Transferase in Different Groups

Table 4: Correlation of eGFR with Serum GGT in different groups (n=150)

Enzymes	Group					
	Group A (CKD with hemodialysis)		Group B (CKD without hemodialysis)		Group C (Healthy)	
Serum gamma-glutamyl transferase	r value	P value	r value	P value	r value	P value
	-0.575	<0.001	-0.354	<0.0010.012	-0.590	<0.001

Pearson's correlation was applied to find out r and p value

Discussion

In this study serum, GGT was significantly higher in CKD with hemodialysis 39.6±10.3 than CKD without hemodialysis 34.8±9.2. Similar type of observation was also found by Liberato et al[10]. They found as in after dialysis serum GGT value increased than the predialysis value which was due to increase oxidative stress or MIA syndrome or DM. Fabrizi et al[8] observed no significant difference in GGT levels between CKD with hemodialysis and healthy people. But this study found serum GGT was significantly higher in CKD with hemodialysis 39.6±10.3 than healthy subjects 18.3±4.1. In this study, serum GGT level was found significantly higher in stage 5 51.00±4.24 than the earlier stages (stage 2,3,4) and it gradually increases with the progression of stages. Caravaca-Fontán et al[11] also found similar type of observation that was elevated level of serum GGT among the CKD stage 4 to 5 but not yet on dialysis and abnormally elevated serum levels of GGT is independently associated with increased mortality in CKD patients, even in patients with no liver disease.

In this study, serum GGT was found gradually increase as per increment of serum creatinine and it was statistically significant but increment of serum GGT was significant and inversely related with eGFR. Similar type of observation was found by Yilmaz et al[12] and found an inverse and significant association between serum GGT level and eGFR in advanced CKD patients (stage 3-5). Serum GGT was gradually increased as per increment of duration of hemodialysis and it was statistically significant among the groups. In this study shows CKD stage 3 was more common than other stages and it was statistically significant. Similar type of observation was found by Hasan et al[13]. They found among the CKD without hemodialysis patients stage 3 was predominant.

Conclusion

The study showed serum GGT level is increased in CKD patients undergoing hemodialysis than in patients with CKD (stage1-5) without undergoing hemodialysis. Thus routine screening for serum GGT level in CKD patients with and without undergoing hemodialysis might help in early diagnosis of liver disease, in prevention of the aggression of hepatic disease in these patients and might help in monitoring, treatment of liver disease in these patients.

Acknowledgements

None

Conflict of Interest

The authors have no conflicts of interest to disclose

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' Contributions

Chowdhury SA, Chowdhury S, Asif M conceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript. Chowdhury SA contributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript. Asif M, Afroz F involved in the manuscript review and editing. All authors read and approved the final manuscript.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board. The written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

How to cite this article: Chowdhury SA, Chowdhury S, Asif M, Afroz F. Serum Gamma-Glutamyl Transferase Enzyme Status in Patients with Different Stages of Chronic Kidney Disease with or without Undergoing Hemodialysis. J Army Med Coll Jashore, 2022;3(1): 28-32

Publication History

Received on: 7 October 2021

Accepted on: 24 November 2021

Published on: 1 January 2022

References

1. National Kidney Foundation . K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis. 2002; 39 : 266. https://www.kidney.org/sites/default/files/docs/ck-d_evaluation_classification_stratification.pdf

2. Winearls C.G. Chronic renal failure. In: Warrel, DA. et al. eds. Oxford Text book of medicine. 4th edn.New York: Oxford University press. 2003; 3: 263-278.

3. Whaley-Connell AT, Sowers JR, Stevens LA, McFarlane SI, Shlipak MG, Norris KC, et al. CKD in the United States: Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES) 1999-2004. Am J Kidney Dis. 2008;51:13-20

4. Rashid HU. Bangladesh renal registry report (1996-1999). Bangladesh Renal J. 2007; 21(1) : 25-8.

5. Ferreira VS, Pernambuco RB, Lopes EP, Morai, CN, Rodrigues MC, Arruda MJ. Frequency and risk factors associated with non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus. Arq Bras Endocrinol Metabol. 2010; 54: 362–368.

6. Dumme, CD, Thom, FS, Veronese FV. Doença renal crônica, inflamação e aterosclerose: Novos conceitos de um velho problema. Rev Assoc Med Bras. 2007;53:446–450.

7. Souza JF, Longui CA, Miorin LA, Sens YA. Gamma-glutamyltransferase activity in chronic dialysis patients and renal transplant recipients with hepatitis C virus infection. Transplant Proc. 2008;40: 1319–1323.

8. Fabrizi F, De Vecchi AF, Qureshi AR, Aucella F, Lunghi G, Bruchfeld A. Gamma-glutamyltransferase activity and viral hepatitis in dialysis population. Int J Artif Organs 2007; 30: 06–15.

9. Nishida C, Uto H, Oketani M, Tokunaga K, Nosaki T, Fukumoto M. Clinical significance of alanine aminotransferase levels and the effect of ursodeoxycholic acid in hemodialysis patients with chronic hepatitis C. J

Gastroenterol 2010; 45: 326–334.
10. Liberato I, Lopes E, Cavalcante M, Pinto T, Moura I, Loureiro-Jr L. Liver enzymes in patients with chronic kidney disease undergoing peritoneal dialysis and hemodialysis. Clinics 2012; 67(2): 131–134
11. Caravaca-Fontán F, Azevedo L, Gonzalez-Candia B, Miguel A, Luna E, Caravaca F. Independent and additive predictive effects of serum gamma-glutamyl tranferase and alkaline phosphatase levels on mortality in patients with chronic kidney disesease. Nephrology Dialysis Transplantation. 2016; 31(1): 439–453.
12. Yilmaz MI, Turgut F, Kanbay M, Saglam M, Sonmez A, Yaman H, et al. Serum gamma-glutamyltransferase levels are inversely related to endothelial function in chronic kidney disease. Int Urol Nephrol. 2012;
13. Hasan MJ, Kashem MA, Rahman MH, Quddush R, Rahman, M, and Sharmeen A. Prevalence of chronic kidney disease and identification of associated risk factors among rural population by mass screening. CBMJ. 2012; 1(1) : 20-6

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 33-36
ISSN : 2789-1135 (Print)

Review Article ***Open Access***

Pathological Entity of C1q Nephropathy: A Review

Nur-E-Jannatul Ferdous[1], Md. Golam Mostofa[2], Raihana Zannat[3], JarinTasnim Promi[4]

[1]Assistant Professor, Department of Pathology, Ashiyan Medical College, Dhaka, Bangladesh; [2]Lieutenant Colonel, Department of Medicine, Armed Forces Medical Institute, Dhaka, Bangladesh; [3]Assistant Professor, Department of Physiology, Ashiyan Medical College, Dhaka, Bangladesh; [4]Lecturer, Department of Pathology, Ashiyan Medical College, Dhaka, Bangladesh.

Abstract

C1q nephropathy is a unique glomerular disease and this entity is purely diagnosed by characteristic mesangial C1q deposition noted on immunofluorescence microscopy.Light microscopic features are diverse comprising minimal change diasease (MCD),focal segmental glomerulosclerosis (FSGS), and proliferative glomerulonephritis. Clinical presentation is also variable, ranging from nephrotic range proteinuria to sub-nephrotic state, with or without haematuria, renal insufficiency in both children and adults.Treatment includes management of the underlying light microscopic lesion while glucocorticoids remain the mainstay of treatment.This concept of 'C1q nephropathy' has periodically advanced since its original.In this paper, the current understanding of pathophysiology, histopathology, diagnostic and therapeutic options of C1q nephropathy is discussed. *[Journal of Army Medical College Jashore, January 2022;3(1):33-36]*

Keywords: C1q nephropathy; nephrotic syndrome; complement pathway; rituximab

Introduction

C1q nephropathy has been described by Jennette and Hipp and is defined by conspicuous C1q in glomerular immune deposits in a dominant or co-dominant fashion in patients with no evidence of systemic lupus erythematosus (SLE)[1-2]. The exclusion criteria also include type 1 membranoproliferative glomerulonephritis having frequent substantial C1q staining in the glomerular immune deposits[3]. The prevalence of C1q nephropathy among patients with renal biopsy varies from 0.2 to 16.0% and seems to be higher in children[4-5]. Complement activation and glomerular antigen-antibody complex formation with additional involvement of alternative complement and letin pathway underlie pathogenesis of c1q nephropathy[6].

C1q nephropathy often manifests as steroid-resistant asymptomatic proteinuria or nephrotic syndrome. Light microscopic features are heterogeneous and comprise no glomerular lesions, focal segmental glomerulosclerosis (FSGS), and proliferative glomerulonephritis. The pathologic features, clinical presentations, and outcomes are based on only a few small studies. Patients with nephrotic syndrome, particularly those with FSGS, showed a poor response to corticosteroid therapy, whereas patients presenting with asymptomatic urinary abnormalities maintained normal renal function. Additional studies are needed to elucidate this heterogeneous glomerular disease[6,7].

More recent modified criteria require ≥2+ (on a scale of 0 to 4+) immunostaining for C1q with a predominantly mesangial distribution, frequently accompanied by IgG and IgM, which may be less intense, equally intense, or more intense, in patients without evidence of SLE. In addition, type1 membrano-proliferative glomerulonephritis, which frequently has intense C1q staining, is an exclusion criterion.

We review the pathogenesis, histological findings, clinical features, therapeutic options, and outcomes in patients with C1q nephropathy.

Complement C1q:Key Factor in Complement Pathway

Complements are a heterogeneous group of 40 proteins circulating in bloodstream. These got activated by specific molecules like autoantibodies, immune complexes and carbohydrate molecules in the surface of microorganism's through the classical pathway, lectin pathway or through a

Correspondence: Dr: Nur-E-Jannatul Ferdous, Assistant Professor, Department of Pathology, Ashiyan Medical College, Dhaka, Bangladesh; Email: lipijannat@yahoo.com; Cell No.: +8801715561365

low-grade spontaneous activation called alternate pathway[7].
The classical pathway: C1q is the first component of the complement cascade. It forms the first component in the classical pathway. Structurally C1 exists as a macromolecular complex consisting of one molecule of C1q and two molecules each of the serine proteases C1r and C1s. The complement cascade initiated by the binding of C1q to fc fragment of IgG or IgM. This binding leads to conformational change in one of the C1r molecule and activates it. This then activates its partner C1r molecule which in turn activates the two C1s molecules. Activated C1s cleaves C4 and C2. C4 is cleaved first and C4b binds to the membrane in the vicinity of C1 and then binds C2. On binding C4b at the membrane surface, C2 becomes susceptible to cleavage into C2a and C2b by the activated C1s enzyme. A smaller C2b fragments diffuse away leaving behind enzymatically active C4b2a complex,the C3 convertase.
The c3 convertase enzyme,C4b2a,now hydrolyse C3,generating C3a and C3b.Some molecules of C3b bind with the C4b2a enzyme to form the membrane-bound,C5 convertase complex C4b2a3b.The C3b components of C5 convertase binds C5, permitting C4b2a to calve C5 into C5a and C5b[8].

Pathogenesis

The pathogenesis of C1q nephropathy is poorly understood.Possible theories include Specialized C1q receptors which help in the binding of immune complexes are found in themesangial cells of the kidneys[9]. C1q deposition in mesangium may be as a result of binding to Fc portion of IgM and IgG either via direct interactions with surface-bound Ig or via trapping of circulating immune complexes.Considering this mechanism, some authors hypothesized C1q nephropathy could represent as a variant of FSGS.However,the exact mechanism of C1q deposition is uncertain.At present, no specific antigen has been identified. Alternatively, the affinity of C1q molecule to a variety of polyanionic substances including DNA, RNA, viral proteins,gram negative bacteria and a variety of immune cells may mean that a direct mechanism may exist, and immuneglobulins may just be an observer in the process. Contrary to this theory,presence of mesangial electron-dense deposits argues against the disease mediated by podocyte injury,hence away from the spectrum of FSGS[10]. The presence of podocyte foot process effacement raises the possibility of "podocytopathy", at leastin a subset of patients[11]. Certain viruses like Epstein Barr Virusand BK virushave also been identified to be associated with C1q nephropathy[12-13]. Rarely, abnormalities in C1q inhibitor protein may pose risk factor for deposition of C1q[14].

Light Microscopy and Clinical Presentation

According to the light microscopy, the histological pattern of C1q nephropathy could be broadly divided as minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS) and immune complex-mediated proliferative glomerulonephritis(GN). The last mentioned group encloses several morphological aspects including focal or diffuse mesangial proliferative GN, post-infectious GN,membrano-proliferative GN and membranous GN.Furthermore,the FSGS group has three variants,that is collapsing cellular and "not otherwise specified" variants4. In a study of Jenette et al. encompassed 15 patients, out of which 2 cases revealed MCD, mesangialhyper cellularityin 3 cases and focal or diffuse proliferative GN in 8 cases(1). In another study by Markowitz et al as many as 17 out of the 19 patients with C1qN reported FSGS on renal histopathology and MCD in 2 cases. A paper on the largest study group correlating clinicopathological changes of C1qN (n=72) reported FSGS in 11(16%), MCD in 27(38%), proliferative glomerulonephritis in 20(28%) and a variable picture in other patients, i.e. tubulointerstitial nephritis and thin basement nephropathy[12]. Occasionally, cresentic glomerulonephritis is seen in some case reports of C1q nephropathy[5]. A further recent paper by Roberti et al,however revealed a predominance of children with diffuse mesangial proliferation with or without segmental sclerosis on histopathology[15].

Immunofluorescence Microscopy

Immunofluorescence microscopy is more specific than light microscopy. For Immunofluorescence microscopy antisera is used against immunoglobulin or compliment components or even proteins like albumin and fibrinogens. The patternof staining is also important in making the specific diagnosis in renal biopsy. The pattern includes granular,linear,mesangial or capillary as well as the anatomical location of the staining.C1q nephropathy is based on demonstration of intense C1q (dominant or co-dominant) , mainly in the mesangium.Immunoglobulins like IgM and IgG are also usually identified,as they serve as ligands for C1q and further activation of classic pathway of compliment cascade. Vizjak et al. in the largest series published so far with 72 cases,reported that the frequency of positivity for IgG,IgA and IgM respectively were 48%,34% and 58%(12). In addition, C3 and C4 were also found at 60% and 25% respectively. A full house pattern with deposits of IgM, IgG, IgA, C1q and C3 was noted in 30.6% of cases, predominantly in those with proliferative GN morphology. Immunological staining for C1q may be seen in many glomerular diseases. Jennette and Hipp found high intensity positivity in a high proportion of cases of proliferative lupus nephritis,membranous lupus nephritis and type 1 membranoproliferative glomerulonephritis (MPGN)[17]. These findings formed the basis of their exclusion of SLE and type 1 MPGN in the diagnostic criteria of C1q nephropathy[16]. Having said that multiple immunoglobulins can be positive, there is a chance that a patient can in fact fulfill the diagnostic criteria for both C1q nephropathy and IgA nephropathy. The latter combination could be avoided to a greater extent as C3 staining is seen more in cases of IgA nephropathy[17].

Electron Microscopy

Amorphouselectron dense deposits in the mesangium are confirmatory of the diagnostic entity in C1q nephropathy. Besides mesangium,deposits can also be seen in subendothelial and subepithelial areas in case of morphological appearance of proliferative glomerulonephritis or focal segmental glomerulosclerosis. Podocytopathy can also be noted . They are more common in the inmune complex mediated subtype and possess podocyte foot process effacement and cytoskeleton condensation to a wider extent[11]. They are more common in patients with nephrotic syndrome or nephrotic range proteinuria than in those with nonnephrotic proteinuria. On rare occasion, tubuloreticular cytoplasmic inclusions in glomerular and peritibular capillary endothelial cells may also be found.

Clinical Presentation

The prevalence of C1q nephropathy is rare, ranging from 0.2 to 2.5% in biopsies from children to adult, to 2.1 to 9.2/6% in pediatric biopsies, to 16.5% among renal biopsies of children with nephrotic syndrome and persistent proteinuria and slightly male predominance at 68%[1,2,4,11]. It generally affects older children and young adults with an average age of 17.8 years along with equal gender distribution.Presentation ranges from asymptomatic proteinuria or hematuria to frank nephritic or nephrotic syndromes. Hypertension is present in about 50.0% of patients and renal insufficiency at the time of diagnosis is quite recurrent[11]. Renal in Two variants of C1q nephropathy are reported MCD/FSGS and immune-complex mediated glomerulonephritis. The latter includes mesangial proliferative glomerulonephritis, membranous nephropathy and membrano-proliferative like glomerulonephritis. Cases of secondary C1q nephropathy have also been reported with viral infection or rarely with rheumatoid arthritis[18]. There have also been some case reports where the patients had presented with rapidly progressive glomerulonephritis to end-stage renal disease (ESRD) as well as renal failure requiring renal replacement therapy[19,20]. A large number of patients present with her persistent proteinuria spontaneous remission has been reported uncommonly[21]. In the course of time renal insufficiency is evident in majority of cases and 3 years renal survival is about 80.0% cases[22].

Management

C1q nephropathy poses a management challenge as its pathophysiology is not well established .and varied clinical presentation.There are no randomized controlled trials that have assessed the treatment of this condition. Glucocorticoids being the mainstay of treatment,current therapy includes treating the underlying light microscopic lesion and outcome vary accordingly. In steroid resistant cases, pulsed methylprednisolone has shown to be effectivesequential therapy with cyclophosphamide, azathioprine, mycophenolatwmofetil, tacrolimus and rituximab used separately or in combination with steroids has shown good clinical response in different studies. A small number of cases have reported the efficacy of rituximab for treating C1q nephropathy,with significant improvement of renal function and clinical manifestations[23-26].

Rituximab is a human/mouse chimeric monoclonal antibody targeting CD2027.Originally it was used to treat B-cell non-Hodgkin's lymphoma but recently used for the treatment of autoantibody related kidney disease, including antineutrophil cytoplasmic antibodies (ANCA) associated with nephritis and membranous nephropathy[28-30].

Conclusion

C1q nephropathy is under recognized with a wide range of the clinicaland histological spectrum. Some author demonstrate it as a part of the variety of FSGS/MCD, while others have described different clinical presentation, histopathology, response to therapy and outcomes,pointing that it may be a combination of disease group than a single entity. Further studies are needed to establish C1q nephropathy as a universally recognized distinct clinical entity. Routine addition of C1q staining in renal biopsy is recommended.

Acknowledgements

None

Conflict of Interest

The authors have no conflicts of interest to disclose

Financial Disclosure

The author(s) received no specific funding for this work.

Authors' Contributions

Ferdous NEJ, Mostofa MG conceived the study and wrote up the draft manuscript. Mostofa MG,Zannat R, Promi JT involved in the manuscript review and editing. All authors read and approved the final manuscript.

How to cite this article: Ferdous NEJ, Mostofa MG, Zannat R, Promi JT. Pathological Entity of C1q Nephropathy: A Review.J Army Med Coll Jashore, 2022;3(1):33-36

Publication History

Received on: 7 October 2021

Accepted on: 24 November 2021

Published on: 1 January 2022

References

1. Jennette JC, Hipp CG; Clq nephropathy: a distinct pathologic entity usually causing nephrotic syndrome. Am J Kidney Dis. 1985;6(2): 103-10

2. Iskandar SS, Broning MC, Lorentz WB: C1q nephropathy: A pediatricclinic-pathologic study. Am J Kidney Dis 1991;18:459 – 465

3. Jennette JC, Hipp CG: Immunohistopathologic evaluation of Clqin 800

renal biopsy specimens. Am J ClinPathol 1985;83(4): 415-20
4. Markowitz, J. A. Schwimmer, M. B. Stokes et al., "Clq nephropathy: a variant of focal segmental glomerulosclerosis," Kidney International, 2003;64(4):1232-1240
5. Srivastava T, Chadba V, Taboada EM, Alon US. C1q nepropathy presenting as rapidyprogressivecresentic glomerulonephritis. PediatrNephrol 2000;14:976-79
6. Devasahayam j,Erode-singaravelu G,Bhat Z,Oliver T,Chandran A,Zeng X,et al.c1q nephropathy:the unique underrecognized pathological entity. Anal Cell Pathol 2015:490413
7. Walport M.J.complement:first of two parts. New England Journal of Medicine, 2001: vol.344,no.14,pp.1058-1066
8. Punt J, Stranford S, Jones P, Owen J.The Complement System. Susan Winslow, KubyImmunoogy, 2019,Eight edition. 6; 187-221
9. Berger S.P, Roos A and Daha M.R.,"Complement andthekidney:what the nephrologist needs to know in 2006?"Nephrology Dialysis Transplant, 2005: vol.12,pp.2613-2619
10. Thomas DB.Focal segmental glomerulosclerosis:a morphological diagnosis in evolution.ArchPathol Lab Med 2009;133(2):217-23
11. A.Vizjak,D.Ferluga,M.Rozic et al."pathology, clinical presentation,andoutcomes of C1qnephropathy,"journal of the American Society ofNephrology, 2008: vol.19,no.11,pp.2237-2244
12. I.S.Lim,K.W.Yun,K.C.Moon, and H.I.Cheong,"proteinuria in a boy with infectious mononucleosis,C1q nephropathy, and Dent's disease,"journal of Korean Medical Science,vol.22.no.5,pp.928-931,2007
13. J.Issac and F.S.Shihab,"De novo C1q nephropathyin the renal allograft of a kidney pancreas transplant recipient:BK virus-induced nephropathy?"Nephron,vol.92,no.2,pp.431-436,2002
14. MiiA,ShimizuA,MasudaY,Fujita E, Aki k,IshizakiM,et al. Current status and issues of C1q nephropathy.ClinExpNephrol.2009;13(4):263-74
15. Roberti I,BaqiN,VyasS,etal,"A single-center study of C1q nephropathy in children ".PediatrNephrol 2009;24:77-82
16. J.C.Jennette and C.G.Hipp,"immunohistopathologic evaluation of C1q in 800 renal biopsy specimens."American Journal of Clinical Pathology, 1985: vol.83,no.4,pp.415-420
17. Emanicipator SN.Benign essential hematuria,IgA nephropathy,and Alportsyndrome.In: Silva FG,DfagatiVD,NadasdyT,editors.Renal Biopsy Interpretation.NewYork:Churchill Livingstone;1996.pp.147-180
18. ArdalanMR,SadreddiniS,Nasri H.C1q Nephropathy in Association with Deforming arthritis.Nephro-Urol Mon.2010;2(2):383-85
19. Srivastava T,Chadha V.C1q nephropathy presenting as rapidly progressive crescentic glomerulonephritis.ClinExpNephrol2009;13(4):263-74
20. Malleshappa P,Ranganath R,Chaudhari AP,Ayiangar A,Lohitaksha S.C1q nephropathy presenting as acute renal failure.Saudi J Kidney Dis Transpl2011;22(2):324-6
21. Nishida M,Kawakatsu H,Komatsu H,Ishiwari K,Tamai M,Sawada T.Spontaneous improvement in a case of C1q nephropathy.Am j kidney Dis.2000;35(5):E22
22. KersnikLevart T,Kenda RB,AvgustinCavic M,FerligaD,Hvala A,Vizjak A.C1q nephropathy in children.PediatrNephrol2005;20(12):1756-61
23. Sinha A, Nast CC, Hristea I, Vo AA, Jordan SC. Resolution of clinical and pathological features of C1q nephropathy after rituximab therapy. ClinExpNephrol. (2011) 15:164-70
24. Yang YH, Lee WS, Cheng CY. C1q nephropathy in a patient complicated with nephrotic syndrome and refactory to steroid therapy. J MicrobiolImmunol Infect. (2020) 53:183-5
25. Bitzan M, Ouahed JD, Krishnamoorthy P, Bernard C. Rituximab treatment of collapsing C1q glomerulopathy: clinical and histopathological evolution. PediatrNephrol 2008;23:1355-61
26. Ramachandran R, Bharati J, Jha V. Successful treatment of C1q nephropathy with CD19 targeted Rituximab therapy, Nephrology. 2017;22:265
27. Pierpont TM, Limper CB, Richards KL. Past, present, and future of rituximab-the world's first oncology monoclonal antibody therapy. Front oncol 2018;8:163
28. Ravani P, Bonanni A, Rossi R, Caridi G, Ghiggeri GM. Anti-CD20 antibodies for idiopathic nephrotic syndrome in children. Clin J Am SocNephrol 2016;11:710-20
29. MacIsaac J, Siddiqui R, Jamula E, Li N, Baker S, Webert KE, et al. Systemic review of rituximabfor autoimmune disease: a potential alternative for intravenous immune globulin. Transfusion 2018;58: 2729-35
30. Musette P,Bouaziz JD. B cell modulation strategies in autoimmune disease: new concepts. Front Immunol 2018;9:622

https://amcj-bd.org/
Journal of Army Medical College Jashore
January 2022, Volume 3, Number 1, Page 37-41
ISSN : 2789-1135 (Print)

Case Series ***Open Access***

Sixth Nerve Palsy: Three Cases of False Localizing Sign

Shah Md. Rajibul Islam[1], Shafiul Ashraf[2], Rezwan Ahmed[3]

[1]Assistant Professor, Head, Department of Ophthalmology, CMH & Army Medical College Jashore, Bangladesh; [2]Assistant Professor, Department of Ophthalmology, Army Medical College Jashore, Bangladesh; [3]Assistant Professor, Department of Ophthalmology, Army Medical College Jashore, Bangladesh

Abstract

Sixth nerve palsy is the commonest isolated cranial nerve palsy. Possessing the longest course, it is susceptible to damage through a myriad of etiologies, hence termed 'false localizing sign'. Though frequently being a benign process with spontaneous recovery, it may be due to serious underlying pathology. Therefore, sixth nerve palsy requires careful clinical workup with tailored investigation. We are presenting three cases of isolated sixth nerve palsy having different etiologies. *[Journal of Army Medical College Jashore January 2022;3(1):37-41]*

Keywords: C1q nephropathy; nephrotic syndrome; complement pathway; rituximab

Introduction

Abducens nerve (Cranial Nerve VI) innervates the lateral rectus muscle and abducts the eye. The nucleus is situated at the dorsal pons and courses superiorly & anteriorly leaving the brainstem at the ponto-medullary junction. It travels along the base of the skull in the subarachnoid space and crosses over the petrous apex and passes through the cavernous sinus. It enters the orbit through the superior orbital fissure, travelling through the annulus of Zinn, reaches the lateral rectus muscle.

Abducens nerve (Cranial Nerve VI) palsy is the commonest ocular motor nerve palsy[1]. Paresis causes esotropia due to unopposed action of the antagonist (Medial rectus). In primary position the eye is esodeviated (towards the nose). The deviation is incomitant and more marked when the patient gazes towards the affected side.

Etiology differs among children and adults. Being the longest cranial nerve, it is susceptible to damage from vast pathological processes; vascular, traumatic, neoplastic, infectious, inflammatory, demyelination & also idiopathic. Microvascular ischemia is the commonest in adults over age of 50 years who are suffering from vascular comorbidities; diabetes mellitus, hypertension, hyperlipidemia[1]. Neoplasms are much more common in children[2]. Aneurysms are uncommon comprising 0 to 3% of the cases[3]. About 22 to 30% cases present as idiopathic[2].

Symptoms associated with abducens nerve palsy depend on the underlying etiology. Diplopia is the commonest presenting symptom. Patients will have horizontal uncrossed diplopia which is greater at distance than at near. The diplopia is also worse in the direction of the palsied muscle and gets better in the contralateral gaze.

In cases due to raised intracranial pressure, patients may experience associated symptoms of headache, pain around the eyes, nausea, vomiting, or pulse synchronous tinnitus. If a patient has a lesion causing the abducens nerve palsy which affects other structures in the brain, other neurologic signs may be observed[4]. In the event of subarachnoid hemorrhage, the patients can present with leptomeningeal irritation and present with cranial nerve palsies[5].

If the etiology of the abducens nerve palsy is a brainstem lesion affecting the sixth cranial nerve fasciculus, there may be associated ipsilateral facial weakness, contralateral hemiparesis, or sensory abnormalities. If the abducens nerve palsy presents together with other ipsilateral cranial nerve palsies, etiology could be a lesion involving the meninges, superior orbital fissure, orbital apex, or cavernous sinus.

Case Presentation

We are presenting three cases of isolated sixth nerve palsy that reported to us having three different etiology.

Correspondence: Maj (Dr) Shah Md Rajibul Islam. MBBS. FCPS. FACS. FICS. Fellow Vitreo-Retina. Classified Ophthalmologist, CMH Jashore & Assistant Professor & HOD, Department of Ophthalmology, Army Medical College, Jashore Cantonment, Jashore, Bangladesh; Email: dr_rajibul_islam@yahoo.com, Cell no: +8801819215339.

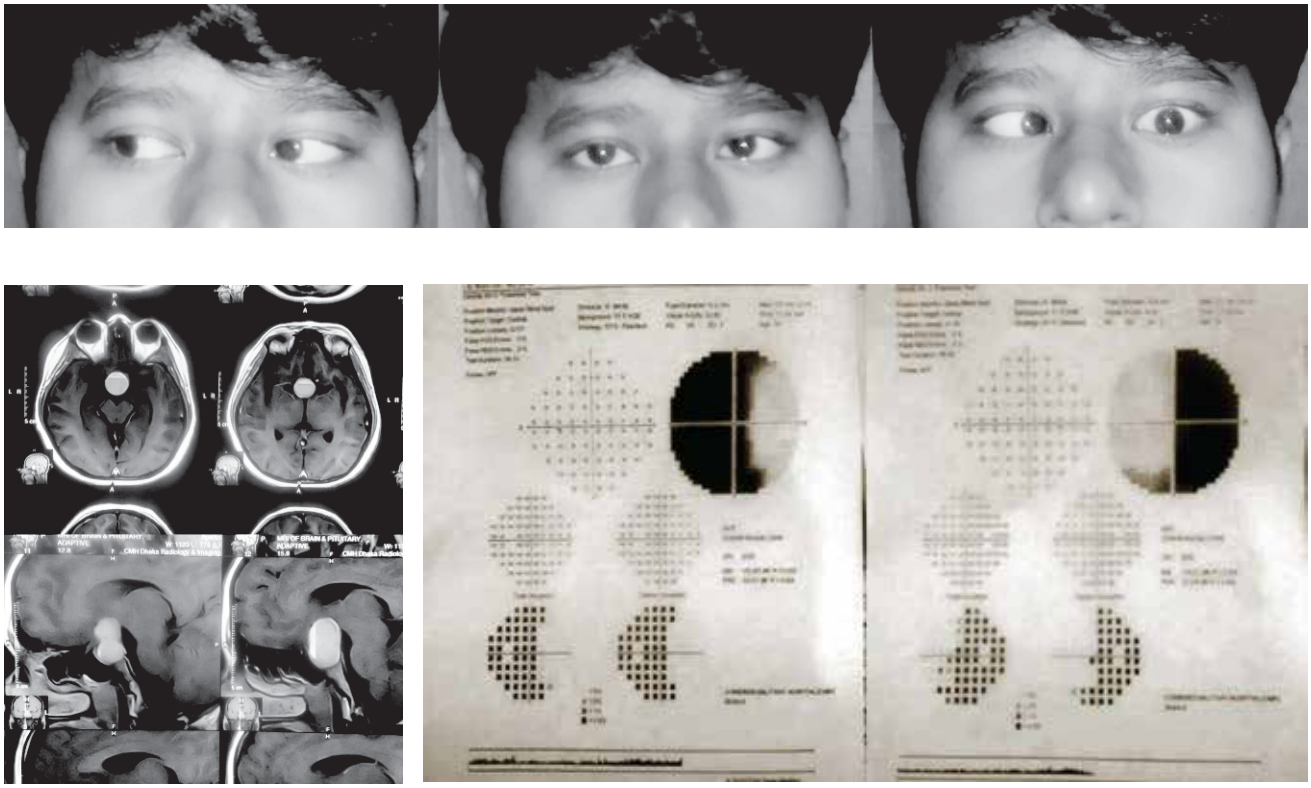
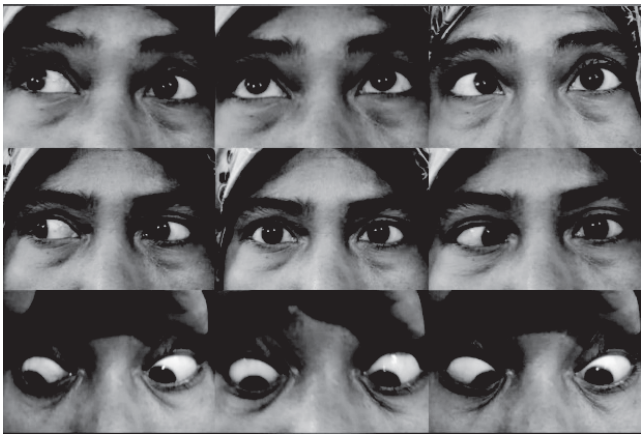
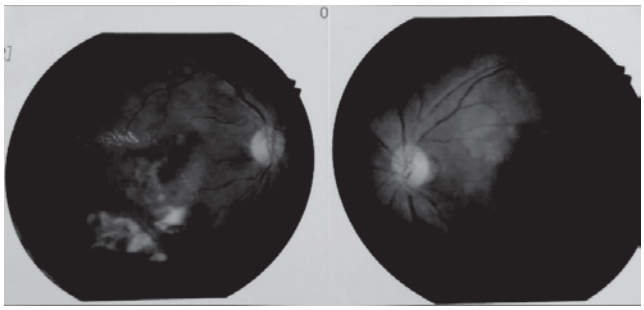


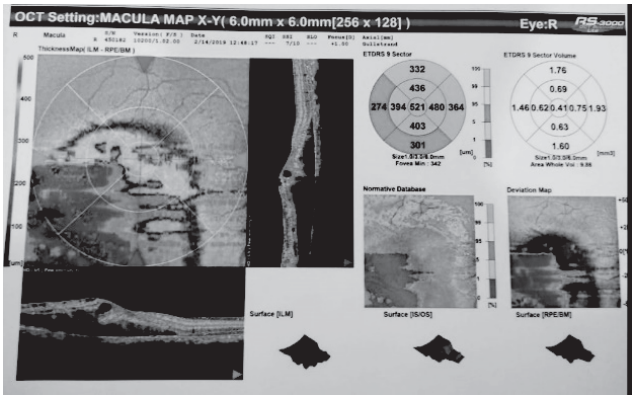
Figure II: A) Left gaze palsy. B) MRI showing solid midline tumor with cystic component, Craniopharyngioma. C) HVFA showing bitemporal hemianopia

Case 1: An 11 year old boy presented to us with dimness of vision, headache and occasional diplopia for approximately 06 months. O/E BCVA was 6/12 OD and 6/9 OS. Normal ocular findings except limited abduction on left gaze (Fig 1). Diplopia was present throughout levoversion, levoelevation & levodepression. MRI revealed a large lobulated soft tissue intensity mass having both solid and cystic components in the sella & suprasellar region extending upto the floor of the third ventricle. Visual field analysis showed bi-temporal hemianopia (Figure I). A working diagnosis of craniopharyngioma was made and he was referred to Neurosurgery department.

Case 2: A 45 year old female presented with intermittent headache for 06 months and blurred vision in right eye for one month. O/E BCVA was 6/24 OD & 6/6 OS. Limited abduction of the left eye (Fig 2). Fundus showed right infero-temporal branch retinal vein occlusion (BRVO) with macular edema (Fig 2). Routine hemogram was normal, she was normotensive and euglycemic. MRI of brain revealed a large internal carotid artery (ICA) aneurysm on the left side







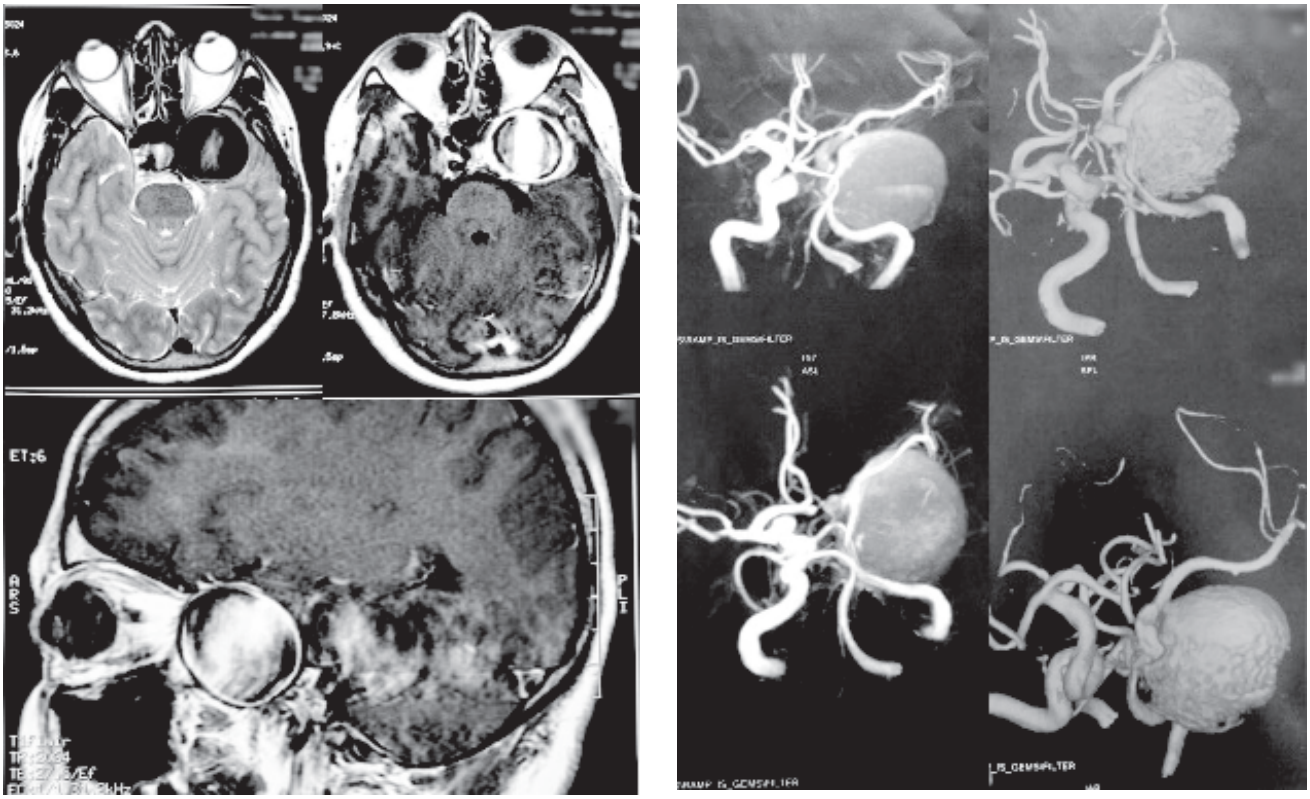


Figure III: A) Nine diagnostic gazes showing left gaze palsy. B) Color fundus photograph showing infero-temporal BRVO with macular edema in right eye. C) OCT Macula showing macular edema. D) MRI brain showing left sided Internal Carotid Artery aneurysm. E) MRA showing aneurysm of internal carotid artery.

(Figure II). MRA was done (Fig 2). Temporary Frosted glass was prescribed for the left eye. She was referred to Neurosurgery department.

Case 3: A 55 year old male reported with sudden onset diplopia on left gaze; noticed by him for two days. O/E: BCVA was 6/6 OU. Ocular findings were normal except limited abduction on left side (Fig 3). Diplopia was present throughout levoversion, levoelevation & levodepression. Routine hemogram was normal, he was diabetic and had hyperlipidemia. He has been suffering from diabetes mellitus for 05 years and was on oral hypoglycemic agent. He was referred to Medicine department for review and controlling of the comorbid conditions. Temporary Frosted glass was prescribed for the left eye. During follow up after 06 months, his conditions improved with no diplopia and almost near normal extra ocular motility (Figure III).

Figure IV: Showing nine diagnostic gazes. A) Left gaze palsy during presentation. B) Follow up after 06 months showing almost complete recovery following good glycemic control.

Table 2: Dermatological conditions' distribution of patients (n=50)

Etiologies of acquired sixth nerve palsy	Schrader[3]	Rucker[6]	Johnston[7]	Robertson[8] (Children)	Rush[9]	Patel[10]	Bagheri[11]	Jung[12]
Sample size	104	607	158	133	419	137	33	486
Etiologies %								
Neoplasm	7	33	13	39	15	5	2	5
Trauma	3	12	32	20	17	12	18	5
Aneurysm	0	3	1	3	3	2	0	2
Ischemic	36	8	16	0	18	16	1	56
Miscellaneous*	30	24	30	29	18	19	6	4
Undetermined**	24	20	8	9	29	26	6	28

*Leukemia, migraine, pseudotumor cerebri, multiple sclerosis;**Undetermined cause. All routine investigations normal, imaging normal.

Discussion

Diagnosis of the manifestation of sixth nerve palsy is not straight forward. It possesses a myriad of etiologies varying with age thus termed false localizing sign. The three cases presented here reminds the underlying varied etiology of Abducens nerve palsy. Patients with micro-vasculopathy tend to have a better prognosis than other etiologies. The underlying etiology dictates the preferred plan of treatment. Treatment varies from observation to neurosurgery depending upon the cause. Thus, it is of utmost importance to find out the underlying etiology in abducens nerve palsy.

Studies on etiology of sixth nerve palsy reports high frequencies of microvascular disease (28.0 to 46.0%) and idiopathic (24.0 to 31.0%)[12]. It is widely reported that microvascular diseases are a common cause of isolated unilateral sixth nerve palsy in patients over 50 years of age[12]. Tamhankar et al1 also reported sixth nerve palsy in 80.6% of patients over 50 years of age was due to microvascular disease. Sixth nerve palsy from aneurysm is low 0 to 6.0% cases[12]. Studies have found high frequency of neoplastic etiology in children 39.0 to 45.0% cases[12].

Recovery rates of sixth nerve palsy is 60-87.3%[13]. Vascular and idiopathic etiologies were associated with higher natural recovery rates than other etiologies of ocular motor nerve palsies[10]. Sanders et al reported 86% experienced resolution of sixth nerve[14].

Conclusion

Sixth nerve palsy being a false localizing sign, warrants examination and tailored investigation. It may not be a benign process. Hence the clinician must consider the potential of a serious neurological process. Early diagnosis is critical in some conditions with sixth nerve palsy.

Acknowledgements

None

Conflict of Interest

The authors have no conflicts of interest to disclose

Authors' Contributions

Islam SMR, Ashraf S, Ahmed R involved in the diagnosis and management of the patients. manuscript review and editing. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Institutional Review Board. All methods were performed in accordance with the relevant guidelines and regulations.

How to cite this article: Islam SMR, Ashraf S, Ahmed R. Sixth Nerve Palsy: Three Cases of False Localizing Sign. J Army Med Coll Jashore, 2022;3(1): 37-41

Publication History

Received on: 7 October 2021

Accepted on: 24 November 2021

Published on: 1 January 2022

References

1. MA Tamhanker V Biousse GS Ying S Prasad PS Subramanian MS Lee. Isolated third, fourth and sixth cranial nerve palsies from presumed microvascular versus other causes: a prospective study. Ophthalmology 2013; 11:2264-2269

2. Husain et al. Egypt J Neurol Psychiatry Neurosurg 2021; 57:162.

3. Shrader EC, Schlezinger NS. Neuro- ophthalmologic evaluation of abducens nerve paralysis. Arch Ophthalmol 1960; 63:84-91.

4. Thurtell MJ, Tomsak RJ, Daroff RB. What do I do now? Neuro-ophthalmology. Oxford, New York; 2011.

5. Parr M, Carminucci A, Al-Mufti F, Roychowdhury S, Gupta G. Isolated Abducens Nerve Palsy Associated with Ruptured Posterior Inferior Cerebellar Artery Aneurysm: Rare Neurologic Finding. World Neurosurg. 2019;121:97-99.

6. Rucker CW. The causes of paralysis of the third, fourth, and sixth cranial nerves. Am J Ophthalmol 1966; 61:1293-1298.

7. Johnston AC. Etiology and treatment of abducens paralysis. Trans Pac Coast Otoophthalmol Soc Annu Meet 1968; 49:259-277.

8. Robertson DM, Hines JD, Rucker CW. Acquired sixth-nerve paresis in children. Arch Ophthalmol 1970; 83:574-579.

9. Rush JA, Younge BR. Paralysis of cranial nerves III, IV, and VI. Cause and prognosis in 1000 cases. Arch Ophthalmol 1981; 99:76-79.
10. Patel SV, Mutyala S, Leske DA, Hodge DO, Holmes JM. Incidence, associations, and evaluation of sixth nerve palsy using a population-based method. Ophthalmology 2004; 111:369-375.
11. Abbas Bagheri, Babak Babsharif, Mohammad Abrishami, Hossein Salour, Maryam Aletaha. Outcomes of surgical and non-surgical treatment for sixth nerve palsy. J Ophthalmic Vis Res 2010; 5:32-37.
12. Eun Hye Jung, Seong-Joon Kim, Joo Yeon Lee & Bum-Joo Cho. The incidence and etiology of sixth cranial nerve palsy in Koreans: A 10-year nationwide cohort study. Nature Research Scientific Reports 2019; 9:18419
13. Park, U. C., Kim, S. J., Hwang, J. M. & Yu, Y. S. Clinical features and natural history of acquired third, fourth, and sixth cranial nerve palsy. Eye (London, England) 2008; 22:691–696.
14. Sanders, S. K., Kawasaki, A. & Purvin, V. A. Long-term prognosis in patients with vasculopathic sixth nerve palsy. American journal of ophthalmology 2002; 134:81–84