ISSN: 2304-0009
eISSN: 2307-7654

Bangladesh Critical Care Journal

Official Journal of Bangladesh Society of Critical Care Medicine

Volume 5, Number 2, September 2017

CONTENTS

Bangladesh Critical Care Journal

bsccmjournal.org

banglajol.info/index.php/BCCJ

Publication of Bangladesh Society of Critical Care Medicine

Dedicated to scientific & professional development of Critical Care Personnel

ISSN: 2304-0009

eISSN: 2307-7654

Volume 5, Number 2, September 2017

PUBLISHED BY:

Dr. Mohammad Asaduzzaman

Publication Secretary

BSCCM

PRINTED AT :

AJ Print Media

112/2, Fakirapool, Dhaka-1000

Mobile : 01991 158182

This publication is a dedication of Bangladesh Society of Critical Care Medicine towards knowledge & professional development of critical care practice in Bangladesh & the whole world. It is published semiannually and accepts original article, review article and case reports. We try to accommodate any content which may help in promotion of knowledge, quality of patient care and research potential amongst concerned personnel. While every effort is always made by the Editorial Board to avoid inaccurate or misleading information appearing in the Journal, information within the individual articles are the responsibility of its author(s). Bangladesh Critical Care Journal and its Editorial Board accept no liability whatsoever for the consequences of any such inaccurate and misleading information, opinion or statement.

Correspondence

Executive Editor; Bangladesh Critical Care Journal

Email: bccj.editor@gmail.com; Web: bsccmjournal.org, banglajol.info/index.php/BCCJ

Bangladesh Critical Care Journal

INFORMATION FOR AUTHORS

Manuscripts prepared following the "Uniform Requirements for manuscripts submitted to biomedical Journals" (http://www.icmje.org/urm_full.pdf) issued by ICMJE (International Committee for Medical Journal Editors) is acceptable to this journal for publishing. Authors are requested to follow the April 2010 update for latest information.

Editorial scope:

- The BCC Journal is intended to promote prompt publication of concise, scientific article based on the study in all fields of medical and health sciences with special predilection to matters concerning critically ill patients & ICU practice.
- Submitted manuscripts should not be previously publishedor currently being considered for publication elsewhere.
- All submitted articles will undergo double blind peer review as per recommendations by subject specific experts selected by editors.
- Reviewed manuscripts will be sent to the corresponding author for appropriate response if it is indicated.
- Acceptance is based on significance, originality, clarity and fulfillment of the criteria of the publication policy of this journal.
- The Editor-in-Chief will make all final decisions regarding acceptance.
- Selection of the reviewed and accepted manuscripts intended for publication in a particular issue will be decided by the Editorial Board.
- Hard copy of rejected manuscripts will be returned if accompanied by stamped or self-addressed envelope.
- Upon acceptance for publication the copyright of the paper automatically transfers to the BCCJ and will not be published elsewhere either in part or whole without written permission of the copyright holder.
- Review articles should be written by a subject expert.

Ethical aspects:

- Clinical trials should have been conducted according to the ethical standards laid down in the 1964 Declaration of Helsinki by World Medical Association; revised 2008 (http://www.wma.net/en/30publications/10policies/b3/17c.pdf).
- Manuscript must contain a statement in the method section that all interventional studies have been approved by the appropriate ethical committee after careful examination of the ethical aspects.
- Permission of the patients or their families to reproduce photographs of the patients where identity is not disguised.
- Author should obtain written permission to reproduce any table or illustration from any other source.

Manuscript submission:

The authors are requested to strictly follow the guidelines below for submission of manuscript to BCCJ for publication. The following documents with manuscripts are to be submitted for publication.

- A cover letter addressed to the Editor-in-Chief of the journal.
- A Title page.
- Abstract and key words in the first page followed by the text, prepared in the format of IMRaD.
- Authors may submit 2 hard copies of all documents and one copy in electronic form written in a CD with adequate labeling.
- Alternately author can submit directly in electronic format (*.doc format as attachment) through email.
- In case of electronic submission, formal cover letter signed by all the authors should be scanned & submitted along with the manuscript.

Cover letter:

- All authors must sign after seeing the manuscript with the statement that they are the only authors.
- It should contain a declaration that this manuscript has not been submitted elsewhere or currently not under consideration in any other journal.
- It should clearly indicate the publication type (Original/Review/Case report/letter etc.)
- Should also mention the expected benefit of the medical science from publishing of this article & the rationale of publishing the article in BCCJ.

Manuscript organization:

Typing

- Double spaced throughout with justified paragraph formatand 5cm margin form the header and 2.5cm margins in all other aspects
- Font type is Times New Roman with font size 12.
- Printed on a good quality A4 80 gm on one side of paper, or formatted as such in electronic format.
- Manuscript should have uniform style, carefully proofread for grammar, spelling and punctuation

- All pages should be numbered consecutively beginning from the title page & number should be placed at bottom center of each page.

Manuscript format

- In general, original articles should be divided into following sections:
- Title page, Abstract, Text, Acknowledgement, References.
- Tables, graphs, illustrations should be appropriately placed in the manuscript with legends & foot notes as expected in printed version.
- Each of the sections is to start on a separate page

Title page:

- Title of the article
- Names of all authors with their designation and institutional affiliations
- Name of the department and institute where the study was undertaken
- Name of the corresponding author with contact address, telephone number, email address
- Disclosure of conflict of interest if any
- Disclosure of sources of funding or sponsor
- A short running head
- 'Key words' representing the article and suitable for electronic search
- Number of tables given
- Number of figures given
- Word count of abstract/summary

Abstract/Summary:

- Structured with headings (Background, Objectives, Methods with statistical analysis, Result & Conclusion) for original works.
- Authors name should not be given.
- Preferably within 250 words.
- No abbreviations in the title and abstract except standard abbreviation.
- A non structured abstract is suggested for review article and case report.

Text:

- IMRaD Format
- Text should be arranged into following sections: Introduction, Methods, Results, Discussions, Acknowledgement, & References

Introduction:

- Statement of the problem with a short discussion of its importance and significance
- Review of the literature related to the problem with pertinent reference
- Objectives/ hypothesis/ benefits expected stated in 1-2 paragraphs

Methods:

- Study type, place and time
- Description of study variables
- Description of study subjects and grouping
- Selection criteria
- Approval of the interventional study involving human subjects by ethical review committee and description of the ethical aspects in such study
- Description of procedure, methods, apparatus, drugs or chemicals as applicable
- Description of statistical procedure with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results

Results:

- Present result in logical sequence in text, table and illustration with most important finding first
- Describe without comment
- Restrict number of tables and figures needed to support assessment of paper
- Do not duplicate data in tables and figures

Tables:

- Simple, self explanatory with brief title, not duplicated in text
- Each table should be numbered in Romans and printed in appropriate place in the text
- Tables should be formatted by Microsoft word & presented with in the *.doc file, Not as a picture.
- Use of many tables is not encouraged

Illustrations:

- All illustrations must be numbered consecutively in Arabic numerals as they appear in the text
- Submit print photograph of each illustration along with its electronic file
- Figure number, title of manuscript, name of the corresponding author and arrow indicating top should be written on a sticky label affixed on the back of each photograph
- Scanned picture, graph, chart with title and figure number should be placed at the appropriate place as expected in the printed version and its original electronic file should be submitted separately also in the CD along with text or by separated file attachments through email.
- Photomicrograph should indicate the magnification, internal scale and the method of staining
- All drugs should be mentioned in their generic form. The commercial name may be used in parenthesis

Acknowledgement:

- Individuals, institution, sponsor, organization or bodies should be acknowledged in the article for their contribution or financial or any form of assistance to the work

References:

- For reference, use author number style (Vancouver) which is based on an ANSI standard adapted by the National Library of Medicine(NLM)
- References should be numbered consecutively in the order in which they are first mentioned in the text
- Identify references in the text, tables and legends by Arabic numerals in superscript
- All citations to electronic references should be presented in numbered references following the text
- The titles of the journals should be abbreviated according to the style used in Index Medicus
- Write names of 6 authors followed by et al. if authors' number is more than six.
- The reference list is not usually verified by the editorial staff or reviewer. It is the total responsibility of author to provide accurate information.
- Consult http://www.nlm.nih.gov/citingmedicine/ for full detail of the referencing system followed by BCCJ.
- Examples of common referencing is given below:
- **Standard journal article:**

Khalil M, Chowdhury MAI, Rahman H, Mannan S, Sultana SZ, Rahman MM, et al Splenic Mass and its relation to age, sex and height of the individual in Bangladeshi People. J Bangladesh Soc Physiol 2008; 3(1): 71-78.

- **Journal article with organization as author:**

  American diabetes Association. Diabetes update. Nursing, 2003 Nov; Suppl: 19-20.

- **Journal article with multiple organizations as author:**

  American Dietetic association; Dietitians of Canada. Position of Dietetic association and Dietitians of Canada: nutrition and women's health. J Am Diet Assoc 2004 Jun; 104(6): 984-1001.

- **Journal article with Governmental body as author:**

  National Institute on Drug Abuse (US); Caribbean Epidemiology Centre; Pan American Health Organization; World Health Organization. Building a collaborative research agenda: drug abuse and HIV/AIDS in the Caribbean 2002-2004. West Indian Med J. 2004 Nov; 53 Suppl 4: 1-78.

- **Standard book with initials for authors:**

  Eyre HJ, Lange DP, Morris LB. Informed decisions: the complete book of cancer diagnosis, treatment and recovery. 2nd ed. Atlanta: American Cancer Society; 2002. 768 p.

- **Contributed chapter of a book:**

  Rojko JL, Hardy WD. Feline lukemia virus and other retroviruses. In: Sherding RG, editor. The cat: diseases and clinical management. New York: Churchill Livingstone; 1989. p. 229-332.

- **Conference Proceedings:**

  Pacak K, Aguilera G, Sabban, E, Kvetnansky R, editors. Stress: current neuroendocrine and genetic approaches. 8th symposium on Catecholamines and Other Neurotransmitters in Stress: 2003 Jun 28-July 3; Smolenice Castle (place of conference), Slovakia. New York (place of publication): New York Academy of Sciences (publisher); 2004 Jun. 590 p.

- **Scientific and Technical Reports:**

  Page E, Harney JM. Health hazard evaluation report. Cincinnati (OH)(Place of publication: National Institute for Occupational Safety and Health (US) (Publisher); 2001 Feb.24 p (Total number of pages). Report No.: HETA2000- 0139-2824

- **Dissertation &Thesis:**

Entire Reference

Kempner JL. Aching heads, making medicine: gender and legitimacy in headache (title) [dissertation]. [Philadelphia]: University of Pennsylvania;2004.271p.

- Alam M. Study of Heart Rate Variability in Adolescent Athletes [M Phil thesis]. [Dhaka]: Bangabandhu Sheikh Mujib Medical University; 2008. 178p.

- **Part of Dissertation &Thesis:**

Mackowski MP. Human factors: aerospace medicine and the origins of manned space flight in the United States [dissertation]. [Tempe (AZ)]: Arizona State University; 2002 May. Part 2, Space medicine; p.188-377.

- Alam M. Heart Rate Variability in Adolescent Athletes [M Phil thesis]. [Dhaka (Bangladesh)]: Bangabandhu Medical University; 2008 July. Appendix (Name of the part) 4 (Number of the part), Classification of Physical Activity Intensity (Title of the part). p.7 (Location of the part).

- **Standard journal article on the Internet:**

  Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. Ann Intern Med [Internet]. 2006Jul4 [cited 2007 Jan 4]; 145 (1):662-9.

  Available from: http://www.annals.org/cgi/ reprint/145/1/62.pdf

- **Journal article on the Internet with organization (s) as author:**

  National Osteoporosis Foundation of South Africa. Use of generic alendronate in treatment of osteroporosis. S Afr Med J [Internet]. 2006 Aug [cited 2007 Jan 9]; 9(8):696-7.

Available from:

http://blues.sabinet.co.za/ WebZ/Authorize?

- **Journal article on the Internet with governmental body as author:**

  Centers for Disease Control and Prevention(US), National center for HIV/AIDS, Hepatitis, STD, and TB Prevention and control of tuberculosis in correctional and detention facilities: recommendations from CDC. Endorsed by the Advisory Council for the elimination of tuberculosis, the national Commission of Correctional Health Care and the American correctional Association. MMWR R Rep [Internet]. 2006Jul7 [cited 2007Jan 9]; 55(RR-9):1-44. Available from: http://www.cdc.gov/ mmwr/preview/ mmwrhtml/rr5509al.htm

- **Journal article on the Internet with no author:**

  Prevention strategies for asthma-secondary prevention. CMAJ [Internet]. 2005 Sept [cited 2007Jan 5]; 173 (6 Suppl): S25-7. Available from: http//:www.cmaj.ca /cgi/content/ full/ 173'6_suppl/S25

- **Journal article on the Internet without standard volume, issue or article number:**

  Jacobs JL, Lee MT, Lindberg M, Kamin C. Problem based learning, multimedia paucity of behavioral issue learning. Med Educ. Online [Internet]. 2005 [cited2005]: [5p]. Available from: http://www.med-ed-online.org/pdf/ 10000006.pdf

Editing and peer review:

- All submitted manuscripts are subject to scrutiny by the Editor in-chief or any member of the Editorial Board.
- Manuscripts containing materials without sufficient scientific value and of a priority issue, or not fulfilling the requirement for publication may be rejected or it may be sent back to the author(s) for resubmission with necessary modifications to suit one of the submission categories.
- Manuscripts fulfilling the requirements and found suitable for consideration are sent for peer review. Submissions, found suitable for publication by the reviewer, may need revision/ modifications before being finally accepted.
- The Editorial Board finally decides upon the merit of the reviewed and revised/modified submission.
- Reviewed accepted manuscript may be sent to the authors, and should be corrected and returned to the editorial office within one week. No addition to the manuscript at this stage will be accepted.
- All accepted manuscripts are edited according to the Journal's style.

Submission Preparation Checklist

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

- The submission has not been previously published, nor is it currently before another journal for consideration (or an explanation has been provided in Comments to the Editor).
- The submission file is in Microsoft Word 97-2003, *.doc file format.
- Where available, URLs for the references have been provided.
- The text is double-spaced; uses a 12-point font; employs italics, rather than underlining (except with URL addresses); and all illustrations, figures, and tables are placed within the text at the appropriate points, rather than at the end.
- The text adheres to the stylistic and bibliographic requirements outlined in the Author Guidelines.

Communication for manuscript submission:

Authors are requested to send online new and revised manuscripts to the following address:

Editor-in-Chief
Bangladesh Critical Care Journal
bccj.editor@gmail.com

Corresponding author should clearly indicate a reply address and preferably an electronic means of communication in the title page.

Copyright:

From the Desk of the Editor

Management of sepsis in resource poor countries: cutting your coat according to your cloth

Gentle S Shrestha

Low and middle-income countries (LMICs) bear the largest part of the global burden of sepsis.[1] In these resource poor countries, outcome of patients with sepsis is poorer and the mortality is higher, when compared to developed nations.[2] Current international guidelines for management of sepsis and septic shock is largely based on studies and research from resource rich settings.[3] Applicability of such guidelines in resource poor settings can be questionable due to difference in availability of trained health care workers, laboratory support, equipments, infrastructure and logistics.[4] Extrapolation of the recommendations may, in some instances, be harmful. In African children with severe infection, administration of a fluid bolus (as recommended by international guidelines) was associated with a higher mortality than restrictive fluid management.[5] Similarly, early initiation of enteral feeding in non-intubated patients with cerebral malaria may increase mortality in resource-poor settings.[6] Recent definition considers sepsis as a life-threatening organ dysfunction caused by a dysregulated host response to infection.[7] Etiology of sepsis in resource poor settings is different than those in developed countries. Malaria, dengue, typhus, leptospirosis and viral hemorrhagic fever contribute significantly to the cause of sepsis. Pathophysiology of sepsis due to these etiologies varies from the bacterial sepsis. Similarly, some principles of management would differ, especially those related to fluid resuscitation and fluid management.[8] For detection of organ dysfunction due to sepsis, the recent definition suggests the use of Sequential Organ Failure Assessment (SOFA) score. An increment of 2 or more points is considered to indicate organ dysfunction. A new bedside clinical score termed quick SOFA (qSOFA) has been suggested to identify the patients with infection, who are likely to have poor outcome.[7] In resource poor settings, effective application of the new definition, and thus calculation of SOFA score, can be challenging due to lack of resources and trained clinicians.[9] Recent recommendations suggest the use of qSOFA to diagnose sepsis in resource-limited settings.[10] However, when compared to SOFA, qSOFA may have limited utility to predict mortality in patients with sepsis in ICU.[11] Early sepsis recognition is one of the key elements that can improve the patient outcome.[12] The tool or scoring system used for diagnosis of sepsis should be validated in resource poor settings and should have simple and easily obtainable values or parameters at bedside.[9,13,14] Besides early detection, initial focused resuscitation, together with proper post-resuscitation monitoring and reassessment can improve outcome in patients with sepsis in resource limited settings.[12] Knowledge and understanding of sepsis if often sub-optimal in the first line health care workers from resource limited settings.[15] Training of medical practitioners about recognition of sepsis, resuscitation and monitoring can improve the care of these patients.[12]

Introduction of early goal-directed therapy (EGDT) for treatment of sepsis and septic shock revolutionized the management of sepsis.[16] However, subsequent multicentric studies showed that EGDT did not confer better results than usual care and was associated with higher utilization of resources and higher cost. Of note, all three multicentric trials after EGDT were conducted in resource rich settings. Early recognition of sepsis, early fluid resuscitation and administration of antibiotics were performed in all patients as the part of usual care. These findings may not be generalized to LMICs where the trained health care workers are limited and mortality of sepsis remains high.[2,15,17] In resource limited settings with scarcity of trained personnel, use of protocols and checklists would depend less on highly specialized knowledge and may improve outcome.[18-20]

Recommendations for management of sepsis in resource poor setting should consider availability of resources, feasibility, affordability and safety; similar to the concept of cutting the coat according to the cloth.[4] Early diagnosis and appropriate management of non-bacterial etiology of sepsis should be considered.[8] Empirical antibiotic selection should be based on local disease epidemiology and antibiotic susceptibility patterns. Due to lack of antimicrobial stewardship programs, multidrug resistant organisms causing sepsis are quite common in resource poor settings.[21] As the ICU capacities and level of care might vary widely even in the resource limited settings, recommendations for management based on availability of diagnostic facilities and training of medical personnel may be reasonable.[22,23] Easily available bedside tools like point-of-care ultrasonography can be a valuable adjunct to facilitate management of these patients.[24,25] There is a dearth of research in resource-poor settings in the field of sepsis management.[26] Future research should focus on need assessment, prognostic scoring and cost-effectiveness evaluation.[18] This largely unexplored field of critical care medicine should be the focus for future research, which would potentially generate good quality evidences and thus may improve the outcome of patients with sepsis in resource poor settings.[26]

Dr. Gentle S Shrestha
MD, FACC, EDIC, FCCP
Intensivist & Anesthesiologist
Tribhuvan University Teaching Hospital
Maharajgunj, Kathmandu, Nepal
Email: gentlesunder@hotmail.com
Phone: +977-9841248584

References:

1. Cheng AC, West TE, Limmathurotsakul D, Peacock SJ. Strategies to reduce mortality for bacterial sepsis in adults in developing countries. PLoS Med 2008;5:e175.
2. Vincent JL, Marshall JC, Namendys-Silva SA, Francois B, Martin-Loeches I, Lipman J, et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. Lancet Respir Med 2014;2:380-6.
3. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016. Intensive Care Med 2017;43:304-77.
4. Mer M, Schultz MJ, Adhikari NK; European Society of Intensive Care Medicine (ESICM) Global Intensive Care Working Group and the Mahidol–Oxford Research Unit (MORU), Bangkok, Thailand. Core elements of general supportive care for patients with sepsis and septic shock in resource-limited settings. Intensive Care Med 2017 Jun 15. doi: 10.1007/s00134-017-4831-z.
5. Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO, et al. Mortality after fluid bolus in African children with severe infection. N Engl J Med 2011;364:2483-95.
6. Maude RJ, Hoque G, Hasan MU, Sayeed A, Akter S, Samad R, et al. Timing of enteral feeding in cerebral malaria in resource-poor settings: a randomized trial. PLoS One 2011;6:e27273.
7. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315:801-10.
8. Dondorp AM, Hoang MNT, Mer M; Sepsis in Resource-Limited Settings-Expert Consensus Recommendations Group of the European Society of Intensive Care Medicine (ESICM) and the Mahidol-Oxford Research Unit (MORU) in Bangkok, Thailand. Recommendations for the management of severe malaria and severe dengue in resource-limited settings. Intensive Care Med 2016 Nov 5. doi: 10.1007/s00134-016-4602-2.
9. Shrestha GS. Composition of the sepsis definition task force. JAMA 2016;316:459-60.
10. Kwizera A, Festic E, Dunser MW. What's new in sepsis recognition in resource-limited settings? Intensive Care Med 2016;42:2030-3.
11. Raith EP, Udy AA, Bailey M, McGloughlin S, Maclsaac C, Bellomo R, et al. Prognostic accuracy of the SOFA score, SIRS criteria, and qSOFA score for in-hospital mortality among adults with suspected infection admitted to the intensive care unit. JAMA 2017;317:290-300.
12. Papali A, McCurdy MT, Calvello EJ. A "three delays" model for severe sepsis in resource-limited countries. J Crit Care 2015;30:861.e9-14.
13. Haniffa R, Pubudu De Silva A, Weerathunga P, Mukaka M, Athapattu P, Munasinghe S, et al. Applicability of the APACHE II model to a lower middle income country. J Crit Care 2017 Jul 13;42:178-183. doi: 10.1016/j.jcrc.2017.07.022.
14. Grissom CK, Brown SM, Kuttler KG, Boltax JP, Jones J, Jephson AR, et al. A modified sequential organ failure assessment score for critical care triage. Disaster Med Public Health Prep 2010;4:277-84.
15. Shrestha GS, Parajuli BP, Banstola A, Upadhyay B, Acharya SP, Bajracharya T. Understanding of severe sepsis and septic shock among emergency department and intensive care unit medical officers in a developing country Nepal: A survey study. BJHS 2016;1:48-51.
16. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-77.
17. Eaton TL, Keener C, Landis K, Stapleton DK, Weissfeld LA, Willochell M, et al. Early, goal-directed therapy for septic shock – A patient-level meta-analysis. N Engl J Med 2017;376:2223-34.
18. Riviello ED, Letchford S, Achieng L, Newton MW. Critical care in resource-poor settings: lessons learned and future directions. Crit Care Med 2011;39:860-7.
19. Levy MM, Dellinger RP, Townsend SR, Linde-Zwirble WT, Marshall JC, Bion J, et al. The surviving sepsis campaign: results of an international guideline-based performance improvement program targeting severe sepsis. Intensive Care Med 2010;36:222-31.
20. Phua J, Koh Y, Du B, Tang Y Q, Divatia JV, Tan CC, et al. Management of severe sepsis in patients admitted to Asian intensive care units: prospective cohort study. BMJ 2011;342:d3245.
21. Dondorp AM, Iyer SS, Schultz MJ. Critical care in resource-restricted settings. JAMA 2016;315:753-4.
22. Dunser MW, Festic E, Dondorp A, Kissoon N, Ganbat T, Kwizera A, et al. Recommendations for sepsis management in resource-limited settings. Intensive Care Med 2012;38:557-74.
23. Hashmi M, Khan FH, Zubairi AB, Sultan ST, Haider S, Aftab S, et al. Developing local guidelines for management of sepsis in adults: Sepsis Guidelines for Pakistan (SGP). Anaesthesia Pain Intensive Care 2015;19:196–208.
24. Lictenstein DA. Point-of-care ultrasound: Infection control in the intensive care unit. Crit Care Med 2007;35:S262-7.
25. Mayo P, Arntfield R, Balik M, Kory P, Mathis G, Schmidt G, et al. The ICM research agenda on critical care ultrasonography. Intensive Care Med 2017 Mar 7. doi: 10.1007/s00134-017-4734-z.
26. Schultz MJ, Dunser MW, Dondorp AM, Adhikari NK, Iyer S, Kwisera A, et al. Current challenges in the management of sepsis in ICUs in resource-poor settings and suggestions for the future. Intensive Care Med 2017;43:612-24.

Original Article

Hypomagnesemia is associated with increase in mortality and morbidity in ICU: Can serum magnesium level be used as prognostic marker in critically ill ICU admitted patients?

Md. Motiul Islam[1], Mohammad Omar Faruq[2], Mohammad Asaduzzaman[3], Amina Sultana[4], Uzzawl Kumar Mallick[5].

Abstract

Objective: *Hypomagnesemia is one of the common electrolyte disorders found in critically ill patients. It is often an incidental finding and usually its importance is ignored. This study was designed to assess the significance of the "impact of hypomagnesemia" on the mortality and morbidity of the ICU patients. Hence the efficacy of hypomagnesemia as prognostic marker was also tested.*

Method: *Prospective cohort study done at the department of Critical Care Medicine, of a tertiary care hospital in the city of Dhaka, Bangladesh (from January 2014 to December 2014) aiming to find out of the differences in mortality & morbidity between two groups of patients one with low and other with normal Mg level.*

Result: *95 adult ICU admitted patients were included in the study and 38% of the study subjects were found to be Hypomagnesemic. The Hypomagnesemic group of patients needed more frequent ventilator support (75% vs 52.54%, p<0.02) and the duration of mechanical ventilator support was also prolonged (3.88±4.10 vs 2.25±3.18, p<0.04, in days). Hypomagnesemic group also needed prolonged ICU stay (9.13 vs 6.27, p<0.01) and total hospital stay (14.94 vs 10.47, p<0.007, days). Hypomagnesemic group of patients had more abnormal total leukocyte count (69.4% vs 47.5%, p <0.05) and more frequent use of inotropic support (61.1% vs 38.9%, p <0.05). The 28 days mortality rate in Hypomagnesemic patients were also high (33.3% vs 11.86%, p<0.01).*

Conclusion: *In this study it was observed that Hypomagnesemia was significantly associated with adverse outcome. So it is better not to ignore this important confounder to predict the outcome of the critically ill ICU admitted patient. Considering the increasing demand of more accurate prognostic marker in critically ill patient, it maybe the high time to utilize serum Mg level systematically for outcome prediction.*

Key wards: *Hypomagnesemia, ICU, mortality and morbidity.*

Introduction:

Magnesium is a very important cation of the human body. It is the fourth most abundant cation in the body and the second most abundant intracellular cation after potassium. Magnesium (Mg) has a very important role in transfer, storage and utilization of energy. More than 300 enzyme systems are regulated and catalyzed by it. [1, 2] Magnesium deficiency is known to be associated with a number of electrolyte abnormalities e.g. hypokalemia, hypocalcemia, hyponatremia and hypophosphatemia. It is also associated with a lot of clinical manifestations such as atrial and ventricular arrhythmias, cardiac insufficiency, coronary vasospasm, sudden death, skeletal and respiratory muscle weakness, bronchospasm, tetany, seizures and other neuromuscular abnormalities.[3,4,5,6] It serves as a co-factor for several enzymes required for electrolyte homeostasis and is also necessary for membrane stability, cell division, and generation of action potentials.[7]

Malnutrition in the intensive care unit (ICU) patients is a widely acknowledged problem that may intensify underlying illnesses and increase the risk of complications.[8] Nutritional assessment upon admission to the ICU is necessary to identify patients at risk and to guide nutritional support during ICU stay.[9] This disorder is often overlooked, although it should probably be searched for systematically because of its significance in predicting prognosis of patients.[10]

Magnesium deficiency commonly occurs in critical illnesses and correlates with higher mortality rate and worse clinical outcome in the intensive care unit patients.[11,12] Magnesium

1. Dr. Md. Motiul Islam, MBBS, MD in Critical Care Medicine. Associate consultant, Medical ICU, Asgar Ali Hospital, 111/1/A Distillary Road, Gandaria, Dhaka- 1204. email:motiulccr16@yahoo.com.
2. Prof. Mohammad Omar Faruq, MD, FACP, FACEP, FCPS, FCCM, Professor, Dept. of Critical Care Medicine, Ibn Sina Hospital, Dhanmondi, Dhaka.
3. Dr. Mohammad Asaduzzaman, MBBS, MD in Critical Care Medicine. Department of Critical Care Medicine, National Institute of Neuroscience, Dhaka, Bangladesh.
4. Dr. Amina Sultana, MBBS, MD in Critical Care Medicine, specialist ICU, United Hospital limited Dhaka.
5. Dr. Uzzawl Kumar Mollick, MBBS, MD in Critical Care Medicine, Department of Critical Care Medicine, National Institute of Neuroscience, Dhaka, Bangladesh.

Corresponding Author:

Dr. Md. Motiul Islam
MBBS, MD Critical Care Medicine.
Associate consultant, Medical ICU, Asgar Ali Hospital,
111/1/A Distillary Road, Gandaria, Dhaka- 1204.
email: motiulccr16@yahoo.com.

also regulates enzymes controlling intracellular calcium, which ultimately affects smooth muscle vasoconstriction, important to the underlying pathophysiology of several critical illnesses.[11] Magnesium deficiency results primarily from gastrointestinal or urinary Mg losses, but malnutrition and decreased dietary Mg intake may hasten the development of Mg depletion.[13] Magnesium therapy is supported by clinical trials in the treatment of symptomatic hypomagnesemia and preeclampsia and is recommended for torsade de pointes.[11]

Hypomagnesemia occurs in 40% of the hospitalized patients,[5] approximately 60% of postoperative patients,[7] about 65% of medical ICU patients,[14] and up to 90% of surgical ICU patients.[15] Hypomagnesemia has been implicated in the development of cardiovascular dysfunction and the systemic inflammatory response syndrome in ICU patients.[15] This study has been conducted to determine the level abnormalities in serum magnesium in critically ill patients at the time of initial ICU evaluation and to study the association of these values with patient's prognosis in terms of mortality and morbidity.

The patients who are admitted to ICU are unstable & critically ill. Most of them need extensive resuscitation & organ support along with expensive interventions & medications. Most of the times it is very important to undergo an initial assessment & to calculate a predictive outcome of the patient. The calculated predicted outcome is then applied for the priority selection of patient's interventions & medications. In a third world country like Bangladesh where most of the people have very low income & limited resources, the calculated outcome prediction may have a great value to utilize the limited resource judiciously.

Till date there are many different scoring systems to predict the outcome of the critically ill ICU patients, but magnesium level is not included to any one of them. Recently the researchers are showing more interest on serum Magnesium level as a predictive marker. Yet more research needed especially in Bangladesh. Moreover this study may help to create physicians awareness to keep an eye on serum magnesium level which is frequently ignored till today.

MATERIALS AND METHODS:

It was a Prospective cohort study where samples were collected by consecutive sampling method. The study was done during the period of January 2014 to December 2014.

The all new admission at intensive care unit who are over 18 years and stays at ICU > 24 hrs were included in the study. The patients recently treated with magnesium (within last 7 days) and with Increased serum createnine (Serum creatinine > 1.2 mg/dl) during admission were excluded from the study.

This prospective cohort study was carried out at the Department of Critical Care Medicine, at a tertiary care hospital in Dhaka city, aiming at finding out the significant mortality & morbidity differences between low & normal magnesium level groups in critically ill ICU admitted patients. The cohort was selected from the critically ill ICU admitted patients by some selection criteria. From the cohort one group was exposed to hypomagnesemia and another group was not exposed to hypomagnesemia. The exposed and unexposed groups were identical to each other. They were all selected after ICU admission and they did not show significant difference of their diagnosis patterns, age distribution and initial mean APACHE II score. After selection of cohort they were followed up for 28 days. The mortality & morbidity within 28 days were recorded. The morbidity was defined as the length of ICU and hospital stay, need and duration of mechanical ventilator support and the occurrences of severe sepsis/septic shock. The study period was of 12 months.

From the study population a total 8 patients were found to be hypermagnesemic (S. Mg level > 2.4 mg/dl). The hypermagnesemic patients were excluded from the study calculation. Normal plasma magnesium concentration was defined as 1.7-2.4 mg/dL (0.7-0.9 mmol, or 1.5-2.0 mEq/L). Hypomagnesemia was defined as the Mg level <1.7 mg/dl & normomagnesemia was defined as the Mg level between 1.7 to 2.4 mg/dl. The overall outcome variables were statistically analyzed to find out any significant difference between the groups.

As it was a prospective cohort study we included as many patients as we could at the given time frame. The cost of the relevant laboratory tests were carried out by the patients as part of their routine management (All the required tests are usually routinely done in the department).

All the enrolled subjects received treatments according to the ICU protocol. Study enrollment did not change the normal treatment procedure. All hypomagnesemic patients were routinely treated with I/V $MgSO_4$. The dose was, In case of mild hypomagnesemia, 4% $MgSO_4$ (w/v) 100ml I/V daily, whereas the same dose was given 12 hourly in case of severe hypomagnesemia. The serum levels were repeated to reassess the Mg status and any persistent hypomagnesemia or iatrogenic hypermagnesemia were handled accordingly.

The outcome was measured by 28 days mortality, length of ICU and hospital stay, need of inotropic support, need and duration of mechanical ventilator support. Appropriate data were collected by using a preformed data sheet. Other necessary data were collected from history sheet and investigation reports.

Collected data were processed and analyzed using Statistical Packages for Social Sciences (SPSS) software version 17. Parametric variables were expressed as mean± standard deviation; non parametric variables were presented as frequency and percentage. Spearman's co-relation test was used for correlation analysis, P value <0.05 was considered statistically significant.

Ethical approval from the proper ethical approval committee was obtained prior to the commencement of the study. Informed written consents were taken from the appropriate persons. The researcher only collected, processed, analyzed & interpretated the data. Patient's confidentiality was strictly maintained.

RESULTS:

During the study period data was collected from 95 study samples. Total 38% (n=36) study subjects had hypomagnesemia and 62% (n=59) had normal magnesium level. From the study subjects 51 patients ware male and 44 patients were female. Total 38.9% of the male patients were hypomgnesemic whereas that was present in 61.1 % cases of female subjects. That means Hypomagnesemia was significantly high in female subjects ($p<0.05$).

The hypomagnesemic and normomagnesemic group of patients were identical to each other. The mean age and mean APACHE II score did not show significant difference between two groups. The diagnosis patterns and co morbidities also did not show any significant difference in chi square test.

Table 1: Shows distribution the disease between two groups:

Systems	Magnesium status		Total	*p value
	Hypomagnesemia	Normomagnesemia		
Pneumonia	05(13.89)	17(28.81)	22	
COPD	02(5.56)	05(8.47)	07	
Stroke	08(22.2)	10(16.9)	18	
CLD	04(11.1)	08(13.6)	12	0.21
Post surgical	08(22.2)	04(6.8)	12	
Others	09(25.0)	15(25.4)	24	
Total	36(100)	59(100)	95	

(Percentages are mentioned within parenthesis)
*Chi-square test

Table 2: Demographic data, disease severity, and outcome according to Mg at admission:

	Low Mg	Normal Mg	p Value
No. of patients n(%)	36(38%)	59(62%)	-
Age, yrs	52.47(±20.84)	55.10(±17.89)	-
APACHE II score (Mean ± SD)	15.75(±6.10)	14.92(±7.91)	0.58
Serum sodium (Mean ± SD)	129.75(±11.87) mmol/L	137.66(±9.52) mmol/L	0.001
Serum potassium(Mean ± SD)	3.52(±0.78) mmol/L	3.95(±0.56) mmol/L	0.003
Serum calcium (Mean ± SD)	7.67 (±1.13) mg/dl	8.22(±0.94) mg/dl	0.01
CRP (Mean ± SD)	167.77(±119.61)	117.09(±96.93)	0.02
Albumin (Mean ±SD)	2.66(±0.72)	2.98(±0.52)	0.01
Abnormal total leukocyte count, n (%)	69.4%	47.5%	0.03
Need ventilator, n (%)	75%	52.54%	0.02
Inotropic support, n(%)	61%	38.9%	0.03
Duration of MV, days (Mean ±SD)	3.88(±4.10)	2.25(±3.18)	0.04
ICU stay days (Mean ±SD)	9.13(±5.70)	6.27(±5.59)	0.01
Hospital stay days (Mean ±SD)	14.94(±7.78)	10.47(±7.60)	0.007
Mortality, n (%)	33.3%	11.86%	0.01

The hypomagnesemic patients needed mechanical ventilator support more frequently (75% vs 52.54%) and for more prolonged duration (3.88± 4.10 vs 2.25 ± 3.18) than the normomagnesemic group. The occurrences of sepsis and septic shock were also likely to be high in Hypomagnesemic group of the study subjects as there were increased frequency abnormal total leukocyte count (69.4% vs 47.5%, $p< 0.05$) and more frequent requirement of inotropes (61.1% vs 38.9%, $p< 0.05$).The mean length of ICU (9.13 vs 6.27, $p<0.01$) and hospital (14.94 vs 10.47, $p<0.007$, days) stay (in days) were also high in the hypomagnesemic group. The mortality rate was also high in Hypomagnesemic group of the study subjects (33.3% vs 11.86% $p<0.01$), the odds ratio of hypomagnesemia for mortality in this study is 3.71.

DISCUSSION:

In human body Magnesium is the 4th most abundant cation.[16] Though its deficiency is a common electrolyte imbalance, till date it is under diagnosed. Magnesium depletion can be present in about one half of all ICU patients. Many study showed that these patients may have significantly higher morbidity and mortality. To identify this type of electrolyte disorder we have to look for the risk factors for this problem. These include poorly controlled diabetes mellitus, alcohol ingestion, severe diarrhea and steatorrhea.[17] Use of a number of pharmacologic agents that induce renal Mg wasting (such as diuretics and aminoglycosides) and sepsis.[18] Manifestations of Mg deficiency include hypokalemia, hypocalcemia, neuromuscular hyper excitability, respiratory muscle weakness and intractable arrhythmias. Mg deficiency may also play a role in the genesis of myocardial ischemia.[15, 18]

The aim of this study was to find the prevalence of hypomagnesemia in critically ill patients and to evaluate the relationship of magnesium level to organ failure, length of ICU and hospital stay, electrolyte disturbance, need and duration of mechanical ventilation and 28 days mortality rate. That means to evaluate the morbidity and mortality in relation of magnesium level.

This study found that in case of hypomagnesaemia mean age was 52.47(±20.84) years and in case of normomagnesemia it was 55.10 (±17.89) years and the mean age did not show significant difference statistically. Hypomagnesaemia had female preponderance (61.1% vs 38.9%, p<0.05). In a study by Mousavi et al.[19] the mean age of hypomangesemic patients was found 60.54 ± 2.06 yrs and there were 252 males (55.7%) and 121 (44.3%) females.

In the present study 38% of the patients had hypomagnesemia and 62% had normomagnesemia. Musavi et al.[19] study found 33% of the patients having hypomagnesemia and 53.8% normomagnesemia is comparable with our study.

In the current study we also found that there was no significant difference between hypo and normomagnesemic group in terms of disease distribution, common co morbidity patterns and mean APACHEII score. Those two groups also did not differ significantly in terms of mean age.

In this study it was found that, there was significantly more use of mechanical ventilator support in hypomagnesemic patient group compared to normomagnesemic (75% vs 52.54%) group. Musavi et al.[19] also found increased rate of mechanical ventilator use in hypomagnesemia (91.1% vs 66.7%). Both the studies showed that the patients with lower serum magnesium levels had increased frequency of mechanical ventilator use.

In case of severe sepsis and septic shock the current study found that, abnormal leukocyte count was more frequent in hypomagnesemia (69.4% vs 47.5%, p<0.05) and they also needed inotropic support more frequently (61.1% vs 38.9%,p<0.05) than normomagnesemia , which ultimately indicates that the hypomagnesemic patients are more prone to develop sepsis and septic shock. Similar result was found by Limaye et al.[20] They showed that occurrence of sepsis were more common in hypomagnesemic patients, among the 29 patients with sepsis hypomagnesemia was higher (20/29 or 69%) as compared to normomagnesemia (8/29 or 28%). The present study found that hypomagnesemia is significantly associated with more frequent use of inotropic support which was 61.1% in hypomagnesemic patients (p<0.05). Compared with Safavi and Honarmand et al.[21] It was found that severe sepsis and septic shock (48%) were most common in hypomagnesemia. The occurrence of hypomagnesemia also was particularly common in patients with sepsis and septic shock. Sepsis was one of the independent risk factors for developing hypomagnesemia during the ICU stay. Magnesium may play an important role in sepsis, as magnesium ions are essential for several important immunologic functions and serve as a natural calcium antagonist, an important step in propagating cellular injury.[22] In animal models, magnesium deficiency increases the production of inflammatory cytokines with increase in lethality associated with endotoxin challenge.[23,24] Showed that progressive magnesium deficiency and hypomagnesemia are strongly associated with increased mortality in experimental sepsis and magnesium replacement therapy provides significant protection from an endotoxin challenge.

Mean length of mechanical ventilation days was higher in hypomagnesemic patients than normomagnesemic (3.88±4.10 vs 2.25±3.18) group. The mean mechanical ventilation days was inversely correlated with serum magnesium level (p>0.04). The mean length of ICU stay was 9.13(±5.70) days in hypomagnesemia. The mean length of hospital stay was 14.94(±7.78) days in hypomagnesemia and 10.47(±7.60) days in normomagnesemia (p>0.007). In the study carried out by Soliman et al.[18] the patients with hypomagnesemia had longer duration of stay in the ICU. They also found that hypomagnesemia was an independent risk factor for the longer ICU stays.

In this study there was significantly increased mortality rate in hypomagnesemic patients compared to normomagnesemia (33.3% vs 11.86%; p<0.01). The relationship between hypomagnesemia and the mortality rate varies from study to study. A higher mortality rate was detected in hypomagnesemic patients when compared with normomagnesemic patients by Chernow et al.[7] (41% vs. 13%), Rubeiz et al.[25] (46% vs. 25%) and Safavi and Honarmand et al.[21] (55% vs. 35%). But Guérin et al.[26] found no difference in ICU mortality between hypomagnesemic and normomagnesemic groups (18% vs. 17%). Soliman et al.[18] observed that patients who develop ionized hypomagnesemia during their ICU stay have higher mortality rates (2-3 times higher). Dabbagh et al.[12] observed higher mortality rates in critically ill-patients with daily magnesium supplementation index (DMSI) <1 g/day in comparison to DMSI > 1 g/day (43.5% vs. 17%). Limaye et al.[20] observed that mortality rate in hypomagnesemic group was 57% when compared with 31% in the normomagnesemic group. Our results showed significant difference in ICU mortality between patients with hypomagnesemia and normomagnesemia on admission.

SUMMARY:

This prospective cohort study was carried out in the Department of Critical Care Medicine (ICU), in a tertiary care hospital in Dhaka city, aiming at finding out the significant mortality & morbidity differences between low & normal magnesium level group, in critically ill patients admitted in ICU. A cohort from critically ill ICU admitted patients were selected by some selection criteria. The cohort had two groups, one of them had hypomagnesemia and another group had normomagnesemia. The cohort was followed up for the next 28 days. The 28 days mortality & morbidity was assessed & recorded. The mortality was defined as the mortality within 28 days of ICU admission. The morbidity was defined as the length of ICU and hospital stay, need for mechanical ventilation and duration of ventilation support and need for inotropic support. The two cohorts were similar to each other in terms of age, co morbidity, disease distributions and initial mean APACHE II score as statistically they showed no significant differences. The study period was of 12 months.

Total 38% of the study subjects were Hypomagnesemic and this group of patients needed mechanical ventilator support more frequently (52.54% vs. 75%, $p<0.02$), required prolonged ventilator support (3.88±4.10 vs 2.25±3.18, $p<0.04$), prolonged ICU stay (9.13 vs 6.27, $p<0.01$) and prolonged hospitalization (14.94vs10.47,$p<0.007$) compared to normomagnesemia (in days). Incidence of severe sepsis and septic shock were also more common in hypomagnesemia as it had significant association with abnormal total leukocyte count (69.4% Vs 47.5%, $p <0.05$) and more frequent use of inotropic support ($p <0.05$). The mortality rate in hypomagnesemic patients was also significantly high (33.3% vs 11.86% $p<0.01$).

CONCLUSION :

In this study it was observed that hypomagnesemia is a common electrolyte imbalance in our study subjects. After summarizing all the observations of this study it can be stated that hypomagnesemia is significantly associated with increased mortality and morbidity.

RECOMMENDATIONS :

In this study we found that serum hypomagnesemia is a very common disorder in critically ill patients and it has significant relationship with the outcome of ICU patients, even after proper correction. So we can make the following recommendations.

- Firstly, every ICU admitted patient should be checked for serum Mg level routinely.
- Secondly, we may propose a modified APACHI score which should include separate point for Serum Mg level.
- Finally, as there was limitation of time and budget our sample size was very small to draw a final conclusion. A general consensus is also important to develop a widely accepted modified scoring system. Further multicentre study with large sample size may be done in future to overcome the problem.

Limitations of our study

1. It was a single center study.
2. Short duration of study.
3. Fewer number of study subjects.
4. Serum Mg level should have been substratified among the hypomagnesaemia group to increase the sensitivity of cut off value of serum Mg level to improve the prognostic accuracy.

REFERENCES:

1. Al-Ghamdi Sm, Cameron Ec, Sutton Ra.Magnesium deficiency, pathophysiologic and clinical overview. Am J Kidney Dis 1994 (1); vol. 24: pp.737-52.
2. Altura Bm, Altura Bt.Role of magnesium in patho-physiological processes and the clinical utility of magnesium ion selective electrodes. Scand J Clin Lab Invest Suppl 1996; vol. 224: pp.211-34.
3. Sanders Gt, Huijgen Hj, Sanders.Magnesium in disease: A review with special emphasis on the serum ionized magnesium. Clin Chem Lab Med 1999; vol.37: pp.1011-33.
4. Fawcett Wj, Haxby Ej, Male Da. Magnesium: Physiology and pharmacology. Br J Anaesth 1999; vol.83: pp.302-20.
5. Whang R, Oei TO, Aikawa JK et al. Predictors of clinical hypomagnesemia. Hypokalemia, hypophosphatemia, hyponatremia, and hypocalcemia. Arch Intern Med 1984; vol.144 (9): pp.1794-6.
6. Speich M, Bousquet B, Nicolas G.Reference values for ionized, complexed, and proteinbound plasma magnesium in man and women. Clin Chem 1981; vol.27: pp.246-8.
7. Chernow B, Bamberger S, Stoiko M et al. Hypomagnesemia in patients in postoperative intensive care. Chest 1989; Vol.95: pp.391-7.
8. Pollack MM, Ruttimann UE, Wiley JS.Nutritional depletions in critically ill children: associations with physiologic instability and increased quantity of care.JPEN J Parenter Enteral Nutr 1985; vol. May-Jun 9(3): pp.309-13.
9. Hulst JM, van Goudoever JB, Zimmermann LJ, Tibboel D, Joosten KF.The role of initial monitoring of routine biochemical nutritional markers in critically ill children. J Nutr Biochem 2006; vol. 17 (1): pp. 57-62.
10. Whang R, Ryder K. Frequency of hypomagnesemia and hypermagnesemia, requested vs routine. JAMA 1990; vol. Jun 13,263(22): pp.3063-4.
11. Tong GM, Rude RK. Magnesium deficiency in critical illness. J Intensive Care Med 2005; vol.20: p.3.
12. Dabbagh OC, Aldawood AS, Arabi YM, Lone NA, Brits R, Pillay M. Magnesium supplementation and the potential association with mortality rates among critically ill noncardiac patients. Saudi Med J 2006; vol.27 (6): pp.821-5.
13. Ryzen E.Magnesium homeostasis in critically ill patients.Magnesium 1989; vol.8 (3-4): pp. 201-12.
14. Ryzen E, Elbaum N, Singer FR, Rude RK.Parenteral magnesium tolerance testing in the evaluation of magnesium deficiency. Magnesium 1985; vol. 4: pp.137- 47.

15. Koch SM, Warters RD, Mehlhorn U.The simultaneous measurement of ionized and total calcium and ionized and total magnesium in intensive care unit patients. J Crit Care 2002; vol.17: pp.203-20.

16. Fox C, Ramsoomair D, Carter C. Magnesium: its proven and potential clinical significance.South Med J 2001; vol.94 (12): pp. 1195- 201.

17. Olerich MA, Rude RK.Should we supplement magnesium in critically ill patients? New Horiz 1994; vol.2 (2): pp.186- 92.

18. Soliman HM, Mercan D, Lobo SS, Melot C, Vincent JL.Development of ionized hypomagnesemia is associated with higher mortality rates. Crit Care Med 2003; vol. 31(4): pp.1082-7.

19. Mousavi SAJ, Salimi S, Rezai M.Serum Magnesium Level Impact on the Outcome of Patients Admitted to the Intensive Care Unit.Tanaffos 2010; vol. 9(4): pp.28-33.

20. Limaye CS, Londhey VA, Nadkar MY, Borges NE.Hypomagnesemia in Critically Ill Medical Patients.JAPI 2011; vol.59: pp.19-22.

21. Safavi M and Honarmand A.Admission hypomagnesemia - Impact on Mortality or Morbidity in critically ill patients, M.E.J. ANESTH 2007; vol.19 (3): pp.645-60.

22. Sayeed Mm, Zhu M, Maitra Sr.Alterations in cellular calcium and magnesium during circulatory/septic shock. Magnesium 1989; vol.8: pp.179-89.

23. Wang P, Ba Zf, Morrison Mh et al.Mechanism of the beneficial effects of ATP MgCl2 following trauma-hemorrhage and resuscitation: Downregulation of inflammatory cytokine (TNF,IL-6) release. J Surg Res 1992; vol.52: pp.364-71.

24. Salem M, Kasinski N, Munoz R. et al. Progressive magnesium deficiency increases mortality from endotoxin challenge: Protective effects of acute magnesium replacement therapy. Crit Care Med 1995; vol.23: pp.108-88.

25. Rubeiz GJ, Thill-Baharozian M, Hardie D, Carlson RW.Association of hypomagnesemia and mortality in acutely ill medical patients. Crit Care Med 1993; vol.21: pp.203–9.

26. Guérin C, Cousin C, Mignot F, Manchon M, Fournier G.Serum and erythrocyte magnesium in critically ill patients. Intensive Care Med 1996; Vol.22: pp.724–7.

Original Article

Prevention of Nosocomial Infection & role of Hand Hygiene Compliance in a Private Hospital of Bangladesh

Begum A[1], Bari MS[2], Azad MAK[3], Hossain I[4], Saha PR[5]

Abstract

Background: *Nosocomial infection (NI) is a major cause of morbidity and mortality of patients attending the healthcare facilities all over the world. Only a few studies regarding this issue have been conducted in Bangladesh.*

Objective: *To describe the load of NI and to assess role of hand hygiene compliance of doctors and nurses regarding its prevention.*

Method: *In this cross-sectional study, medical records of all patients admitted from January 2014 to June 2014 were reviewed and data were collected from patients who had diagnosis of NI. Collected data includes month wise number of NI patients, types of NI, organism responsible for NI and hand hygiene compliance of doctors and nurses. Regarding hand hygiene compliance only critical care areas were considered.*

Results: *During the study period, a total of 8769 patients were admitted in all inpatient departments and critical care areas (cardiac intensive care unit, neonatal intensive care unit, general intensive care unit, coronary care unit, general high dependency unit and cardiac high dependency unit) of the hospital and number of NI was 201 (2.29%). The highest NI was respiratory tract infection (63%) and the lowest was skin & soft tissue infection (2%). Predominant organisms responsible were E. coli (16%), acinetobacter species (15%), Pseudomonas species (14%), Klebsiella species (13%), Serratia species (13%) and Candida species (13%). The highest average hand hygiene compliance (67.67%) and lowest NI (1.14%) was observed in June 2014.*

Conclusion: *In this study, NI rate was the lowest when the hand hygiene compliance was the highest. So, it is obvious that implementation of hand hygiene may be one of the important measures to prevent NI. So, hospitals should have strict guidelines and review measures to prevent this man made phenomenon. All these efforts will not only reduce patient morbidity, but will also reduce the use of antibiotics and healthcare costs of the country.*

Key Words: *Nosocomial infection (NI), Hand Hygiene Compliance.*

Introduction:

Nosocomial infection is an infection occurring in a patient during the process of care in a hospital or other health care facility which was not present or incubating at the time of admission.[1] NI can affect patients in any type of setting where they receive care and even may appear after discharge. However, an asymptomatic patient may be considered infected if pathogenic microorganisms are found in a body fluid or at a body site that is normally sterile, such as cerebro-spinal fluid or blood.[2] Infections acquired by staff or visitors to the hospital or other healthcare setting and neonatal infection that result from passage through the birth canal may also be considered nosocomial infections.[3]

The highest frequencies of NIs were reported from hospitals in the Eastern Mediterranean and South-East Asia Regions (11.8 and 10.0% respectively), with a prevalence of 7.7 and 9.0% respectively in the European and Western Pacific Regions.[4] Annually, this results in 5000 deaths with a cost to the National Health Service of a billion pounds in United Kingdom. On average, a patient with NI spent 2.5 times longer in hospital, incurring additional costs of £3000 more than an uninfected patient. A few studies have been conducted in Bangladesh to measure the load of NI. In a study conducted in general surgery and burn unit of Dhaka Medical College Hospital revealed that burden of NI was 46.2%.[5] Pneumonia and surgical-site infection are most common NI followed by gastrointestinal infection, urinary tract infection, and primary bloodstream infection.

Pathogens that cause such infections are termed nosocomial pathogens. People become infected with bacteria, viruses, fungi and parasites when these micro-organisms spread through the air, through direct or indirect contact or when

1. Dr. Afsana Begum, Department of Medicine, United Hospital Limited, Dhaka, Bangladesh
2. Dr. Md. Shafiqul Bari, Department of Medicine, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh. E-mail : drsbari_69@yahoo.com
3. Dr. Md. Abul Kalam Azad, Department of Surgery, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh.
4. Dr. Md. Iqbal Hossain, Consultant, Department of Medicine, United Hospital Ltd., Dhaka, Bangladesh. E-mail : iqbal.hossain@uhlbd.com
5. Dr. Pradip Ranjan Saha, Consultant, Department of Medicine, United Hospital Ltd., Dhaka, Bangladesh. E-mail : pradip.saha@uhlbd.com

Corresponding Author:

Dr Afsana Begum
Consultant (Medicine)
United hospital limited, Gulshan – 02, Dhaka, Bangladesh
E mail: afsana_75@yahoo.com
Phone: +880-1819503771

infected blood or body fluids enter the body. The risk of infection is higher in places where people gather, and the impact is magnified in hospitals and long-term care facilities because patients are already ill and at particular risk of infection due to medical interventions and "hands-on" care. The severity is greatest among those who are elderly, very young, have weakened immune systems or have one or more chronic conditions. Of greatest concern are the bacteria that

are resistant to multiple types of antibiotics. More than 50% of NI are caused by bacteria that are resistant to at least one type of antibiotic.[6] Infection can easily spread from patient to patient through the hands of healthcare workers during treatment or personal care or by touching contaminated shared surfaces, such as bathrooms, toilets or equipments. Even the simple act of holding a loved one's hand can risk spreading infection if hands haven't been correctly washed. While direct person-to-person touch is the primary pathway, the healthcare environment itself can be a route of transmission. Bacteria can exist on many objects in the patient environment (e.g. bedrails, telephones, call buttons, taps, door handles, mattresses, chairs). Some of those bacteria can survive for a long time—in some cases for many weeks and even months. Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* (*C. difficile*) are two of the most well-known bacteria that are able to adapt and survive in the healthcare environment long enough to cause infection.[7]

In 1985, the Centers for Disease Control and Prevention's (CDC's) Study on the efficacy of NI control reported that hospitals with four key infection control components—an effective hospital epidemiologist, one infection control practitioner for every 250 beds, active surveillance mechanisms, and ongoing control efforts, can reduce NI rates by approximately one third.[8] Infection control programs are cost-effective, but their implementation is often hindered by a lack of support from administrators and poor compliance by doctors, nurses, and other health workers. Hand hygiene is the single most important measure for prevention and control of NI and can significantly reduce the burden of disease, particularly in developing countries. Unfortunately, compliance with recommended hand hygiene procedures has been unacceptably poor, with mean baseline rates of 5% to 81%.[9]

Objective:

To describe the load of NI and to assess role of hand hygiene compliance of doctors and nurses regarding its prevention.

Method:

This is a cross-sectional study which is conducted in United Hospital Limited, Dhaka, Bangladesh. Medical records of all patients admitted in all inpatient departments and critical care areas from January 2014 to June 2014 were reviewed. Patients having diagnosis of NI with culture positive materials where sample were taken 48 hours after admission were considered. Patients with incomplete information, NI patients with culture negative materials and those who left the hospital against medical advice were excluded from the study. An infection control team was formed which included an infection control doctor and an infection control nurse. At the same time an infection control committee was also formed which comprises consultants from all specialties of hospital, chaired by senior consultant of microbiology. To prevent nosocomial infection two measures were taken,1) a guideline of antibiotic therapy which was based on infection site, possible organisms responsible for infection and local resistance pattern were supplied to all departments and were advised to follow it strictly and 2) implementation of hand hygiene practice (Hand washing and hand disinfecting with alcohol based hand rub). Effective hand washing was described as the application of a plain (non-antimicrobial) or antiseptic (antimicrobial) soap onto wet hands; then vigorous rubbing together of both hands to form a lather, covering all the surface of the palms, tops of the hands, base of the fingers, between the fingers, back of the fingers, fingers tips, fingernails, thumb and wrists for one minute. Alcohol hand-rub uses alcohol instead of water. The process of alcohol hand-rub starts by applying a sufficient amount of the alcohol based hand-rub product (liquid, gel or foam) according to the manufacturer's recommendation (usually between 3 to 5 ml), and spreading it all over the hands, especially the areas between fingers, thumbs and finger nails. To see the compliance, a vigilance team was also formed. For study purpose, emphasis was given on hand hygiene practice only and regarding this hand hygiene practice, only critical care areas (cardiac intensive care unit, neonatal intensive care unit, general intensive care unit, coronary care unit, general high dependency unit and cardiac high dependency unit) were considered.

Collected data included month wise number of NI patients, types of NI, organism responsible for NI and hand hygiene compliance of doctors and nurses in critical care areas from January 2014 to June 2014. Statistical analysis was done using SPSS version 16 (SPSS Inc., Chicago, USA) and results are presented as frequency and percentage with charts and tables.

Results:

Distribution of NI patients

During study period a total 8769 patients were admitted in the hospital among which 2.29% patients were diagnosed as NI [Table 1]. The highest (3.5%) NI occurred in January 2014 and the lowest (1.14%) in June 214.

Types of NI

In this study the highest NI was respiratory tract infection (63%) followed by urinary tract infection (21%), blood stream infection (10%) surgical site infection (4%) and skin & soft tissue infection (2%) [Figure 1].

Microbial organism causing NI

The predominant organisms responsible for NI were *E.coli* (16%), *Acinetobacter* species (15%), *Pseudomonas* species (14%), *Klebsiella* species (13%), *Serratia* species (13%) and *Candida* species (13%) [Table 2].

Hand hygiene compliance

The highest average hand hygiene compliance was observed in June 2014 (67.67%). Among doctors, the highest hand hygiene compliance (94%) was noted in neonatal intensive

care unit in March 2014 and June 2014 and the lowest (37%) was noted in general high dependency unit in January 2014. Among nurses, the highest hand hygiene compliance (86%) was also noted in neonatal intensive care unit in March 2014 and the lowest (39%) was noted in cardiac high dependency unit in February 2014 [Figure 2].

Discussion:

In this study, month wise distribution of NI from January 2014 to June 2014, types of NI, organisms responsible for NI and hand hygiene compliance of doctors and nurses as a prevention strategy in the United Hospital Limited, Bangladesh was described. This study showed NI rate was 2.29% which is similar to the result of a survey (2.4%) conducted by infection control unit of BIRDEM hospital in 2004.[10] On the contrary, findings from two other studies conducted in Dhaka Medical College Hospital revealed that NI rate were much higher (46.2% and 38%).[5, 11] Similarity of results between United Hospital and BIRDEM Hospital was probably due to similarity of infection control policy of these institutes. But the rate of NI was much higher in Dhaka Medical Hospital possibly because the study was conducted in surgery unit of this institute where chance of wound infection is common. Louis et al. conducted a study in Europe and the prevalence of NI was 20.6% which is also much higher than our study probably because that study was conducted to the see the NI among patients of intensive care units only where chance of cross infection rate is very high as a result of use of mechanical ventilation, other invasive procedures, long hospital stay and finally less immunity of the patients.[12]

Majority of NI in this study was respiratory tract infection but two other studies conducted in Dhaka Medical College Hospital showed wound infection was the predominant NI.[5, 11] In United Hospital, patients from all departments were included but studies conducted in Dhaka Medical College Hospital, patients from surgery units and burn unit were included and possibly this is the main reason of this disparity. In EPIC study conducted by Louis et al. majority of infection was pneumonia that is similar to our study.[12] This is because majority of patients included in both studies were from critical care units.

Predominant organisms in this study were *E. coli, Acinetobacter species, pseudomonas species, Klebsiella species, Serratia species* and *candida species.* Two other studies conducted in Bangladesh by Zaman et al. and Mohiuddin et al. in 1992 and 2008 respectively showed that the predominant organism was *E. coli* followed by *Pseudomonas* and *Staphylococcus aureus*.[13, 14] This reflects the changing pattern of organism responsible for NI as a result of changing pattern of drug resistance.

The importance of hands in transmission of hospital infections has been well demonstrated and can be minimized with appropriate hand hygiene practice. Compliance with hand washing however is frequently suboptimal. This is due to a variety of reasons including: lack of appropriate accessible equipment, high staff to patient ratios, allergy to hand washing products, insufficient knowledge of staff about risk and procedures, long duration recommended for washing and the time required.[15,16] This study showed that among doctors, the highest hand hygiene compliance (94%) was noted in neonatal intensive care unit and the lowest (37%) was noted in the general high dependency unit and among nurses, the highest hand hygiene compliance (86%) was also noted in neonatal intensive care unit and the lowest (39%) was noted in cardiac high dependency unit. Hand hygiene compliance rates in different developed countries rarely exceed 50% and in the USA it is 50%, 42% in the Switzerland and 32% in the UK.[17] It is noted in this study that in the month of June 2014 hand hygiene compliance rate was highest and NI rate was lowest at that time. In a study conducted by Chen et al. in Taiwan showed that an increase in hand hygiene compliance from 43.3 to 95.6 percent was directly related with an 8.9 percent decrease in NI with a net benefit of more than $5.2 million.[18] In another study conducted in Argentina by Rosenthal et al showed that improvement in hand washing in ICUs from 23.1% to 64.5% were associated with reduction in NI 47.55 per 1000 patient-days to 27.93 per 1000 patient-days.[19] So, it is obvious that hand hygiene is an important strategy for prevention of NI.

Conclusion:

NI is a global threat and its impact on health and economy is considerable but certainly it is preventable. In this study it was noted that in the month of June 2014 when hand hygiene compliance was the highest and NI was the lowest. So, it is obvious that hand hygiene practice is the cornerstone in the prevention of NI. In Bangladesh, infection control program in hospitals has been recognized only in early 2000. Only few hospitals of the country have designated infection control programs and only a few has an antibiotic policy of its own. So, our recommendation is to introduce NI and its prevention in the undergraduate and post graduate medical curriculum to aware our future doctors of this man made phenomenon. We also recommend establishing infection control policy and surveillance system in all government and private hospital in our country. These efforts will not only reduce patient morbidity, but also reduce the use of antibiotics and health care costs of the country.

Limitations:

Only culture positive cases were included in this study and many patients with actual NI having culture negative specimen and NI acquired from other health care facilities were not taken into consideration. So, true burden of NI in our context might not be reflected in this study. Hand hygiene compliance in this study could not be evaluated in general wards and in the cabin due to lack of vigilance team in these areas. Besides this, nosocomial infection in hospital staffs was not calculated in this study.

Tables:

Table 1: Month wise distribution of NI patients.

Month	Number of admitted patients	Number of NI patients (%)	p value
January 2014	1285	45 (3.50)	
February 2014	1360	34 (2.50)	0.142
January 2014	1285	45 (3.50)	
March 2014	1620	47 (2.90)	0.373
January 2014	1285	45 (3.50)	
April 2014	1489	35 (2.35)	0.079
January 2014	1285	45 (3.50)	
May 2014	1447	22 (1.52)	0.001
January 2014	1285	45 (3.50)	
June 2014	1568	18 (1.14)	0.001
Total	**8769**	**201 (2.29)**	**------**

Table 2: Hand hygiene compliance in different departments.(CICU - Cardiac Intensive Care Unit, NICU - Neonatal Intensive Care Unit, GICU - General Intensive Care Unit, CCU - Coronary Care Unit, GHDU - General High Dependency Unit, CHDU- Cardiac High Dependency Unit)

Unit	January 2014				February 2014				March 2014				April 2014				May 2014				June 2014			
	Doctor (%)	Nurse (%)	P value	Average	Doctor (%)	Nurse (%)	P value	Average	Doctor (%)	Nurse (%)	P value	Average	Doctor (%)	Nurse (%)	P value	Average	Doctor (%)	Nurse (%)	P value	Average	Doctor (%)	Nurse (%)	P value	Average
CICU	59	52	0.319	60.15	73	67	0.354	60.24	64	66	0.769	67	70	71	0.876	61.03	83	78	0.372	60.06	67	71	0.540	67.57
NICU	87	81	0.247		90	82	0.103		94	86	0.059		93	77	0.001		56	70	0.040		94	81	0.005	
GICU	44	62	0.010		56	58	0.775		63	67	0.553		53	53	1.000		45	60	0.033		74	57	0.001	
CCU	48	56	0.257		45	64	0.007		46	68	0.002		60	54	0.113		45	53	0.257		65	55	0.148	
GHDU	37	43	0.386		45	40	0.474		56	64	0.248		52	61	0.199		50	55	0.479		58	66	0.243	
CHDU	39	43	0.565		48	39	0.199		59	59	1.000		43	46	0.669		83	78	0.372		48	59	0.118	

Figures:

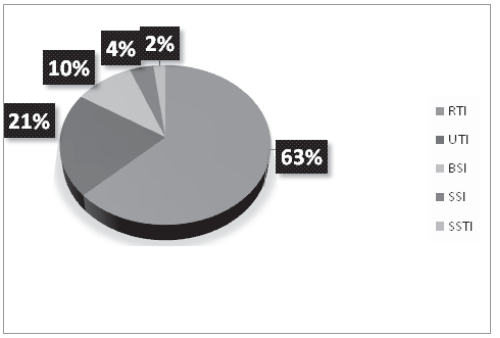


Figure 1: Types of NI. (RTI – Respiratory tract infection, UTI – Urinary tract infection, BSI – Blood stream infection, SSI – Surgical site infection, SSTI – Skin & soft tissue infection)

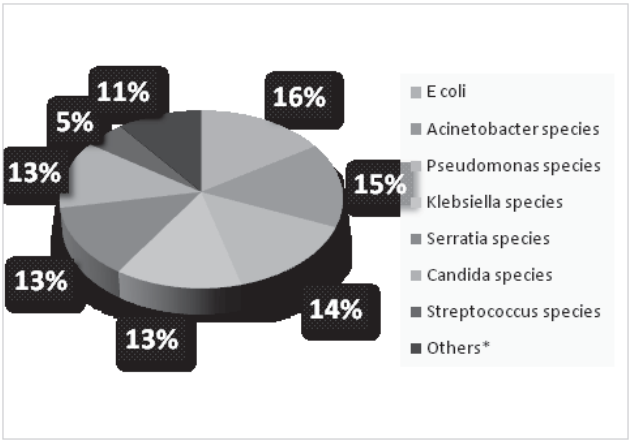


Figure 2: Microbial organisms causing NI. (*Others = *Staphylococcus* spp, *Citrobacter*, *Providencia* spp, *Enterobacter* spp, *Proteus* spp)

References:

1. World Health Organization. The burden of health care-associated infection worldwide. Retrieved on September 3, 2016, from http://www.who.int/gpsc/country_work/burden_hcai/en/
2. Chikere CB, Omoni VT, Chikere BO. Distribution of potential nosocomial pathogens in a hospital environment. Afr J Biotechnol 2008; 7: 3535-9.
3. Lolekha S, Ratanaubol B, Manu P. Nosocomial infection in a teaching hospital in Thailand. Phil J Microbiol Infect Dis 1981; 10: 103-14.
4. Mayonwhite RT, Ducel G, Kereselidge T, et al. An international survey of the prevalence of hospital acquired infection. J Hosp Infect 1988; 11: 43-48.
5. Farukuzzaman. Positive associations of nosocomial infections in surgical wards with etiological clinical factors. Bratisl Lek Listy 2011; 112(5): 273-7.
6. Mauldin PD, Salgado CD, Hansen IS, et al. Attributable Hospital Cost and Length of Stay Associated with Health Care-Associated Infections Caused by Antibiotic-Resistant Gram-Negative Bacteria. Antimicrobial Agents and Chemotherapy 2010; 54(1): 109-15.
7. Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. BMC Infectious Diseases 2006; 6: 130.
8. Haley RW, Culver DH, White J, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am J Epidemiol 1985; 121: 182-205.
9. Doebbeling BN, Stanley GL, Sheetz CT, et al. Comparative efficacy of alternative hand-washing agents in reducing nosocomial infections in intensive care units. N Engl J Med 1992; 327(2): 88-93.
10. A survey on hospital acquired infection in BIRDEM hospital. Infection Control Unit, BIRDEM 2004.
11. Hussain T, Fazal MA, Ahmed A, et al. Nosocomial infection-A cross-sectional study in the surgical wards of Dhaka Medical College Hospital. J of Preventive and Social Med 1991; 10(2): 10-13.
12. Louis V, Bihari MB, Suter P, et al. The prevalence of nosocomial Infections in intensive care units in Europe. European Prevalence of Infection in Intensive Care (EPIC) Study. JAMA 1995; 274: 639–44.
13. Zaman MA, Ahmed ANN, and Chowdhury MZU, et al. Surveillance study of Hospital acquired infection. J of Bangladesh College of Physicians and Surgeons 1992; 10(1): 9-13.
14. Mohiuddin M, Haq JA, Hoq MM, et al. Microbiology of Nosocomial Infection in Tertiary Hospitals of Dhaka City and Its Impact. Bangladesh J Med Microbiol 2010; 4(2): 32-38.
15. CDC guidelines for hand washing and hospital environmental control. Am J Infect Control 1986; 14:110–29.
16. Larson EL. APIC guideline for hand washing and hand antisepsis in health care settings. Am J Infect Control 1995; 23:251–69.
17. Takahashi I, Turale S. Evaluation of individual and facility factors that promote hand washing in aged-care facilities in Japan. Nurs Health Sci 2010; 12(1): 127-34.
18. Chen YC, Sheng WH, Wang JT, et al. Effectiveness and Limitations of Hand Hygiene Promotion on Decreasing Healthcare–Associated Infections. PLoS One 2011; 6(11): e27163.
19. Rosenthal VD, Guzman S, Safdar N. Reduction in nosocomial infection with improved hand hygiene in intensive care units of a tertiary care hospital in Argentina. Am J Infect Control 2005; 33(7): 392-7.

Bangladesh Crit Care J September 2017; 5 (2): 88-92

Original Article

Serum Lipase Amylase Ratio in Predicting Aetiology, Severity and Outcome of Acute Pancreatitis in a Tertiary Care Hospital

Majharul Haque[1*], Golam Azam[2*], Debashis Kumar Sarkar[3], Anisur Rahman[4]

Abstract

Background: *Acute pancreatitis is a relatively common disease with variable prevalence in different countries. Different modalities are available for predicting aetiology, severity and outcome of acute pancreatitis with different sensitivity and specificity. Moreover, some are not widely available, some are very expensive. A single, cheap, widely available marker with high sensitivity and specificity is yet to be identified. The present study intends to find out the utility of serum lipase amylase ratio in predicting the aetiology, severity and outcome of acute pancreatitis.*

Methods: *This prospective, observational study was done at the Department of Gastrointestinal Hepatobiliary & Pancreatic Disorders (GHPD), BIRDEM General Hospital, Dhaka, during the period of July 2014 to March 2016. A total of 71 patients with acute pancreatitis were included. Complete blood count, serum amylase, serum lipase, serum calcium, liver function test, renal function test, fasting lipid profile, ultrasonography of whole abdomen, CT scan of upper abdomen and arterial blood gas (ABG) were done in all patients. Statistical analysis was done with SPSS version 16.*

Results: *Among 71 patients, 23(32.4%) were due to biliary cause, 15(21.1%) were due to hypertriglyceridaemia, 4(5.6%) were due to alcohol and 22(31%) were due to unknown causes. 45 (63.4%) patients had mild attack, 10(14.1%) patients had moderate attack and 16(22.5%) patients had severe attack of acute pancreatitis. Out of 71 patients, 17(23.9%) developed complication whereas 54(76.1%) developed no complication. Serum lipase amylase ratio in patients with biliary pancreatitis was 1.40±0.39 and in patients with non-biliary pancreatitis was 2.39±0.84(p <0.001). Again, serum lipase amylase ratio in patients with acute alcoholic pancreatitis was 2.89±0.79 and in patients with non-alcoholic acute pancreatitis was 1.95±0.81 (p=0.002). Serum lipase amylase ratio in patients with acute pancreatitis due to hypertriglyceridaemia was 2.75±0.68 and in patients with acute pancreatitis due to other than hypertriglyceridaemia was 1.62±.65(p< 0.001). This study showed that serum lipase amylase ratio was <2.0 in acute biliary pancreatitis and this ratio was >2.5 in acute alcoholic pancreatitis and in acute pancreatitis due to hypertriglyceridaemia. Serum lipase amylase ratio in patients with mild acute pancreatitis was 1.95±0.89; in patients with moderately severe acute pancreatitis the ratio was 2.37±0.92 and in patients with severe acute pancreatitis, the ratio was 2.22±0.70. The difference of lipase amylase ratio among these groups of patients was not statistically significant (p=0.273). Mean lipase amylase ratio among the patients without complication of acute pancreatitis was 2.03±0.92 whereas this ratio among the patients with complication was 2.17±0.68. This difference of lipase amylase ratio was not statistically significant (p=0.557).*

Conclusion: *Role of serum lipase amylase ratio in predicting the aetiology and severity of acute pancreatitis has been addressed in several recent studies. This study was another attempt to achieve this goal. Predicting the aetiology of acute pancreatitis by such a cheap tool will guide further diagnostic work up and management strategy will avoid unnecessary investigations.*

Key word: *Serum lipase, serum amylase, acute pancreatitis.*

Introduction :

The incidence of acute pancreatitis appears to be increasing. As the population is becoming increasingly overweight, the incidence of gallstones, the most common cause of acute pancreatitis is rising.[1] The incidence of acute pancreatitis in England, Denmark, and the United States varies from 4.8 to 38 per 100,000 patients. However, estimates of incidence are inaccurate because the diagnosis of mild disease may be missed, and death may occur before diagnosis in 10% of patients with severe disease.[2] Acute pancreatitis is defined physiologically as an acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ system.

Many conditions predispose to acute pancreatitis to varying degrees. Gall stone and alcohol are the most common causes. Other causes include hypertriglyceridaemia, hypercalcaemia, post ERCP, drugs, helminthes, pancreatic carcinoma, pancreatic divisum etc. The laboratory markers for diagnosing acute pancreatitis are serum levels of amylase and lipase. Serum Amylase rises within 6 to 12 hours of onset and is cleared fairly rapidly from the blood. It remains elevated for three to five days in uncomplicated attacks. Serum amylase activities may be normal in 19–32% of cases at the time of hospital admission, as a result of delayed presentation or exocrine pancreatic insufficiency—for example, secondary to chronic alcohol abuse.[3] Serum amylase also may be falsely normal in hypertriglyceridemia-associated pancreatitis.[4] The sensitivity of serum lipase for the diagnosis of acute pancreatitis is similar to that of serum amylase and is between 85% and 100%.[5] Lipase may have greater specificity for pancreatitis than amylase. Serum lipase is always elevated on the first day of illness and remains elevated longer than the serum amylase.[6] Serum lipase amylase ratio can be a useful

marker for predicting aetiology of acute pancreatitis. Devanath *et al.* (2009) showed that the sensitivity and specificity to predict alcoholic acute pancreatitis with lipase-amylase ratio at >4 was 84% and 59% respectively.[7]

Once the diagnosis is established, patients are classified as having mild, moderately severe or severe pancreatitis. The Atlanta criteria defines severity by the presence of organ failure or pancreatic necrosis on dynamic contrast–enhanced CT scan.[8] Other acceptable markers of severe pancreatitis include three or more of Ranson's 11 criteria for non-gallstone pancreatitis[9] and an Acute Physiology and Chronic Health Evaluation (APACHE-II) score of greater than eight.[10] Local complication of acute pancreatitis includes acute peripancreatic fluid collection (APFC), pancreatic pseudocyst, acute necrotic collection (ANC) and walled-off pancreatic necrosis (WOPN). Other complications include splenic infarction splenic / portal vein thrombosis and gastric outlet dysfunction. Systemic complications include renal, circulatory or respiratory organ failure or exacerbation of serious pre-existing comorbidities.[11] This study is intended to evaluate the relationship between serum lipase amylase ratio and acute pancreatitis, which may reveal the predictive value to determine the aetiology, severity and outcome of acute pancreatitis.

Materials and methods

The study was a hospital based prospective, observational and longitudinal study done at the department of Gastrointestinal Hepatobiliary and Pancreatic Disorders (GHPD), BIRDEM General Hospital, Dhaka, Bangladesh during the period of July 2014 to March 2016. Patients with acute pancreatitis aged above 18 years admitted to GHPD of BIRDEM General Hospital, Dhaka, were included in this study. Patients admitted with abdominal pain and diagnosed as acute pancreatitis by clinical history, physical examination and different imaging modalities were included in the study.

The following types of patients were excluded from this study: Known case of chronic kidney disease, chronic pancreatitis, patient unwilling to give voluntary consent to participate in the study and patient attending after 24 hours of onset of abdominal pain. Demographic and clinical variables were age, sex, BMI, duration of hospital stay, abdominal pain, severity of pain, radiation of pain, fever, co-morbid illness, smoking, alcohol, drug history, family history, history of previous attack, vital parameters and GCS score. Laboratory variables were hemoglobin level, haematocrit, WBC count, serum electrolyte, serum calcium, random blood sugar, HbA1c, blood urea, BUN, serum creatinine, liver function test, serum amylase, serum lipase, serum lipase amylase ratio, fasting lipid profile, serum LDH, ABG, CA 19.9, USG, CT scan findings.

Acute pancreatitis was defined by the presence of two of the following criteria: (1) symptoms, such as epigastric pain, consistent with the disease; (2) a serum amylase or lipase greater than three times the upper limit of normal; or (3) radiologic imaging consistent with the diagnosis, usually using CT or MRI. Biliary pancreatitis was considered when the patient with diagnosis of acute pancreatitis with no history of alcohol abuse and imaging techniques showing gall stones or biliary sludge. Biliary pancreatitis was also considered if serum ALT is > 150 U/L with a specificity of 96%.[12] Hypertriglyceridaemia induced acute pancreatitis was defined when fasting serum triglyceride level within 24 hours of admission >1000 mg/dl.[13]

Alcoholic pancreatitis was defined when acute pancreatitis in a patient with history of heavy alcohol consumption (>50 gm/day) for more than 5 years was considered as acute alcoholic pancreatitis.[13] Lipase amylase ratio was calculated on serum lipase and amylase values (expressed as multiples of the upper limit of normal), each of which was obtained on admission (preferably from the same sample) or at least within 24 hours of admission.[7] Severity of pancreatitis was assessed by revised Atlanta criteria where mild acute pancreatitis was defined by absence of organ failure and local or systemic complication, moderately severe acute pancreatitis was defined by transient organ failure that resolves within 48 hours and/ or local or systemic complications, severe acute pancreatitis was defined by presence of persistent single or multiple organ failure lasting for >48 hours.[14]

Outcome of acute pancreatitis was categorized into acute pancreatitis without any complication, acute pancreatitis with complication and death from sequel of acute pancreatitis. Organ failure was defined according to the Modified Marshall Scoring System, a universally applicable scoring system for identifying organ failure.

Data were collected in a pre-designed data-sheet which contains questionnaire, clinical findings and biochemical and imaging findings.

1. Dr. Majharul Haque, FCPS (Medicine), MD (Gastroenterology), Junior consultant (Medicine), Narayangonj General Hospital, email: majharhq@gmail.com
2. Dr. Golam Azam, MD (Hepatology). Associate Professor, Department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD), BIRDEM General Hospital, Shahbag, Dhaka, Bangladesh. email: drgolamazam@gmail.com
3. Dr. Debashis Kumar Sarkar, MD (Gastroenterology), OSD, deputed to BIRDEM General Hospital, Dhaka, Bangladesh.
4. Dr. Anisur Rahman, FCPS. Professor, Department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD), BIRDEM General Hospital, Shahbag, Dhaka,.Bangladesh.

*Dr. Majharul Haque and Dr. Golam Azam had equal contributions and will be considered as principal authors.

Corresponding Author:

1. Dr. Majharul Haque, FCPS (Medicine), MD (Gastroenterology), Junior consultant (Medicine)
Narayangonj General Hospital, email: majharhq@gmail.com
2. Dr. Golam Azam, MBBS, MD (Hepatology)
Associate Professor, Department of Gastrointestinal
Hepatobiliary and Pancreatic Disorders (GHPD)
BIRDEM General Hospital, Shahbag, Dhaka
Postal Code-1000. Bangladesh
E-mail: drgolamazam@gmail.com

Statistical analysis

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean, standard deviation, and categorical variables as frequencies and percentages. The differences between groups were analyzed by unpaired t-test, chi-square (X^2) test, and ANOVA test. Correlation between variables was measured by Spearman correlation coefficient test. A p-value <0.05 was considered as significant.

Ethical consideration

Prior to the commencement of this study, the research protocol was approved by the local ethical committee. The aims and objective of the study along with its procedure, alternative diagnostic methods, risk and benefits were explained to the patients in easily understandable local language and then informed consent was taken from each patient. It was assured that all records would be kept confidential and the procedure would be helpful for both the physician and patients in making rational approach regarding management of the case.

Results

A prospective observational study was carried out to evaluate serum lipase amylase ratio as a predictor of aetiology, severity and outcome of acute pancreatitis. Total 71 patients with acute pancreatitis were enrolled in this study after admission in GHPD with certain inclusion criteria.

Table 1: Demographic, clinical and biochemical characteristics of the study population n(%)

Parameters (n=71)	Result
Age (years)	44.35±16.90
Sex (Male)	37(52.1)
Contributing factor	
Smoking	24(33.8)
Alcohol	11(15.5)
DM	47(66.2)
OCP	5(7.0)
Tea/ coffee	49(69.0)
BMI	25.88±2.95
Clinical features	
Fever	20(28.2)
Abdominal pain	71(100.0)
Duration of hospital stay	7.8±2.5
Hct	32.9±7.5
HbA_{1c}	7.8±1.7
Blood urea nitrogen	21.7±7.2

Values are expressed as mean ± SD. Values within the bracket are expressed as percentage.

Mean age of the patients was 44.35±16.90. 52.1% of the patients were male. Among the patients, 33.8% were smoker, 15.5% were alcoholic, 66.2% were diabetic, 7% patients used to take OCP and 69% patients used to take tea/coffee. 28.2% patients had fever where as all (100%) patients had abdominal pain. Mean duration of hospital stay was 7.8±2.5. Mean Hct level was 32.9±7.5, mean HbA1c was 7.8±1.7, mean blood urea level was 21.7±7.2 (table-1).

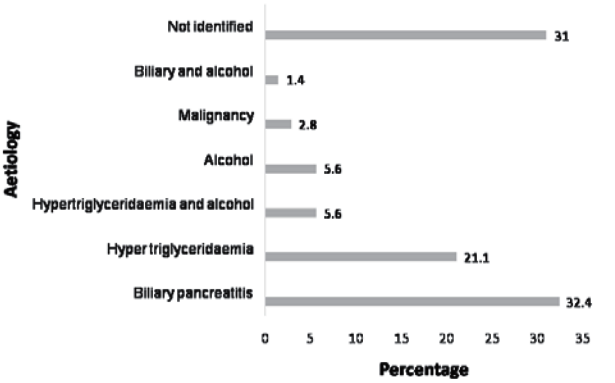


Figure 1: Distribution of patients according to aetiology (n=71)

Among the patients, 32.4% were due to biliary pancreatitis, 21.1% were due to hypertriglyceridaemia, 5.6% were due to alcohol, 5.6% were due to both alcohol and hypertriglyceridaemia, 2.8% were due to malignancy, 1.4% were due to biliary and alcohol and in 31% cases, no cause could be identified (figure-1).

Table 2: Association between serum lipase amylase ratio and acute biliary pancreatitis

Type of acute pancreatitis	n(%)	L-A ratio (Mean±SD)	p value
Biliary pancreatitis	23(32.4)	1.40±0.39	<0.001
Non biliary pancreatitis	48(67.6)	2.39±0.84	
Total	71(100.0)	2.07±0.86	

Unpaired t test was done to measure the level of significance.

Serum lipase amylase ratio in patients with biliary pancreatitis was 1.40±0.39 and in patients with non biliary pancreatitis was 2.39±0.84. This difference was statistically significant (p <0.001) (table-2).

Table 3: Association between serum lipase amylase ratio and acute alcoholic pancreatitis

Type of acute pancreatitis	n(%)	L-A ratio (Mean±SD)	p value
Alcoholic	9(12.7)	2.89±0.79	0.002
Non alcoholic	62(87.3)	1.95±0.81	
Total	71(100.0)	2.06±0.89	

Unpaired t test was done to measure the level of significance

Serum lipase amylase ratio in patients with acute alcoholic pancreatitis was 2.89±0.79 and in patients with non alcoholic acute pancreatitis was 1.95±0.81. This difference was also statistically significant (p=0.002) (table-3).

Table 4: Association between serum lipase amylase ratio and acute pancreatitis due to hypertriglyceridaemia

Type of acute pancreatitis	n(%)	L-A ratio (Mean±SD)	p value
Hypertriglyceridaemia	28(39.4)	2.75±0.68	<0.001
Non-hypertriglyceridaemia	43(60.6)	1.62±0.65	
Total	71(100.0)	2.06±0.89	

Unpaired t test was done to measure the level of significance

Serum lipase amylase ratio in patients with acute pancreatitis due to hypertriglyceridaemia was 2.75±0.68 and in patients with acute pancreatitis due to other than hypertriglyceridaemia was 1.62±0.65. This difference was also statistically significant (p<0.001) (table-4).

Table 5: Association of serum lipase amylase ratio with severity of acute pancreatitis (based on revised Atlanta criteria)

Severity of acute pancreatitis	n(%)	L-A ratio (Mean±SD)	p value
Mild	45(63.4)	1.95±0.89	0.273
Moderately severe	10(14.1)	2.37±0.92	
Severe	16(22.5)	2.22±0.70	

ANOVA test was done to measure the level of significance

Serum lipase amylase ratio in patients with mild acute pancreatitis was 1.95±0.89; in patients with moderately severe acute pancreatitis, the ratio was 2.37±0.92 and in patients with severe acute pancreatitis, the ratio was 2.22±0.70. The difference of lipase amylase ratio among these groups of patients was not statistically significant (p=0.273) (table-5).

Table 6: Association between serum lipase amylase ratio and outcome of acute pancreatitis

Outcome of acute pancreatitis	n(%)	L-A ratio (Mean±SD)	p value
No complications	53(74.6)	2.03±0.92	0.557
Complication	18(25.4)	2.17±0.68	

Unpaired t test was done to measure the level of significance

Mean serum lipase amylase ratio among the patients without complication of acute pancreatitis was 2.03±0.92 whereas this ratio among the patients with complication was 2.17±0.68. This difference of lipase amylase ratio was not statistically significant (p=0.557) (table-6).

Discussion

Acute pancreatitis is a relatively common disease with incidence of 5 – 80 per 100,000 population, although its prevalence varies in different countries.[15] Different modalities are available for predicting aetiology, severity and outcome of acute pancreatitis with different sensitivity and specificity. Moreover some are not widely available, some are very expensive. A single, cheap, widely available marker with high sensitivity and specificity is yet to be identified. Serum lipase amylase ratio determined within first 24 hours of hospitalization may contribute in this regard. A prospective, longitudinal study was carried out to assess serum lipase amylase ratio as a predictor of aetiology, severity and outcome of acute pancreatitis.

In this study, 71 patients diagnosed as a case of acute pancreatitis were included. Among them, 21(29.6%) patients were within 31-40 years age group and only 10(14.1%) patients were above 60 years of age. Mean age was 44.35±16.90 (mean±SD) with minimum age 18 years and maximum age 95 years (table 2). Among the patients, 37(52.1%) patients were male and 34(47.9%) patients were female (table 1). In a study by found the mean age of acute pancreatitis of 47 years among which 55 % were male and 45% were female.[16] The mean age and sex difference of the above study correlate with this study.

It is observed that, there is a relation between DM and acute pancreatitis that may be due to hypertriglyceridaemia. In this study, majority (66.2%) of the patients had DM. This can be explained by the inclusion of patients from a tertiary level diabetic hospital. Out of 71, 24(33.8%) patients were smoker, 11(15.5%) patients were alcoholic. Mean BMI was 25.88±2.95. Mean haematocrit after admission was 32.9±7.5. Mean blood urea nitrogen was 21.7±7.2 and mean HbA_{1c} was 7.8±1.7. Average duration of hospital stay was 7.8±2.5 days.

In this study, 23(32.4%) cases were due to biliary pancreatitis, 15(21.1%) cases were due to hypertriglyceridaemia, 4(5.6%) cases were due to alcohol, 4(5.6%) cases were due to hypertriglyceridaemia and alcohol, 2 (2.8%) cases due to malignancy, 1(1.4%) case due to biliary and alcohol and 22 (31%) cases were due to unknown cause (figure 1). Al-Karawi *et al* found that 67.5% cases of acute pancreatitis were due to biliary cause; alcohol was responsible in 1.8% of cases and 17% cases were due to unknown cause.[17] In another study, found gall stone as aetiology in 34.1% of cases and alcohol in 33.6% cases and hypertriglyceridaemia in 12.3% of cases.[18] Low prevalence of alcohol as aetiology of acute pancreatitis in present study is due to social custom as well as religious belief. On the other hand, high prevalence of hypertriglyceridaemia in the present study is due to increased prevalence of DM among the study population.

This study showed more than half of the patients (63.4%) had mild acute pancreatitis according to revised Atlanta criteria, 14.1% cases had moderately severe attack and 22.5% of cases had severe attack of acute pancreatitis (figure 2). Cho *et al*. found 13% cases as severe acute pancreatitis, 8% cases as moderately severe and 79% cases as mild acute pancreatitis in their study which is similar to present study.[15]

Out of 71 patients, 17(23.9%) developed complication where as 54(76.1%) developed no complication. Albulushi *et al.*

found 32% patients that developed complication of acute pancreatitis in their study.[16]

Serum lipase amylase ratio in patients with biliary pancreatitis was 1.40±0.39 and in patients with non biliary pancreatitis was 2.39±0.84. This difference was statistically significant (table 3; p <0.001). Again, serum lipase amylase ratio in patients with acute alcoholic pancreatitis was 2.89±0.79 and in patients with non alcoholic acute pancreatitis was 1.95±0.81. This difference was also statistically significant (table 4; p=0.002). Serum lipase amylase ratio in patients with acute pancreatitis due to hypertriglyceridaemia was 2.75±0.68 and in patients with acute pancreatitis due to other than hypertriglyceridaemia was 1.62±0.65. This difference was also statistically significant (table 5; p< 0.001).

This study showed that serum lipase amylase ratio was <2.0 in acute biliary pancreatitis and >2.5 in acute alcoholic pancreatitis and in acute pancreatitis due to hypertriglyceridaemia. Devanath *et al.* found serum lipase amylase ratio >4.0 in acute alcoholic pancreatitis and <4.0 in patients with acute pancreatitis due to biliary and miscellaneous causes.[7] There is no study that showed lipase amylase ratio difference among patients with acute pancreatitis due to hypertriglyceridaemia and due to other causes.

Serum lipase amylase ratio in patients with mild acute pancreatitis was 1.95±0.89; in patients with moderately severe acute pancreatitis the ratio was 2.37±0.92 and in patients with severe acute pancreatitis, the ratio was 2.22±0.70. The difference of lipase amylase ratio among these groups of patients was not statistically significant (Table 6; p= 0.273). Devanath *et al.* also didn't find any statistically significant difference in lipase amylase ratio among different severity of acute pancreatitis.[7]

Mean serum lipase amylase ratio among the patients without complication of acute pancreatitis was 2.03±0.92 whereas this ratio among the patients with complication was 2.17±0.68. This difference of lipase amylase ratio was not statistically significant (table 8; p=0.557). Pezzilli*et al.* also found lipase amylase ratio unable to predict the outcome of acute pancreatitis.19

Conclusion:

This study evaluated serum lipase ratio as a predictor of aetiology, severity and outcome of acute pancreatitis. Serum lipase amylase ratio was <2.0 in acute biliary pancreatitis whereas this ratio was >2.5 in patients with acute pancreatitis due to alcohol and hypertriglyceridaemia. Serum lipase amylase ratio in mild AP was lower than that observed in moderately severe and severe AP; but this difference was not statistically significant. Again, serum lipase ratio was lower among patients who did not develop complication than those who developed complication; this difference also was not statistically significant. These findings were similar to other studies.

Serum lipase amylase ratio on admission of patients with acute pancreatitis may be used as a predictor of aetiology of acute pancreatitis. Further study is needed with larger sample size.

References :

1. Mann DV, Hershman MJ, Hittinger R. Multicentre audit of death from acute pancreatitis. Br J Surg 1984;81:890-3.
2. Lankisch PG, Schirren CA, Kunze E. Undetected fatal acute pancreatitis: Why is the disease so frequently overlooked? Am J Gastroenterol 1991;86:322.
3. Matull WR, Pereira SP, O'donohue JW. Biochemical markers of acute pancreatitis. Journal of Clinical Pathology 2006; 59(4):340-4.
4. Agarwal N, Pitchumoni CS, Sivaprasad AV. Evaluating tests for acute pancreatitis. Am J Gastroenterol 1990;85:356.
5. Gullo L. Familial pancreatic hyperenzymemia. Pancreas 2000;20:158.
6. Gwodz GP, Steinberg WM, Werner M. Comparative evaluation of the diagnosis of acute pancreatitis based on serum and urine enzyme assays. Clin Chim Acta 1990;187:243.
7. Devanath A, Kumari J, Joe J, Peter S, Rajan S, Sabu L. Usefulness of lipase amylase ratio in acute pancreatitis in south Indian population. Indian Journal of Clinical Biochemistry 2009;24(4):361-5.
8. Bradley EL. A clinically based classification system for acute pancreatitis. Arch Surg 1993;128:586.
9. Ranson JHC, Rifkind RM, Roses DF. Prognostic signs and the role of operative management in acute pancreatitis. SurgGynecolObstet 1975;139:69.
10. Knaus WA, Draper EA, Wagner DP. Apache II: A severity of disease classification system. Crit Care Med 1985;13:818.
11. Sarr MG. 2012 revision of the Atlanta Classification of acute pancreatitis. Polskie archiwum medycyny wewnętrznej 2013;123(3):120.
12. Tenner S, 2016. Acute pancreatitis. In: M. Feldman, eds. Sleisenger and Fordtran's Gastrointestinal and liver disease.volume 1. 10th ed. USA: Elsevier, 970-86.
13. Tenner S, Baillie J, Dewitt J, Vege SS. Management of Acute Pancreatitis. Am J Gastroenterol 2013;218(2):54.
14. Banks PA, Bollen TL, Dervenis C. Classification of acute pancreatitis—2012: Revision of classification and definitions by international consensus. Gut 2013;62:102-11.
15. Cho JH, Kim TN, Chung HH, Kim KH. Comparison of scoring systems in predicting the severity of acute pancreatitis. World J Gastroenterol 2015;21(8):2387-94.
16. Albulushi A, Siddiqi A, Alqarshoubi I, Aladawi M, Alkhadhouri G, Farhan H. Pattern of Acute Pancreatitis in a Tertiary Care Center in Oman. Oman Medical Journal 2014;29(5):358-61.
17. Al-Karawi MA, Mohamed AE, Dafala MM, Yasawi MI, Ghadour ZM. Acute pancreatitis in Saudi patients. Saudi J Gastroenterol 2001;7(1):30-33.
18. Chang MC, Su CH, Sun MS, Huang SC, Chiu CT, Chen MC. Etiology of acute pancreatitis--a multi-center study in Taiwan. Hepatogastroenterology 2003;50(53): 1655-7.
19. Pezzilli R, Billi P, Miglioli M, Gullo L. Serum amylase and lipase concentrations and lipase/amylase ratio in assessment of etiology and severity of acute pancreatitis. Dig Dis Sci. 1993;38(7):1265-9.

Bangladesh Crit Care J September 2017; 5 (2): 93-96

Original Article

Ultrasound guided emergency cannulation of internal jugular vein in coagulopathic adult patients – a prospective observational pilot study.

Gentle Sunder Shrestha[1], Sabin Koirala[2], Arjun Gurung[3], Prakash Chand[4]

Abstract

Aim: *This study aims to evaluate the safety of ultrasound guided emergency cannulation of internal jugular vein in coagulopathic adult patients.*

Methods: *Adult subjects admitted in the intensive care unit, undergoing emergency cannulation of internal jugular vein under real time ultrasonographic guidance with platelet count less than 50,000/cu mm and/or international normalized ratio (INR) more than 1.5 were enrolled. Major and minor complications during the procedure were noted.*

Results: *Internal jugular vein was successfully cannulated in all the patients. The mean INR of patients having minor complications (provided that platelet count > 50000) was found to be 3.07 with 95% confidence interval(CI) being 2.37-3.77. The mean platelet count of patients having minor complications (provided that the INR<1.5) was found to be 27428 with 95% CI being 19428-36000. There was a significant relationship between margin of safety and occurrence of minor complications (>7mm vs 7mm or less; p value 0.027). Number of attempts while performing internal jugular vein cannulation was associated with minor complications (mean 1.5 with CI 1.2-1.78 vs mean 1.08 with 95% CI 1.00-1.25; p value 0.023). No major complications were reported during the study regardless of platelet count, INR, margin of safety or number of attempts.*

Conclusions: *Emergency cannulation of internal jugular vein may be safely performed in coagulopathic adult patients under real-time ultrasound guidance when performed by an experienced physician.*

Key-words: *Central Venous Cannula (CVC), Coagulopathic Patient, Internal Jugular Vein, Point of Care Ultrasound (POCUS), Venous Cannulation.*

Introduction:

Central venous cannulas are important portals for vascular access and for the assessment of changes in intravascular volume. Central venous cannulas permit the rapid administration of fluids, insertion of pulmonary artery catheters (PACs) or central venous O_2 ($ScvO_2$) saturation monitoring, insertion of transvenous electrodes, monitoring of central venous pressure (CVP), and for treatment of venous air embolism.[1]

Developing nations lack the advanced blood banks and procurement of blood products in short time is not only challenging but is near impossible. However, with the advancement in health care and increase in life expectancy, sicker patients are being managed in intensive care units (ICUs). It is not uncommon for the treating physician to face a coagulopathic patient who needs urgent central venous cannulation, when there is little time to wait for blood products to correct coagulopathy.

Central vein cannulation in a critically ill patient with coagulopathy is a challenge to an anesthesiologist and intensivist due to increased risk of complications. The challenge of successfully cannulating the internal jugular vein with minimal complication is aided by the use of real time ultrasonography. G Ruesz have suggested that ultrasound guided CVC placement without routine correction of coagulation abnormalities may be safe in the ICU.[2]

Real time ultrasonography helps cannulation of central veins under direct visualization, thus reducing the chances of complications. Another advantage that USG cannulation offers is the visualization of vessels in hypotensive patients in whom carotid artery is difficult to palpate for landmark identification.[3]

With the advent of portable and affordable ultrasound

1. Dr. Gentle Sunder Shrestha, Intensivist and Anaesthesiologist, Department of Anaesthesiology, Institute Of Medicine, Tribhuvan University Teaching Hospital, Kathmandu;
2. Dr. Sabin Koirala, Anaesthesiologist, Department of Anaesthesiology and Critical Care, Grande International Hospital, Kathmandu;
3. Dr. Arjun Gurung, Anaesthesiologist, Department of Anaesthesiology, Institute Of Medicine, Tribhuvan University Teaching Hospital, Kathmandu;
4. Dr. Prakash Chand, Medical Officer, Department of Critical Care Medicine, Alka Hospital Pvt Ltd, Jawalakhel, Lalitpur, Nepal.

Corresponding Author:

Dr. Gentle Sunder Shrestha
Intensivist and Anaesthesiologist
MBBS, MD Anaesthesiology, FACC, EDIC, FCCP
Lecturer, Department of Anaesthesiology,
Tribhuvan University Teaching Hospital, Institute Of Medicine,
Maharajgunj, Kathmandu, Nepal
Email: gentlesunder@hotmail.com
Phone: +977-9841248584

machines, the availability and the possibility to procure ultrasound machine in ICUs of even the resource limited settings is becoming more realistic. The demand for blood products is ever increasing, making timely procurement of blood products to correct coagulopathy a bigger challenge in resource limited places. We planned this prospective observational study to evaluate the safety of ultrasound guided emergency cannulation of internal jugular vein in coagulopathic adult patients when there is inadequate time for correction of coagulopathy for safe cannulation and when the demand for central venous access appears to outweigh the risk.

Subjects and Methods:

Adult subjects admitted in the intensive care unit undergoing emergency cannulation of internal jugular vein under real time ultrasonographic guidance with platelet count less than 50,000/cu mm and/or international normalized ratio (INR) more than 1.5 were enrolled in the study after obtaining a written informed consent. Patients with coagulopathy and semi-emergent indication for central venous cannulation, when there is time for correction of coagulopathy, were excluded from study.

All patients had cannulation of the internal jugular performed using the Seldinger technique. Subjects were placed in a head down position with the head turned slightly to the side opposite to that of cannulation. The skin of the anterior and lateral neck was prepared using antiseptic solution and draped. The ultrasound probe used was a 6-10 L38 MHz linear transducer SonoSite turbo unit (SonoSite®, Micromaxx, Bothwell, WA, USA). The probe was covered with a sterile sheath and sterile ultrasound gel was applied to the inside of the sheath. Each cannulation was performed by an experienced anaesthesiologist with a minimum of 3 years of experience in cannulation of central veins and a minimum of 100 ultrasound guided cannulations of internal jugular vein. Following information were recorded: indication for central venous cannulation, platelet count, prothrombin time, INR, side of internal jugular vein cannulated, mechanical ventilation status of the patient, diameter of internal jugular vein (mm), margin of safety (mm), number of attempts, approach (short / long axis) and success of cannulation.

Margin of safety was the distance between midpoint of internal jugular vein and the lateral border of carotid artery. Diameter of internal jugular vein and margin of safety were measured at the same level and in the same head position of the patient as during cannulation.

A short axis image of the internal jugular vein was obtained by placing the transducer in a transverse orientation on the patient's neck at the level of the cricoid cartilage. The needle was inserted at 60 degrees to the vertical and advanced toward the vein employing gentle aspiration on the attached syringe. Entry to the vein was confirmed by visualizing indentation of the anterior wall of the vein followed by blood in the syringe and by visualising the tip of the needle inside the vein. Confirmation of guide wire placement was performed by scanning the vein in both short and long axis planes.

Complications if present were recorded and were categorized as major or minor. Complications like carotid puncture, carotid cannulation, pneumothorax, haemothorax, haemodynamically significant or life threatening bleeding and airway compromise attributable to bleeding were categorized as major complications. Superficial haematoma either visible or palpable and superficial oozing from cannula site were categorized as minor complications.

Results:

A total of 25 cases were enrolled in the study. Technical success was achieved in all the cases. The mean INR of patients having minor complications (provided that platelet count > 50000/cu mm) was found to be 3.07 with 95% CI of 2.37-3.77 (Table 1). The mean platelet count of patients having minor complications (provided that the INR<1.50) was found to be 27428/cu mm with 95% CI being 19428-36000/cu mm (Table 2). None of the patients had the combination of platelet count less than 50000/cu mm and INR more than 1.50. Margin of safety was found to be related to the occurrence of minor complications and the association was statistically significant (Table 3 and 4). Number of attempts for cannulation was found to be associated with the occurrence of minor complications and the association was statistically significant (Table 5 and 6). Major complications such as carotid puncture, pneumothorax, hemothorax, hemodynamically significant bleeding or airway compromise were not reported during the study regardless of platelet count, INR, safety of margin or number of attempts.

Discussion:

Cannulation of a large central vein is the standard clinical method for monitoring central venous pressure and is also performed for a number of additional therapeutic interventions, such as providing secure vascular access for the administration of vasoactive drugs or to initiate rapid fluid resuscitation. Frequently, the central venous location is the only site available for intravenous access.[4] Due to the spectrum of usage of the central venous catheter, its requirement is increasing in medical practice. Sometimes coagulation disorders are present in patients with indication of central venous cannulation. Coagulation disorders pose a challenge as there are increased chances of complications like hemorrhage from the insertion site, hematoma formation and hemothorax. Usually, correction of coagulopathy is sought before the procedure. However, it is unclear whether fresh frozen plasma (FFP), platelet concentrate or platelet rich plasma (PRP) should be administered prior to attempted catheterization when coagulopathy is not severe. Although correction of coagulopathy may be possible, it may not be beneficial, it may be impossible to administer the corrective transfusion factor owing to lack of venous access or the condition may not be correctable by transfusion alone.[5]

Each year several million units of fresh-frozen plasma (FFP) are transfused all over the world. Recent data demonstrate that annual FFP usage has been steadily rising. Much of the plasma that is administered is used for the purpose of correcting coagulopathy before performing an invasive

diagnostic procedure. This practice appears to be common despite the fact that most consensus guidelines do not recommend FFP for this indication when the coagulopathy is not severe. This practice exposes patients to the complications associated with transfusion of blood products and is costly. Furthermore, it promotes the use of pre-procedural laboratory testing, which also has costs and may unnecessarily delay the procedures. It can also lead to fluid overload in certain group of patients. The supposition underlying these transfusions is that even a mildly elevated INR is associated with excessive bleeding in the setting of an invasive procedure and that an intervention is needed for safety.[6] In our study we came across no major complication in any of the cases with coagulopathy. Occurrence of minor complications was significant when the INR was more than 3 in patients with platelet count more than 50,000.

The mean platelet count of patients having minor complications (provided that the INR<1.50) was found to be 27428 (95% CI: 19428-36000). In our study we found that minor complications were significant when the platelets count was below 27,000 in presence of normal INR. Doerfler et al also had similar results. They have mentioned that central venous cannulation can be done safely by a skilled clinician even in patients with hemostasis problems and complications were encountered only when the platelet count was below 6000.[7] Slichter et al suggested that attention should be focused on providing aggressive platelet therapy for active bleeding rather than transfusing platelets prophylactically. Therapeutic platelet transfusions have been documented to control bleeding, and mortality rates are not increased when comparing patients receiving therapeutic to that seen in patients receiving prophylactic platelet transfusions.[8] Zeidler et al have mentioned that the risk of non-severe bleeding was increased only in patients with platelet counts below 20000, but not with platelet counts between 20000 and 49000. They have suggested pre-procedural platelet transfusions only in patients with platelet counts below 20000.[9] Weigand et al have also concluded from their study that transfusion of blood products prior to CVC insertion is not necessary in most cases. A delay of CVC insertion waiting for blood products seems to be unjustified, particularly in view of complication rates.[10] Another study has concluded that ultrasound guided central venous cannulation in patients with liver disease and coagulopathy is a safe and is a highly successful modality. In their study, mean INR was 2.17 ± 1.16 whereas median platelet count was 149.5 (range 12-683) × 10^9/L. No major vascular or non-vascular complications were recorded in their patients.[11] Another study has also questioned the prophylactic plasma and platelet transfusion in the critically ill patient. They have suggested thromboelastometry based restrictive transfusion management may reduce unnecessary plasma and platelet transfusion, and might reduce the incidence of transfusion-related adverse events and transfusion-associated hospital costs.[12]

Availability of compact portable ultrasound has been a boon for the anesthesiologist/intensivist facilitating bed side ultrasonography by the non-radiologist. Point of care ultrasound (POCUS) is rapid, accurate, repeatable, inexpensive, noninvasive and without the risk of radiation and thus has became an extension of the clinical examination. The use of POCUS ranges from various bedside diagnostic utility to facilitate real time guidance for central venous cannulation.[13] Some studies show that despite a strong level of evidence and recommendations for using ultrasound guidance during CVC placement and availability of USG in all the units, only half of CVC insertions were ultrasound-guided. They concluded that compliance with this recommendation needs to be improved.[14] POCUS should be included in the teaching courses of residents in anesthesiology and critical care. On the basis of our study, the usual practice of pre-procedural correction of coagulopathy can be questioned. However, being a pilot study, our study has the limitation of enrolling only a small number of patients. Larger multi-centric studies need to be performed to test the validity of the findings of this small study.

To conclude, urgent central venous cannulation may be safely performed by an experienced anesthesiologist /intensivist using sonography in coagulopathic critically ill patients.

Tables:

Table 1. INR of patients having minor complications provided the platelet count is more than 50,000/cumm

		95% Confidence Interval	
		Lower	Upper
Mean	3.07	2.37	3.77
Median	2.90	2.10	4.20
Std. Deviation	1.06	0.46	1.21
Minimum	2.10		
Maximum	4.20		
Range	2.10		

Table 2. Platelet count of patients having minor complications provided the INR is less than 1.50

		95% Confidence Interval	
		Lower	Upper
Mean	27428.57	19428.57	36000.00
Median	24000.00	15000.00	40000.00
Std. Deviation	12380.86	7181.32	14466.71
Minimum	12000.00		
Maximum	40000.00		
Range	28000.00		

Table 3. Relationship between margin of safety and occurrence of minor complications:

			Minor Complications		Total
			No	Yes	
Margin of safety (mm)	≤ 7	Number of patients	4	9	13
		% within minor complications	30.8%	75.0%	52.0%
	> 7	Number of patients	9	3	12
		% within minor complications	69.2%	25.0%	48.0%

Table 4. Statistical significance between margin of safety and occurrence of minor complications:

	Value	Asymptotic Significance (2-sided)
Pearson Chi-Square	4.891	0.027

Table 5. Relationship between number of attempts and occurrence of minor complications:

			Minor Complications		Total
			No	Yes	
Number of attempts	1	Number of patients	12	6	18
		% within minor complications	92.3%	50.0%	72.0%
	2	Number of patients	1	6	7
		% within minor complications	7.7%	50.0%	28.0%

Table 6. Statistical significance between number of attempts and occurrence of minor complications:

	Value	Asymptotic Significance (2-sided)
Pearson Chi-Square	5.540	0.019

Acknowledgement:

None

Conflict of Interest:

None

References:

1. Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC. Clinical anesthesia. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009.
2. Reusz G, Langer C, Egervari G, Sarkany P, Csomos A. Safety of ultrasound-guided central venous access in critically ill patients with uncorrected coagulopathy. Critical Care 2013;17(Suppl 2):P173.
3. Agarwal A, Singh DK, Singh AP. Ultrasonography: a novel approach to central venous cannulation. Indian J Crit Care Med 2009;13:213-6.
4. Miller RD, Eriksson LI, Fliesher LA, Wiener-Kronish JP, Young WL. Miller's Anesthesia. 7th ed. Philadelphia: Churchill Livingstone; 2009
5. Mumtaz H, Williams V, Hauer-Jensen M, Rowe M, Henry-Tillman RS, Heaton K et al. Central venous catheter placement in patients with disorders of hemostasis. Am J Surg 2000;180:503-5.
6. Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. Transfusion 2005;45:1413-25.
7. Doerfler ME, Kaufman B, Goldenberg AS. Central venous catheter placement in patients with disorders of hemostasis. Chest 1996;110:185-8.
8. Slichter SJ. Relationship between platelet count and bleeding risk in thrombocytopenic patients.Transfus Med Rev 2004;18:153-67.
9. Zeidler K, Arn K, Senn O, Schanz U, Stussi G. Optimal preprocedural platelet transfusion threshold for central venous catheter insertions in patients with thrombocytopenia. Transfusion 2011;51:2269-76.
10. Weigand K, Encke J, Meyer FJ, Hinkel UP, Munder M, Stremmel W et al. Low levels of prothrombin time (INR) and platelets do not increase the risk of significant bleeding when placing central venous catheters. Med Klin (Munich) 2009;104:331–5.
11. Singh SA, Sharma S, Singh A, Singh AK, Sharma U, Bhadoria AS. The safety of ultrasound guided central venous cannulation in patients with liver disease. Saudi J Anaesth 2015;9:155–60.
12. Gorlinger K, Saner FH.Prophylactic plasma and platelet transfusion in the critically ill patient:just useless and expensive or even harmful? BMC Anesthesiol 2015;15:86.
13. Abu-Zidan FM. Point-of-care ultrasound in critically ill patients: Where do we stand? J Emerg Trauma Shock 2012;5:70–1.
14. Zieleskiewicz L, Muller L, Lakhal K, Meresse Z, Arbelot C, Bertrand PM et al. Point-of-care ultrasound in intensive care units: assessment of 1073 procedures in a multicentric, prospective, observational study. Intensive Care Med 2015;41:1638–47.

Bangladesh Crit Care J September 2017; 5 (2): 97-100

Original Article

Echocardiographic assessment of cardiac dysfunction in maintenance hemodialysis patients

Md Zahid Alam[1], Mohammad Zakir Hossain[2]

Abstract

Background and Objectives: *The hemodialysis (HD) procedure may acutely induce regional left ventricular systolic dysfunction. This study evaluated the echocardiographic parameters in patients with End Stage Renal Disease (ESRD) on HD and to correlate those with clinical findings, more specifically to see whether there is any change in ejection fraction (EF) by developing new regional wall motion abnormality (RWMA) after hemodialysis, and to correlate these changes with the symptoms & hemodynamic condition of the patients.*

Methodology: *This prospective observational study was carried on a total of 100 adult ambulant patients with end stage renal disease (ESRD) on maintenance hemodialysis in the department of Hemodialysis, BIRDEM General Hospital, Shahbag, Dhaka. Their echocardiogram was done 30 min before and after the hemodialysis.*

Result: *It was revealed that majority of the patients were above 60 years (39%), and male to female ratio of about 3:2. The study subjects had diabetes mellitus (79%), hypertension (96%), dyslipidemia (42%), and family history of ischemic heart disease (24%). Chest pain and breathlessness were present in 31% and 42% subjects respectively before hemodialysis. Palpitation (23%), dizziness (19%), oedema (43%) and raised JVP (15%) were seen in the study subjects. Mean (±SD) serum creatinine level was 9.38 (±2.22) mg/dl and hemoglobin level was 9.0 (±1.08) g/dl. Ejection fraction (EF) before hemodialysis were ≥55, 40-54 & 30-39 in 62%, 34% and 4% study subjects respectively and after hemodialysis it was ≥55, 40-54 & 30-39 in 44%, 46% and 10% study subjects respectively. After HD, left ventricular failure (LVF) occurred in 32% subjects. HD-induced regional left ventricular systolic dysfunction occurred in total 36 patients (36%) and total 14 (14%) patients developed LVF 30 minutes after dialysis. Patients with hemodialysis-induced left ventricular systolic dysfunction were more in those who had worse predialysis EF. Blood pressure, heart rate, chest pain, palpitation, raised Jugular Venous Pressure (JVP) and edema did not differ significantly before and after hemodialysis. Simple regression analysis revealed that the hemodialysis procedure significantly ($P<0.05$) induce regional left ventricular systolic dysfunction.*

Conclusions: *HD acutely induces regional wall motion abnormalities in a significant proportion of patients. It occurs within 30 min after hemodialysis and is not related to changes in blood pressure, heart rate, JVP and oedema.*

Key words: *Hemodialysis (HD), Ejection fraction (EF), End Stage Renal disease (ESRD).*

Introduction:

Chronic kidney disease (CKD) is a worldwide public health problem.[1] CKD may culminate into renal failure which requires treatment with dialysis or transplantation - the most visible outcome of CKD. However, ischemic heart disease (IHD) is also frequently associated with CKD, which is important because individuals with CKD are more likely to die of IHD than to develop kidney failure.[2,3] IHD in CKD is treatable and potentially preventable, and CKD appears to be a risk factor for IHD. Dialysis patients with ischemic heart disease may not necessarily have large-vessel coronary disease. Patients may have ischemia secondary to the combined effects of volume overload and left ventricular hypertrophy (LVH), which causes increased oxygen demand, and small vessel coronary disease, which causes decreased oxygen supply. Patients with CKD also have a high prevalence of arteriosclerosis and remodeling of large arteries.[4] Remodeling may be due to either pressure overload, which is distinguished by wall hypertrophy and an increased wall-to-lumen ratio, or flow overload, which is characterized by a proportional increase in arterial diameter and wall thickness.[3] Patients with CKD also have a high prevalence of cardiomyopathy. [5] Hypertension and arteriosclerosis result in pressure overload and lead to concentric LVH (increased wall-to-lumen ratio), whereas anemia, fluid overload, and arteriovenous fistulas result in volume overload and primarily lead to left ventricular dilatation with LVH. These structural abnormalities may lead to diastolic and systolic dysfunction and may be detectable by echocardiography. Clinical presentations of cardiomyopathy include heart failure and ischemic heart disease, even in the absence of arterial vascular

1. Dr. Md Zahid Alam, FCPS (Medicine), Associate Professor, Dept of Cardiology, BIRDEM General Hospital, Shahbag, Dhaka-1000

2. Dr. Mohammad Zakir Hossain. Senior Medical Officer, Dept of Hemodialysis, BIRDEM General Hospital, Shahbag, Dhaka-1000

Corresponding Author:

Dr. Md Zahid Alam
Associate Professor
Dept of Cardiology
BIRDEM General Hospital, Shahbag, Dhaka-1000
email: ilazybear@yahoo.com

disease.[3] Cardiac failure develops in as many as 25 to 50% of HD patients and confers a dramatic reduction in probability of survival.[6] In addition, a significant percentage of cardiac mortality is due to sudden death,[7] which seems to be temporarily related to the dialysis procedure.[8] Myocardial ischemia may be precipitated by HD; a variety of studies have confirmed dialysis-induced myocardial ischemia.[9] Short intermittent HD treatments exert significant hemodynamic effects, and 20 to 30% of treatments are complicated by intradialytic hypotension.[6]

Echocardiography is a non-invasive diagnostic technique which provides information regarding cardiac function and hemodynamics. In clinical practice, visual (eye ball) assessment via Two-Dimensional (2D) Echocardiography provides a rapid evaluation of regional systolic function.[10] Determining the spectrum of echocardiographic abnormalities in these patients can change our vision in prevention of mortality in this group of chronically ill patients. In this study, we assessed the effects of hemodialysis on global and regional LV systolic function by serial echocardiography before and after dialysis using the routine systolic measurements for clinical practice that are recommended by the American Society of Echocardiography.[11]

Materials and methods

This prospective observational study was carried out to evaluate 100 adult subjects of known ESRD on maintenence hemodialysis in hemodialysis unit of BIRDEM General Hospital, Shahbag, Dhaka with the general objective to determine the echocardiographic parameters in patients with ESRD on haemodialysis and to correlate those with clinical findings. All ambulent adult patients (above 18 years of age) of both sex on maintainance HD (both twice or thrice weekly dialysis schedule) attending in hemodialysis unit. We excluded those patients who were irregular and less than three months on maintenance HD, not willing to be included in the study, and known psychiatric cases. The objective of the study was discussed in details with the patients or their attendants before their decision to enroll themselves into the study and written consent was taken. Clinical examination, relevant biochemical tests and Echocardiography were done and data collected in a pre-designed structured data collection sheets. Echocardiography was done before and after hemodialysis. Echocardiogram was done by a single cardiologist to avoid subjective variation of RWMA and EF. Demographic information was prospectively recorded and substantiated by means of inspection of medical record. Information included was the subject's age, gender, medical and clinical history, followed by conduction of the study. All the relevant collected data were compiled on a master chart first. Then organized by using scientific calculated and standard statistical formulas, percentage was calculated to find out the proportion of the findings. Data entry and analysis were done using SPSS for windows version 17.0. Output of data and graphical representation was done using Microsoft Office chart and Microsoft-Word. *p*-value was considered as significant when it was <0.05. The results were presented in tables, figures, diagrams etc.

Results

All subjects under experiment (n=100) were divided into age, sex, associated risk factors, and presenting clinical features.

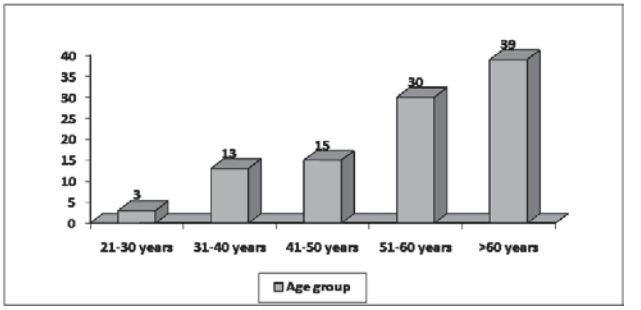


Figure 1: Age group distribution of the study subjects

It was shown in our study that majority of the patients were above 60 years of age (figure 1) and among the study subjects, 59% were male and the rest 41% were female.

The study subjects had hypertension (96%), diabetes mellitus (79%), dyslipidaemia (42%), family history of IHD (24%), tobacco intake (21%), and alcohol intake (2%) as pre-existing risk factors of IHD. *p*- value was achieved by ANOVA test and was considered as significant when it was less than 0.05. No significant difference was observed between male and female.

Presenting complaints were chest pain (31%), breathlessness (42%), cough (44%), dizziness (19%), and palpitation (23%). Sixty five percent subjects were anaemic. Forty three percent subjects had generalized edema. Raised JVP was observed in fifteen percent subjects. Dehydration was present in six percent subjects. Cyanosis was absent in all subjects. *p*-value was achieved by ANOVA test and was considered as significant when it was less than 0.05. No significant difference was observed among the different age or sex groups. Mean (±SD) baseline hemoglobin of the study population was 9.0(±1.08) g/dl, creatinine was 9.38 (±2.22) mg/dl, and blood urea was 102.18(±70.07).

Table I: EF before and after hemodialysis

Ejection fraction (%)	Before hemodialysis (Frequency/percent)	After hemodialysis (Frequency/percent)
≥55	62%	44%
40- 54	34%	46%
30-39	4%	10%

Table II: Effect of hemodialysis on cardiovascular status

Cardiovascular status	Frequency	Percent
As before	42	42.0
Improved	40	40.0
Deteriorated	18	18.0
Total	100	100.0

Discussion

In this study, we found that LV regional systolic dysfunction developed after hemodialysis in about one-third of patients (36%). Hemodialysis-induced regional LV systolic dysfunction and thus reduction of EF was mostly associated with pre-existent LV dysfunction, but it was not associated with age, sex or baseline renal status, ie, predialysis serum creatinine and blood urea level. The present study confirms earlier observations that hemodialysis may acutely induce regional LV dysfunction in a substantial proportion of patients.[12-14]The reason of almost similar type of result can be explained by the nature of the study population: our study population had diabetes, background cardiovascular history, and some of them had pre-existing LV systolic dysfunction like previous study. However, some previous studies showed a lower incidence of HD-induced reduction of EF.[15,16] It can be explained by the absence of diabetes and pre-existing cardiac disease in their study population. A second explanation might be the difference in the method used for the evaluation of regional LV systolic dysfunction. We used standard echocardiographic evaluation of regional LV function according to the guidelines of the American Society of Echocardiography,[11] which is validated for routine clinical application.

Some previous studies,[17,18] however, showed that almost all the post-dialysis patients developed significant LV systolic dysfunction (ie reduced EF). The main reason of this finding is that they used PET (Positron Emission Tomography) to detect HD-induced cardiac ischemia. PET – a nuclear machine which detects the metabolic process of the body, is no doubt, a better tool than conventional echocardiography to detect very minor ischemia.[18]

Univariate analysis suggested that traditional risk factors such as diabetes and previous history of CVD are related to a higher risk of cardiovascular events. On the other hand, age, smoking, and hypercholesterolemia were not risk factors for the occurrence of cardiovascular outcome. Although some studies showed a higher prevalence of traditional risk factors in the population with CKD than in the general population,[19] high rates of cardiovascular complications have not been fully explained by such risk factors.[20,21] Additionally, factors known to be non-traditional, such as anaemia, malnutrition, inflammatory state, alterations in calcium-phosphorus product, among others, have been implicated as independent factors associated with cardiovascular complications in dialysis patients.[22-25] In our study, however, these factors did not correlate with the adverse cardiac outcome, because variables in our study are limited to only HD-induced change in EF .

An important limitation of this study is the lack of angiographic evaluation of coronary arteries and therefore, the inability to correlate the echocardiographic findings with underlying coronary artery disease. This limitation should be considered in future studies on the effect of hemodialysis on LV function. A second limitation is the lack of a validated echocardiographic definition of HD-induced regional LV systolic dysfunction. In this study, hemodialysis-induced LV systolic dysfunction was defined as an increase in wall motion abnormality in two or more LV segments compared with predialysis. The use of other cutoff values would have influenced the prevalence of this entity as well as its association with outcome, because survival decreased with an increasing number of segments developing abnormal function during hemodialysis.

Another two limitations are, whether the reduction of EF was during or after HD was not certain. Because one study showed that reduction of EF was different during different time of HD and mostly occurred during early phase of HD.[15] However, some studies showed that repeated HD may improve LV dysfunction over time.[26,27] As our study was only two-session study, our study did not support this finding.

However, our study has several strengths. First, compared to recent trials, this study is much larger study that evaluated the acute effect of hemodialysis on LV global and regional systolic function. Second, we used routine and clinically applicable echocardiographic methods to evaluate global and regional LV systolic function. Third, the echocardiographic analysis of regional LV systolic function was performed by a single technician who was blinded to the order of echocardiography studies.

References :

1. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. US Renal Data System, USRDS 1998 Annual Data Report. Bethesda M: 1998. Available at: http://www.usrds.org/adr_1998.htm. Accessed September 12, 2003.
2. Shulman NB, Ford CE, Hall WD. Prognostic value of serum creatinine and effect of treatment of hypertension on renal function: results from the hypertension detection and follow-up program. The Hypertension Detection and Follow-up Program Cooperative Group. Hypertension 1989;13(S5):I80–93.
3. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh j, Culleton B, Hamm LL, et al. Kidney Disease as a Risk Factor for Development of Cardiovascular Disease. A Statement From the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation 2003;108:2154-69.
4. London GM, Marchais SJ, Guerin AP, Metivier F, Adda H. Arterial structure and function in end-stage renal disease. Nephrol Dial Transplant 2002;17:1713–24.
5. Foley RN, Parfrey PS, Harnett JD, Kent GM, Martin CJ, Murray DC, et al. Clinical and echocardiographic disease in patients starting end stage renal disease therapy. Kidney Int 1995;47:186–92.
6. Harnett JD, Foley RN, Kent GM, Barre PE, Murray D, Parfrey PS. Congestive heart failure in dialysis patients: Prevalence, incidence, prognosis and risk factors. Kidney Int 1995;47: 884–90.
7. Bleyer AJ, Russell GB, Satko SG. Sudden and cardiac death rates in hemodialysis patients. Kidney Int 1999;55:1553–9.
8. Bleyer AJ, Hartman J, Brannon PC, Reeves-Daniel A, Satko SG, Russell G. Characteristics of sudden death in hemodialysis patients. Kidney Int 2006;69:2268–73.
9. Selby NM, McIntyre CW. The acute cardiac effects of dialysis. Semin Dial 2007;20:220–8.

10. Esmaeilzadeh M, Parsaee M, Maleki M. The role of echocardiography in coronary artery disease and acute myocardial infarction. J Tehran Heart Cent 2013; 8(1): 1–13.

11. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography: Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18: 1440–63.

12. Dasselaar JJ, Slart RH, Knip M, Pruim J, Tio RA, McIntyre CW, et al. Haemodialysis is associated with apronounced fall in myocardial perfusion. Nephrol Dial Transplant 2009; 24: 604–10.

13. McIntyre CW, Burton JO, Selby NM, Leccisotti L, Korsheed S, Baker CS, et al. Hemodialysis-induced cardiac dysfunctionis associated with an acute reduction in global and segmental myocardial blood flow. Clin J Am Soc Nephrol 2008; 3: 19–26.

14. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysisinduced repetitive myocardial injury results in global and segmental reduction in systolic cardiac function. Clin J Am SocNephrol 2009; 4: 1925–31.

15. Assa S, Hummel YM, Voors AA, Kuipers J, Westerhuis R, de Jong PE, et al. Hemodialysis-Induced Regional Left Ventricular SystolicDysfunction: Prevalence, Patient and DialysisTreatment-Related Factors, and Prognostic Significance. Clin J Am Soc Nephrol 2012; 7: 1615–23.

16. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysisinduced cardiac injury: Determinants and associatedoutcomes.Clin J Am Soc Nephrol 2009; 4: 914–20

17. McIntyre CW, Burton JO, Selby NM, Leccisotti L, Korsheed S, Baker CSR, et al. Hemodialysis-Induced Cardiac Dysfunction Is Associated with an Acute Reduction in Global and SegmentalMyocardial Blood Flow. Clin J Am Soc Nephrol 2008;3:19–26.

18. Siqueira TMA, Ferreira PAM, Monteiro FC, Filho NS, Ferreira ASP, Neto ES, et al. Echocardiographic Parameters as Cardiovascular Event Predictors in Hemodialysis Patients. Arq Bras Cardiol 2012; 99(2): 714-23.

19. Longenecker JC, Coresh J, Powe NR, Levey AS, Fink NE, Martin A, et al.Traditional cardiovascular disease risk factors in dialysispatients comparedwith the general population: the CHOICE Study. J Am Soc Nephrol 2002; 13(7): 1918-27.

20. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovasculardisease in chronic renal disease. Am J Kidney Dis 1998; 32: S112-9.

21. Zoccali C, Mallamaci F, Tripepi G. Novel cardiovascular risk factors in endstage renal disease.J Am Soc Nephrol 2004; 15: S77-80.

22. Weiner DE, Tighiouart H, Vlagopoulos PT, Griffith JL, Salem DN, Levey AS, et al. Effects of anemia and left ventricular hypertrophy on cardiovascular disease in patients with chronic kidney disease. J Am Soc Nephrol 2005;16(6): 1803-10.

23. Kakiya R, Shoji T, Tsujimoto Y, Tatsumi N, Hatsuda S, Shinohara K, et al. Bodyfat mass and lean mass as predictors of survival inhemodialysis patients.Kidney Int 2006; 70(3): 549-56.

24. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. A malnutritioninflammation score is correlated with morbidity and mortality inmaintenance hemodialysis patients. Am J Kidney Dis 2001; 38(6): 1251-63.

25. Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM. Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. J Am Soc Nephrol 2004; 15(8): 2208-18.

26. Yazdani I, Ahmed S, Yaqoob Z. Evaluation of the Effect of Haemodlalysis on Cardiac Dysfunction in Patients of Chronic Renal Failure**.** JPMA 1998; 48: 230-2.

27. Jefferies HJ, Virk B, Schiller B, Moran J, McIntyre CW. Frequent Hemodialysis Schedules Are Associated with Reduced Levels of Dialysis-induced Cardiac Injury (Myocardial Stunning). Clin J Am Soc Nephrol 2011; 6: 1326–32.

Bangladesh Crit Care J September 2017; 5 (2): 101-105

Original Article

Early Laparoscopic Cholecystectomy in acute cholecystitis and its sequlae: Experience in tertiary care hospital

Md. Ezharul Haque Ratan[1], Hasina Alam[2]

Abstract

Background: *Acutecholecystitis (AC) is a common surgical condition requiring emergency hospitalization. Traditionally, these patients were treated conservatively, followed by delayed surgery six weeks or longer after acute event has subsided. Recently, early emergency cholecystectomy at same admission is suggested. This has the advantage of reduced length of stay (LOS) in hospital without any significant increase in complication rate. Moreover, conservative management is not always successful. We are here, observing the feasibility of emergency cholecystectomy in practical setting.*

Method: *Between March 2008 and March 2017, 483 patients were admitted in a surgical unit of BIRDEM general hospital with the diagnosis of acute cholecystitis or its complications. The patients were assessed clinically with laboratory and imaging investigations. We planned early laparoscopic cholecystectomy (ELC) in all case, as soon as assessment and resuscitation were completed, irrespective of duration from symptom onset. Cases were analyzed for gender, age, operation time, volume of blood loss, conversion to open surgery, post-operative complication and length of hospital stay.*

Results: *A total of 483 patients with AC and its sequlae were admitted, between March 2008 and March 2017 in a single unit of a tertiary care hospital which deals most of the diabetic patients of the country. Among them 477 patients were treated with emergency or urgent laparoscopic cholecystectomy (LC). The earlier the patient presented for surgery and those who were treated with antibiotics were easier to operate. Incidence of gangrene and perforation were more among those with acalculus cholecystitis. Surgical procedures were the most difficult in those presented beyond two weeks of symptom onset. Consequently operation time was over 100 minutes and blood loss was more than 250ml in such cases. Fortunately none required conversion to open procedure. Subhepatic drain were used in 17 cases. Subcutaneous simple tube drain in umbilical port was used in those with gangrene, perforation and transmural gall bladder wall pyogenic infection. Consequently umbilical port infection were very low (3cases, 0.6%). One patient presented with subhepatic fluid collection, 6 weeks after emergency LC. Laparotomy was done and found to have altered blood and pseudo-aneurysm of cystic artery (chronic blood loss from one of its lateral twig). Length of stay (LOS) in hospital were short (mean-1.8days, range: 20hours-4 days) except those with bile leak (5, 8 and 9 days respectively). None of the cases had bile duct injury or uncontrolled bleeding. There was no mortality in this series.*

Conclusion: *Early laparoscopic cholecystectomy (ELC) has proved to be an effective and safe day case surgical procedure for AC and their complications. It provides much benefits with low complication and conversion in experienced hands.*

Key words: *Laparoscopic cholecystectomy (LC), Early laparoscopic cholecystectomy (ELC), Delayed laparoscopic cholecystectomy (DLC), Acute cholecystitis (AC), Length of stay (LOS)*

Introduction:

Acute cholecystitis (AC) and its complications remain among most common surgical condition which require emergency hospitalization. These patients are commonly treated initially non-operatively followed by delayed surgery six weeks or longer after acute event has subsided [1]. Recently, there has been significant paradigm shifts in management of such cases to early surgery at same admission with the advantage of reduced length of stay (LOS) in hospital while complications rate remain the same [2]. Moreover, conservative management is not always successful. About one fifth of the cases, who were waiting for delayed surgery, had persistent symptoms or developed another acute attack requiring intervention before planned operation [3].

Controversy persists regarding the optimal timing for intervention in AC. Some follow the policy of emergency surgery in 24-96 hours after onset of symptoms while others suggest early surgery in acute phase within 3 days after admission and still others define 'early' as ranging from 24hours to 7 days from diagnosis or onset of symptoms [4,5]. The Tokyo guidelines of the Japanese society of hepatobiliary

1. Dr. Md. Ezharul Haque Ratan, MS (General Surgery), Associate professor, Surgery, Ibrahim Medical College and BIRDEM General Hospital, Shahbagh, Dhaka-1000, Bangladesh

2. Dr. Hasina Alam, FCPS (General Surgery), Registrar, Surgery, Ibrahim Medical College and BIRDEM General Hospital, Shahbagh, Dhaka-1000, Bangladesh

Corresponding Author :

Dr. Md. Ezharul Haque Ratan, MS (General Surgery)
Associate professor, Surgery
Ibrahim Medical College and BIRDEM
Room no-445, BIRDEM General Hospital
Shahbagh, Dhaka-1000, Bangladesh
Tel-01711172547, Email- ezhar65@gmail.com

pancreatic surgery suggested that emergency cholecystectomy was indicated for patients with symptoms within 72 hours while that of the national institute for health and care excellence (NICE) recommended that AC should be treated within seven days of diagnosis[7].

While accepting early surgery for AC, consensus is still lacking regarding technical aspects, whether open or laparoscopic cholecystectomy is to be done. Considering presence of inflammation, oedema, necrosis and adhesion are unfavorable for safe dissection [2], 48.7% of AC are operated with the open technique. Some literature and Tokyo guideline 2013 have shown concern about supposedly higher mortality rates in emergency laparoscopic cholecystectomy (AL) in AC. According to some author, conversion rate to open procedure is also higher during LC in acute phase [8, 9]. On the other hand, some randomized controlled trials [10- 13] and meta-analysis[14-16] recommended acute phase LC with the advantage of fewer complications, less operative blood loss and shorter post-operative LOS[6]. Gonzalez Rodrigueg FJ et al considered urgent LC 72 hours after onset of symptoms to be difficult and associated with higher risk of complications[16]. While some studies found no difference in conversion rate, morbidity and LOS between patients with symptoms less or more than 72 hours.

Many of our patients present late due to financial or personal constrains, ignorance, fear of operation, delayed diagnosis, and getting treatment in another hospital. Delay also occurs due to failure of conservative management, recurrent symptoms before planned operation or due to optimization of medical condition for possible safe anaesthesia. Whatever may be the cause of delay, progressive inflammation may lead to complication like gangrene and perforation of the gallbladder and pericholecystic abscess formation compelling urgent surgery. The feasibility and safety of LC for AC and its sequelae 7 days after symptom onset in patients who were unable to receive earlier surgery are unclear. This retrospective study was aimed to observe the feasibility and safety of emergency and urgent LC in AC and its sequelae during persisting symptoms in same admission.

Materials and methods

Between March 2008 and March 2017, 483 patients were admitted in a surgical unit of BIRDEM general hospital with a diagnosis of acute cholecystectomy or its complications. The patients were assessed clinically (Murphy's sign or right upper quadrant abdominal pain or tenderness or mass & fever) with laboratory tests (leukocytosis, liver & pancreatic enzymes) and imaging (ultrasound examination and computed tomography in selected cases). Diagnostic and/or therapeutic endoscopic retrograde cholangiopancreatography (ERCP) was done in those with suspected biliary tree stone or pathology. We planned laparoscopic cholecystectomy in all cases as soon as assessment and resuscitation were completed irrespective of duration from symptom onset. Surgery was delayed in seven patients for five days after antiplatelet agent has stopped or for ERCP. Six patients were excluded from this study as their surgery was due to high risk for emergency surgery (poor general condition, cardiac function, renal function, or recent stroke). Emergency LC was done in rest of the patients (477), by a single attending surgeon using standard four port technique. Carbon dioxide was used for peritoneal insufflation maintaining a pressure between 10 and 12 mmHg. The gallbladder was decompressed by aspirating its contents. The cystic artery and duct were skeletonized and sealed using hem-o-lock individually. Cystic duct was ligated or transfixed with 1-0 vicryl in selected cases (wide and /or fragile). Saline irrigation was done in all cases. A subhepatic tube drain was placed in those with perforated or gangrenous cholecystitis or pericholecystic abscess. Gallbladder were removed through umbilical port. Those having gangrene, perforation, transmural infection or spillage of stone were placed in 'glove-bag' before removal. Histopathological examination of resected gall bladder was routinely performed to confirm acute cholecystitis. Cases were analyzed for gender, age, operation time, volume of blood loss, conversion to open surgery, post-operative complication and length of hospital stay. Operation time was defined as beginning with skin incision and ending when dressing has been placed over ports.

Results

A total of 483 patients with AC and its sequelae were admitted, between March 2008 and March 2017 in a single unit of a tertiary care hospital which deals most of the diabetic patients of the country. Among them 477 patients were treated with emergency or urgent laparoscopic cholecystectomy. As most of the cases were evaluated in emergency or outpatient department, preoperative hospital stay were only few hours for resuscitation except inpatient referred cases, those required ERCP,with acute pancreatitis or on anti-platelet drugs. Patients demographics are shown in Table I. The ASA scores of the patients were classified as 1E (n=81, 17%), 2E (n=181, 59%) and 3E (n=115, 24%). Table-2 shows clinical, imaging and laboratory characteristics of the patients. The patient numbers underwent LC on the days after symptom onset were as follows- 23 (day 0), 47 (day 1), 71 (day 2), 76 (day 3), 63 (day 4), 55 (day 5), 47 (day 6), 33 (day 7), 44 (day 8-14), 18 (day 15 and beyond). Operative findings of the patients are demonstrated in Table 3. The earlier the patient presented for surgery and those who were treated with antibiotics were easier to operate. Incidence of gangrene and perforation were more among those with acalculus cholecystitis. Among six patients with acute pancreatitis, two were in ICU for initial days of management and surgery were done one day after stepping down to ward or cabin. Surgical procedures were the most difficult in those presented beyond two weeks of symptom onset. Consequently operation time was over 100 minutes and blood loss was more than 250ml in such cases (Table 4). Fortunately none required conversion to open procedure. Subhepatic drain were used in 17 cases, most of which were removed 2-3 days postoperatively except three, who had bile leak due to total gangrene of gall bladder and cystic duct. Bile discharge dried up in 4th, 7th and 9th post-operative day respectively. Subcutaneous simple tube drain in umbilical port was used in those with gangrene,

perforation and transmural gall bladder wall pyogenic infection ; removed in first follow up on 7th post-operative day, consequently umbilical port infection were very low (3 cases, 0.6%). One patient presented with subhepatic fluid collection, 6 weeks after emergency LC. Laparotomy was done and found to have altered blood and pseudo-aneurysm of cystic artery (chronic blood loss from one of its lateral twig). Length of stay (LOS) in hospital were short (mean-1.8 days, range: 20 hours-4 days) except those with bile leak (5, 8 and 9 days respectively). None of the cases had bile duct injury or uncontrolled bleeding. There was no mortality in this series.

Discussion

Early LC (emergency, urgent, expedited) is a feasible treatment option in patients with AC [1].

Gall stone related complications develop in 1-4% of patients per year such as AC. Since pre-laparoscopic era early surgery has shown advantage in terms of hospital stay and reoperation time[2]. Modern trend is towards an increased rate of early laparoscopic cholecystectomy (ELC) for AC. But the exact time point of ELC in AC is still a matter of debate. Tokyo Guidelines 2013 preferred to perform LC within 72 hours of symptom onset[6], whereas NICE recommended LC in AC within 7 days of diagnosis[7]. Till now there is no published document on LC beyond 7 days of onset of AC. We have treated all of our patients (except 6 out of 483, 1.2%) who presented with AC or its sequelae irrespective of its severity, time of appearance from symptom onset and treatment received. All these cases were analyzed retrospectively for efficacy and safety of urgent LC during acute phase. We did not require any conversion during operation. Some author considered potentially serious complications and conversion rates were higher in early LC in AC[17, 18]. But facts are changing with time and expertise. A meta-analysis demonstrated a reduction in overall mortality rate with LC in AC performed in the same admission[2]. LC in late phase of AC (4-7 days) till 2004 was reported to have higher conversion rate to open surgery, while recent studies revealed equivalent hospital stay and lower conversion rate of 3% in early phase and 8% in late phase of AC[1]. In one of our study including all cases of LC, we found that chronic symptom in elderly male and fibrosed contracted GB at imaging (USG or CT scan) were independent predictors of procedure conversion during LC. They concluded that ELC in late phase is superior to delayed laparoscopic cholecystectomy (DLC)[6-8] weeks after AC subsided with conservative treatment. One study from UK demonstrated that a third of their patients were readmitted with recurrent symptoms often more than once while awaiting for DLC[7].

We operated most of our cases within 24 hours after admission. As expected, we found that severity of AC increases with time from its onset, thickening and hardening of GB wall leads to difficulty in handling and dissection with conventional instruments, neovascularization increased blood loss from adhesions associated GB surface. The sooner the LC is attempted, the easier and less time consuming with least bleeding - the procedure can be accomplished. Pericholecystic oedema creates an easy dissection plain especially in those who received antibiotics. These facts increased operation time but did not increase perioperative complication or hospital stay. Meta-analysis found that bile leak rate had no relation with technique (open or laparoscopy).Severity of bleeding in AC, treated either by open or laparoscopy, was not significantly different [2]. It also confirmed reduced mortality, morbidity and post-operative hospital stay without increasing the operation time,reduced operative haemorrhage rates, less expensive, and resulted in better quality of life when AC was treated with ELC compared to DLC. Patience, taking time in dissection, keeping operation field as clean as possible by taking care of 'first drop of blood', clear identification of structures of the region before division, use of telescope with an angle (we used 45^0)when needed, were important tricks in successful completion of LC in complicated AC cases.

One of our female patients required readmission and laparotomy, 6 weeks after ERCP followed by LC for common bile duct stone and AC, due to subhepatic fluid collection. Rest of our patients recovered without any intraabdominal consequences. Cases with gangrenous and perforated cholecystitis or per-operative tear of GB with spillage of stones were common in late presented cases which were managed with copious saline irrigation, removal of stone and GB in a 'glove-bag' and use of a subhepatic drain, hence outcome was not affected in terms of mortality or LOS in hospital. As we assessed most of our patients before admission, LOS in hospital was much less than other series. The total expenditure of treatment was not documented but a rough overview of cost involvement assessed. Other options of management of AC using antibiotics alone or in combination with percutaneous cholecystectomy followed by DLC were associated with no difference in operative time or conversion rate, but LOS, readmission and costs were higher than ELC [19]. Strength of the study is that all AC cases, fit and willing to undergo ELC were included, irrespective of severity and duration of disease onset. Weakness of the study is that it is a retrospective study.

Conclusion

Emergency and urgent laparoscopic cholecystectomy in acute cholecystitis and its sequlae appears to be effective and safe at any time during persisting symptoms. It has the benefit of minimum conversion rate, morbidity, mortality and short hospital stay. Technical difficulties of the procedure are proportional to the time of surgery since onset of the symptoms. The procedure in late presenting cases are associated with longer operation time and more blood loss without influencing operative complications.

However large randomized controlled trials are needed to draw a solid conclusion and firm recommendation.

Conflict of interest-None

Funding-None

Ethical approval-Not applicable

Table-I : Patients' Demographic

March 2008 - March 2017		
Total number of patients –		477
Gender–	Male –	181 (38%)
	Female	296 (62%)
Mean Age-	49.9 years (22-68 years)	

Table-II : Clinical, imaging and laboratory characteristics

Clinical features	No of patients
ASA 1E - 81(17%)	
2E - 181(59%)	
3E - 115 (24%)	
Time from onset of symptoms to admission	-8.2 (0.5-16) days
Murphy's sign/Right upper quadrant tenderness or mass	-396 (83%)
Tempurature (>37^0 C)	- 267(56%)
USG/CT/MRCP findings - Enlarged distended gall bladder	- 324(68%
-Wall thickness	- 3.6(2-8mm)
-Pericholecystic oedema	- 391((82%)
-Swollen oedematous pancreas	- 6 (1.3%)
-Abdominal fluid collection	- 6 (1.3%)
Leucocyte count	- 13,200 (6700 - 24300)/ cmm

Table-III : Operative findings

Findings	No of patients
Simple calculous acute cholecystitis	-405 (84.9%)
Acute cholecystitis with dense adhesion	-31 (6.5%)
Acalculous acute cholecystitis	-17 (3.5%)
Gangranous cholecystitis	-12 (2.5%)
Perforated cholecystitis	-06 (1.3%)
Gall stone with acute pancreatitis	-06 (1.3%)

Table-IV : Outcome of emergency laparoscopic cholecystectomy

Conversion to open surgery	nil
Operation time	68 (35-122) minutes
Blood loss	140 (10-350) ml
Use of sub-hepatic drain	19 (4%)
Use of umbilical port drain	54(11.3%)
Complications-	
Bile leakage	3(0.6%)
Sub-hepatic fluid collection	1(0.2%)
Wound infection (ports)	3(0.6%)
Length of stay in hospital	1.8days (20hours- 9 days)
Readmission for pain	1(0.2%)

References :

1. Christos S, Omar J, Rahul D, George Z, Nagy H, Emmanouil Z,Is early laparoscopic cholecystectomy for acute cholecystitis preferable to delayed surgery? IntJsurg(2012);10:250-8.
2. Federico C, Fausto C, Michele P, Federico G,Stefano F, Salomone DS et al, Open versus laparoscopic cholecystectomy in acute cholecystitis. Systematic review and meta-analysis. Int J Surg(2015); 18:196-204.
3. T. Siddiqui, A.MacDonald, P.S. Chong, J.T. Jenkins, Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis of randomized clinical trials. Am J Surg(2008);195:40-7.
4. Yamashita Y, Takada T, Kawarada Y, Nimura Y, HirotaM, Miura F et al. Surgical treatment of patients with acute cholecystitis :Tokyo guidelines. J HepatobiliaryPancreatSurg(2007);14:91-97.
5. Zhu MW, Gu XD, Xiang JB,Chen ZY. Comparison of clinical safety and outcomes of early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis. Scientific world journal(2014)
6. G. Shinke, T Noda, H. Hatano, J Shimizu, M. Hirota, A. Takata et al. Feasibitity and safety of urgent laparoscopic cholecystectomy for acute cholecystitis after 4 days from symptom onset. J Gastrointest Surg (2015);19:1787-93.
7. S Bokhari, U Walsh, K Qurashi, L Liasis, J Watfah, M Sen et al. Impact of dedicated emergency surgical unit on early laparoscopic cholecystectomy for acute cholecystitis. Ann R CollSurgEngL (2016);98:107-15.
8. S. Cheema, A.E. Brannigan, S.Johnson, P.V. Delaney, P.A Grace, Timing of laparoscopic cholecystectomy in acute cholecystitis.Ir J Med Sci(2003);172:128-31.
9. E.H.Livingston, R.V. Rege, A nationwide study of conversion from laparoscopic to open cholecystectomy. Am J Surg(2004);188:205-11.
10. Lo CM, Liu CL, Fan ST, Lai EC, Wong J, Prospective randomized study of early versus delayed Laparoscopic cholecystectomy for acute cholecystitis. Ann Surg(1998);227:461-7.

11. Laipb, Kwong KH, Leuug KL, Kwok SP, Chan AC, Chung SC, Lauv WY: Randomized trial of early versusdelayedlaparoscopic cholecystectomy for acute cholecystitis, Br J Surg (1998);85:764-7.

12. Chandler CF, Lane JS, Ferguson P, Thompson JE, Ashley SW. Prospective evaluation of early versus delayed laparoscopic cholecystectomy for treatment of acute cholecystitis. Am Surg(2000);66:896- 900.

13. Lua H, Lo CY, Patil NG, Yuen WK. Early versus delayed-interval laparoscopic cholecystectomy for acutecholecystitis:A meta-analysis. SurgEndos 2006;35:553-60.

14. Shikata S, NoguchiY, Fukui T. Early versus delayed cholecystectomy for acute cholecystitis:A meta- analysis of randomized controlled trials. Surg Today 2005;35:553-60.

15. Siddidui T, MacDonald A, Chong PS, Jenkins JT. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis:A meta-analysis of randomized clinical trials.Am J Surg 2008;195:40-7.

16. Gurusamy K, Samraj K, Gluud C, Wilson E, Davidson BR, Meta-analysis of randomized controlled trials on the safety and effectiveness of early versus delayed cholecystectomy for acute cholecystitis.Br J Surg 2010;97:141-50.

17. A. Cuschieri, F. Dubbins, J. Moulel,et al. The European experience with laparoscopic cholecystectomy.Am J Surg (1991);161:385-7.

18. C.K.Kum, P.M.Goh, J.R.Isaac, et al. Laparoscopic cholecystectomy for acute cholecystitis. Br J Surg(1994);81(11):1651-4.

19. Feza YK, Aydincan A, Mahir K, Ali H, YahyaE,Gokhan M. Emergency cholecystectomy vs percutaneous cholecystectomy plus delayed cholecystectomy for patients with acute cholecystitis.HepatobiliaryPancreat Dis Int (2014);13:316-22.

20. Gonzalez-Rodriguez FJ, Paredes-Cotore JP, PontonC,Rojo Y, Flores E, Luis-Calo ES et al. Early or delayed laparoscopic cholecystectomy in acute cholecystitis? Conclusions of a controlled trial. Hepatogastroenterology(2009);56:11-6.

21. Conlon K. The gallbladder and bile ducts. In Norman SW, Christopher JK Bulstrode, Ronan O'Connell . Bailey and Love's Short practice of surgery.26th edition. CRC Press: UK; 2013:1097-1117.

22. Danny Rosin,A comparison of laparoscopic cholecystectomy for acute cholecystitis both within and beyond 72hours of symptom onset during the emergency admission.World J Surg (2012);36:2659-60.

Bangladesh Crit Care J September 2017; 5 (2): 106-109

Original Article

Pattern of Dyslipidemia in different type of Myocardial Infarction

Md. Zahid Alam[1], Aparna Rahman[2], Shabnam Jahan Hoque[3], S.M. Rezaul Irfan[4], Md. Babul Miah[5], Mohammad Shakhawat Hossain[6]

Abstract

Background: *Dyslipidemia is one of the main risk factors with prognostic significance in relation to coronary heart disease. Aggressive treatment has been recommended in acute coronary syndrome (ACS). We examined pattern of dyslipidemia in ST Elevation myocardial infarction (STEMI) and Non- ST elevation myocardial infarction (NSTEMI). We also compare the lipid status in between two types of myocardial infarction (MI).*

Methods: *This cross sectional observational study was carried out enrolling 100 subjects with ST elevation and Non ST elevation Myocardial Infarction, in the Department of Cardiology, BIRDEM General Hospital, Shahbag, Dhaka, over a period of six months from January 2012 to June 2012. Fasting lipid profile was done in next morning of admission in both type of MI.*

Results: *Mean age and gender difference was significant between STEMI and NSTEMI. Mean Cholesterol (chol), Triglyceride (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) were not statistically significant between male and female groups. All mean cholesterol, TG, HDL, LDL were significantly high in older age group. The Mean cholesterol (220.7±28.1Vs208.4±20.9), triglyceride (182.8±34.4 Vs 147.4±28.9), HDL (35.14±5.7 Vs 41.65±3.8) and LDL (160.7±26.2 Vs148.3±16.8)were also statistically significant between STEMI and NSTEMI groups ($p<0.05$).*

Conclusion: *Dyslipidemia is the dominating coronary risk factors. It could be concluded that significant differences are observed between two types of MI. Lipid status is relatively more uncontrolled in ST elevated MI and must be managed with all possible therapeutic modules to minimize further complications.*

Key Words: *ST-segment Elevation Myocardial Infarction (STEMI), NSTEMI (Non-ST-segment Elevation Myocardial Infarction), Acute Coronary Syndrome (ACS), Myocardial Infarction (MI), Cholesterol, Triglyceride(TG), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL).*

Introduction:

Coronary artery disease (CAD) particularly myocardial infarction secondary to atherosclerosis of coronary arteries remains the leading cause of morbidity and mortality worldwide.[1] Atherosclerosis is a chronic, multifocal immuno-inflammatory; fibroproliferative disease of medium sized and large arteries mainly driven by lipid accumulation.[2] Elevated levels of total and low density lipoprotein cholesterol (TC and LDL-C),elevated levels of triglycerides (TG) and low levels of high density lipoprotein cholesterol(HDL-C) are important risk factors for CAD.[3] LDL-C is considered as 'bad cholesterol' since too high level of this cholesterol is associated with an increased risk of coronary artery disease and stroke.

The fundamental etiologic mechanism shared by all the forms of ACS is an imbalance between myocardial oxygen supply and demand. The most common cause of ACS is thrombus formation over a preexisting atherosclerotic plaque that has undergone disruption or erosion. [4] The contrasting scenario is for the thrombus to fully occlude the arterial lumen, resulting in an acute Q-wave myocardial infarction (commonly with ST elevation). Unstable angina (UA)/ NSTEMI primarily caused by a nonocclusive thrombus benefit from a treatment regimen including anti-thrombotic and antiplatelet agents.[5,6]

Methodology:

This prospective observational study was done in the Department of Cardiology, BIRDEM General Hospital, Shahbagh, Dhaka during the period of January 2012 to June 2012 with the general objective to assess the pattern of dyslipidemia in hospital patient with ST Elevation versus Non ST Elevation Myocardial Infarction. During the study period 100 consecutive subjects aged 25-75 years suffering from STEMI and NSTEMI who presented with chest discomfort, palpitation or shortness of breath with either ECG change(ST elevation / depression ,T wave changes) or raised Troponin I were enrolled. Patient with chronic stable angina, unstable angina, non-cardiac chest pain, congenital or valvular cases and shortness of breath for other than ischemic heart disease were excluded from our study. Study subjects were collected from admitted patient in CCU referred from emergency department and also from in-patient department of the respective discipline with acute coronary syndrome. We did fasting lipid profile in next morning of admission and assess the pattern and differences of all parameter of lipid in two types of MI. Dyslipidemia was considered according to ATP III guideline with Serum Total cholesterol > 200 mg/dl ,TG >150 mg/dl, LDL >100 mg/dl, HDL <40 mg/dl (male) and <50 mg/dl (female). Ethical permission was approved by appropriate authority. Data were analyzed using SPSS version 17.0 and p value <0.05 was considered as significant.

Results:

Age distribution of the study subjects (n=100)

100 consecutive patients were included in the study, of which 42 had STEMI and 58 had NSTEMI. The mean age and age distribution of the STEMI and NSTEMI groups were given in Table I.

Table I: Age distribution of the study

Age group (Years)	STEMI (n=42) n (%)	NSTEMI (n=58) n (%)	Statistical test
25-39	06 (14.3)	11 (19.0)	
40-49	08 (19.0)	14 (24.1)	
50-59	16 (38.1)	19 (32.8)	
60 and above	12 (28.6)	14 (24.1)	
Mean±SD	48.36±10.18	51.29±11.55	0.024
Age range	33-68	33-68	

Table II: Association between lipid profile with age (n=100)

Lipid profile	Age (years)				Statistical test
	25-39 (n=17)	40-49 (n=22)	50-59 (n=35)	≥60 (n=26)	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Cholesterol (mg/dl)	195.7±20.1	215±12.14	220±2.14	218±13.14	0.001
Triglyceride (mg/dl)	152.8±24.4	190±19.3	170±29.4	200±9.3	0.001
HDL (mg/dl)	37.14±2.9	33.14±1.7	31.4±2.3	39.14±1.7	0.001
LDL (mg/dl)	120.7±10.2	150.7±13.2	157±8.5	148±2.65	0.001

Gender distribution of the study subjects (n=100)

In STEMI group, male were 33% and 67% were female. In NSTEMI group, 43% subjects were male and 57% were female (Fig-I).The male female ratio 1:2 (STEMI) and 1:1.3 (NSTEMI).

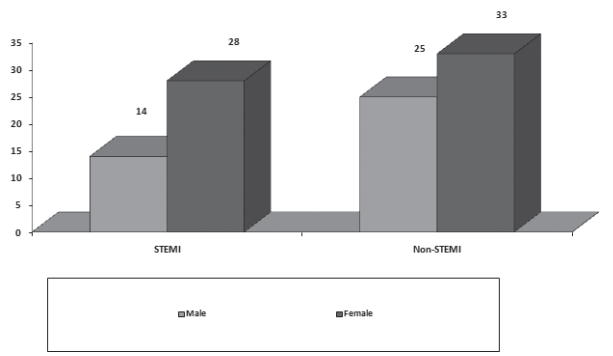


Figure I: Gender distribution of different MI

Association between lipid profile with sex (n=100)

Mean cholesterol, triglyceride, HDL and LDL were not statistically significant between male and female groups which are shown in Table III.

Table III: Association between lipid profile with sex

Lipid profile	Male (n=39) Mean±SD	Female (n=61) Mean±SD	Statistical test
Cholesterol (mg/dl)	209.2±28.1	218.7±21.3	0.058
Triglyceride (mg/dl)	167.8±35.1	174.3±30.1	0.326
HDL (mg/dl)	37.4±3.8	38.7±4.9	0.163
LDL (mg/dl)	152.3±18.2	159.1±24.2	0.136

Lipid profile of the study subjects (n=100)

Mean cholesterol, triglyceride, HDL and LDL were statistically significant between STEMI and NSTEMI groups.

Table IV: Lipid profile of the study subjects

Lipid profile	STEMI (n=42) Mean±SD	NSTEMI (n=58) Mean±SD	Statistical test
Cholesterol (mg/dl)	220.7±28.1	208.4±20.9	0.013
Triglyceride (mg/dl)	182.8±34.4	174.4±28.9	0.001
HDL (mg/dl)	35.14±5.7	41.65±3.8	0.001
LDL (mg/dl)	160.7±26.2	148.3±16.8	0.005
TC/HDL	6.2	5.0	-
TG/HDL	5.2	4.1	-

Discussion:

CAD is a complex and multifactorial process that manifests as stable angina, unstable angina or myocardial infarction. Myocardial infarction comprises a group of symptoms attributed to obstruction of the coronary arteries. Myocardial infarction usually consists of ST elevation myocardial ST elevation myocardial infarction and non ST elevation infarction and non ST elevation myocardial infarction[7]. Both myocardial infarction causes significant mortality and morbidity in acute onset as well as in chronic course of disease. The atherosclerotic process underlies each of these pathologies. Indeed, clinical symptomatology in CAD is frequently triggered by a thrombus formation on an eroded or ruptured atherosclerotic, lipid-rich plaque characterized by a thin fibrous cap.[8] With the aim to show pattern of lipid profile in patient with ST Elevated versus Non ST Elevated Myocardial Infarction this present study was carried enrolling 100 subjects in the Department of Cardiology, BIRDEM General Hospital, Dhaka. The findings of the study are discussed on basis of related previous study concerning the chief objective of the study.

In STEMI group, male were 33.3% and 66.7% were female. In non-STEMI group, 43.1% subjects were male and 56.7% were female. The difference was statistically significant between STEMI and NSTEMI. Other study findings[9,10] were comparable with the gender distribution of this present study. Mean total cholesterol (209.2±28.1 Vs 218.7±21.3), triglyceride (167.8±35.1 Vs 174.3±30.1), HDL (37.4±3.8 Vs 38.7±4.9) and LDL (152.3±18.2 Vs 159.1±24.2) were higher in female than male but statistically insignificant ($p>0.05$). Our results do not match with other study where these parameters (TC, TG, LDL) were higher in male than female. Addulla Abdelaziz et al also describe high level of HDL in female than male, which is consistent with our study.[11]

It was observed that mean age of STEMI and NSTEMI groups were 48.36±10.18 and 51.29±11.55 years respectively with an age range from 33 to 68 years. Majority of (38.1%, 32.8%) the respondents (STEMI vs NSTEMI) were found in the age group of 50-59. STEMI vs Non-STEMI subjects were found in 28.6% and 24.1% cases respectively above 60 years age group. Mean age difference was significant between STEMI and NSTEMI. Burazeri et al[12] found that mean age of the study subjects with STEMI was 59.1±8.7 years in their study.Mean ±SD of total cholesterole, HDL, LDLwere significantly high in 50-59 age group. Triglycerides was high in above 60 years age group. Differences of all parameter of lipid profile is statistically significant in diferrent age group.

Dyslipidemia, manifested by elevated levels of total and low density lipoprotein cholesterol, triglycerides (TC, LDL-C, TG), low levels of high density lipoprotein cholesterol (HDL-C) is an important risk factor for CAD. These were the common laboratory findings among the subjects with STEMI and NSTEMI.[14,15] Regarding pattern of dyslipidemia in our study [table IV], we found that high levels of TC (more than 200mg/dl), LDL (more than 130 mg/dl) ,TG (more than 150 mg/dl) were found in both STEMI and NSTEMI patients. Low levels of HDL (less than 40 mg/dl) were also found in both types of MI. Our results also revealed that the TC/HDL ratio was more than five (TC/HDL>5) and TG/HDL ratio was more than four (TG/HDL>4) in both groups. According to the American Heart Association, the goal is to keep TC/HDL ratio < 5 and TG/HDL <4. A higher ratios indicates a higher risk of heart disease; a lower ratio indicates a lower risk. Our results also revealed that there was significant difference of lipid parameter between patients with STEMI and NSTEMI.

1. Dr. Md. Zahid Alam, FCPS (Medicine), Associate Professor, Department of Cardiology, BIRDEM General Hospital, Shahbag, Dhaka.
2. Dr. Aparna Rahman, MD (Cardiology), Senior medical officer, Department of Cardiology, BIRDEM General Hospital, Shahbag, Dhaka.
3. Dr. Shabnam Jahan Hoque, FCPS (Medicine), D-card, Junior Consultant, Department of Cardiology, BIRDEM General Hospital, Shahbag, Dhaka.
4. Dr. S.M. Rezaul Irfan, FCPS (Medicine), Assistant professor, Department of Cardiology, BIRDEM General Hospital, Shahbag, Dhaka.
5. Dr. Md. Babul Miah, MRCP (UK), Senior medical officer, Department of Cardiology, BIRDEM General Hospital, Shahbag, Dhaka.
6. Dr. Mohammad Shakhawat Hossain, MD (Cardiology), Senior medical officer, Department of Cardiology, BIRDEM General Hospital, Shahbag, Dhaka.

Corresponding Author:

1. Dr. Md. Zahid Alam
FCPS (Medicine)
Associate Professor
Department of Cardiology
BIRDEM General Hospital, Shahbag, Dhaka
email: ilazybear@yahoo.com
2. Dr. Aparna Rahman
MBBS, MD (Cardiology)
Senior medical officer
Department of Cardiology
BIRDEM General Hospital, Shahbag, Dhaka.
email: aparnadr28@gmail.com

*Both Md. Zahid Alam and Aparna Rahman will be considered as first author because of their equal contribution in this article.

There was study regarding comparison of lipid profile between MI and UA . Guler *et al*.[16] and Esteghamati *et al*.[17]who reported that Low levels of HDL were significantly low in subjects with MI compared to those with UA. In our study group HDL is significantly low in STEMI than NSTEMI.

Conclusion

In conclusion, this study revealed that pattern of dyslipidemia were same between two groups. But there is significant difference of all parameters of lipid profile between STEMI and NSTEMI.Based on these results, we can recommend to pay more attention to serum lipids for prevention of acute coronary syndrome .Furthermore, we have to control lipid profile more aggressively in STEMI to prevent further unwanted complications. Our study limitation is the absence of correlation of in hospital outcome with lipid status. Original sample size was small in relation to huge number of population, As well as the study period was only six months so large sample could not be included.

References:

1. Humayun H, AzharMK.Prevlence of hyperlipidemia in patients suffering from coronay arterydisease.PJC1999;10:9-14.
2. Murray CJL, Lopez AD. The global burden of disease: a comprehensive assessment of mortality and disability from disease, injuries and risk factors in 1990 and projected to 2020. Harvard School of Health, Boston (Mass) (1996)
3. Yadav AS and Bhagwat VR: Lipid Profile Pattern in Anginal Syndrome Patients From MarathwadaRegion of Maharashtra State Journal of Medical Education & Research 2012;2(2):12-15.
4. The World Health Report 1999: The Double Burden: Emerging Epidemics and Persistent Problems. WHO 1999.
5. World Health Statistics 2008: WHO. Available at: http:// www.who.int/whosis/whostat/EN_WHS08_TOCintro.pdf.
6. Ibrahim MM, Appel LJ, Rizk HH, Helmy S, Mosley J, Ashour Z, et al. Cardiovascular risk factors in normotensive and hypertensive Egyptians. J Hypertens 2001;19:1933-40.
7. Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction--summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients with Unstable Angina). J Am Coll Cardiol 2002;40:1366-74.
8. Libby P: The molecular mechanisms of the thrombotic complications of atherosclerosis. J Intern Med 2008;463,517−47.
9. Frank V, Aguirre FV, Younis LT, Chaitman BR. Early, and 1- year clinical outcome of patients evolving non-ST elevation versus ST elevation myocardial infarction after thrombolysis. Results from the TIMI II study. Circulation 1995;91:2541-8.
10. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST elevation myocardial infarction-summary article: a report of the American college of cardiology/American heart association task force on practice guidelines. J Am Coll Cardiol 2002;40:1366-74.
11. Addulla Abdelaziz, Mohamed S. Fawzy Prevalence and Pattern of Dyslipidemia World J Med Res 2014;3:19-28.
12. Burazeri G, Goda A, Sulo G, Stefa J, Roshi E, Kark JD. Conventional Risk Factors and Acute Coronary Syndrome during a Period of Socioeconomic Transition: Population-based Case-control Study in Tirana, Albania. Croat Med J. 2007; 48(2): 225–33.
13. Yadav AS, Bhagwat VR: Lipid Profile Pattern in Anginal Syndrome Patients FromMarathwada Region of Maharashtra State. Journal of Medical Education & Research 2012;2(2),12-15.
14. Wood D, De Backer G, Faergeman O, Graham I, Mancia G, Pyorala K. Prevention of coronary heart disease in clinical practice: recommendations of the second joint task force of European and other societies on coronary prevention. Eur Heart J 1998; 19:1434-1503.
15. Kuzuya N. Guidelines for dining out for diabetics. Nippon Rinsho 2002;60:697-705.
16. Guler E, Gecmen C, Guler G, Karaca1 O, Agus H, Gunes H, Batgerel U, Elveran A, Esen A: Adding lipoprotein(a) levels to the GRACE score to predict prognosis in patients with non-ST elevation acute coronary syndrome. Kardiologia Polska 2013;7: 695–701;
17. Esteghamati A, Abbasi M, Nakhjavani M, Yousefizadeh A, Basa A, Afshar H: Prevalence of diabetes and other cardiovascular risk factors in an Iranian population with acute coronary syndrome. Cardiovascular Diabetology 2006; 5:15

Bangladesh Crit Care J September 2017; 5 (2): 110-112

Original Article

Laparoscopic cost effective management of cholecystoduodenal fistula

Md. Ezharul Haque Ratan[1], Hasina Alam[2], Md. Abdul Karim[3].

Abstract

Introduction: *Contraindication to laparoscopic surgery is decreasing with time, expertise and innovation. One such uncommon condition is cholecystoduodenal fistula (CDF), now increasingly managed with laparoscopic technique. We are reporting eight such incidentally diagnosed cases during laparoscopic operation, which were successfully and cost-effectively managed with traditional laparoscopic instruments.*

Materials and Methods: *During March 2008 to March 2017, 1500 patient underwent laparoscopic cholecystectomy for benign gall bladder condition or their complications, eight of these having chronic dyspeptic symptoms of gallstone, were found to have cholecystoduodenal fistula, intraoperatively. All cases were managed laparoscopically using common laparoscopic instruments without any special gadgets and extra costs. Medical records of eight cases were reviewed for age, sex, operative technique, intra and post-operative complications and length of stay in hospital.*

Results: *Five patients were male and three were female with a mean age of 63 years. All of them had gall stones at abdominal ultrasound and cholecystoduodenal fistula were found intraoperatively. Fistula tract was dissected, cleaned and sealed with combination of intracorporeal simple transfixation ligation and interrupted stitches to invert the stump within the duodenal wall in transverse fashion. All eight had uneventful postoperative course with hospital stay of 4-7 (mean 5) days.*

Conclusion: *In expert hands cholecystoduodenal fistula can successfully and safely be managed laparoscopically using common instruments and logistics with slight modification of open technique without extra cost.*

Key words: *Cholecystoduodenal fistula (CDF),Cholecystoenteric fistula (CEF), laparoscopic technique.*

Introduction:

Since the first successful case in 1982, laparoscopic cholecystectomy (LC) has become the favored treatment as well accepted by surgeons and patients for gall bladder lesions worldwide [1].With time and increasing experience laparoscopic cholecystectomy has successfully been attempted in all kinds of benign gall bladder pathology [5] and their complications. One such condition is cholecystoenteric fistula (CEF), an abnormal spontaneous tract with bile drainage from the gall bladder to one or more adjacent bowel loop. It is though uncommon, a well-recognized complication of gall stone disease (75%)[2, 3] but can be due to peptic ulcer or neoplasm[4]. During acute cholecystitis adjacent serosal surface become inflamed and adherent of gall bladder. Raised intra cholecystic pressure and gangrene of gall bladder wall leads to penetration of bile to bowel, forming cholecystoduodenal fistula [5]. Its incidence has been reported as 3-5% in cholelithisasis and 0.15-4.8% among patients who undergo biliary tract surgery[6]. Cholecystoduodenal type (CDF) has the highest incidence (up to 80%) among cholecystoenteric fistula. The symptoms of cholecystoduodenal fistula are non-specific, often resemble those due to gall stone[3], rarely diagnosed pre-operatively and almost always discovered during cholecystectomy[6]. At inception of laparoscopic surgery cholecystoduodenal fistula was considered an absolute contraindication for laparoscopic cholecystectomy. Now it is a relative contraindication to laparoscopic cholecystectomy, while it is not a contraindication to some surgeons[6, 8]. Now increasing number of surgeons are managing cholecystoduodenal fistula laparoscopically with a conversion rate of 58.8%. Laparoscopic stapling techniques are used to seal the fistula and have been proved to be flexible and safe method[2, 3, 9]. However, stapling devices are expensive, not always available and require certain level of expertise of the surgeon. We are reporting eight cases of cholecystoduodenal fistula managed successfully by laparoscopic ligation and suture technique using traditional laparoscopic instruments. All these cases were discovered during an attempt to perform laparoscopic cholecystectomy.

1. Dr. Md. Ezharul Haque Ratan, MS (General Surgery), Associate professor, Surgery, Ibrahim Medical College and BIRDEM General Hospital, Shahbagh, Dhaka-1000, Bangladesh
2. Dr. HasinaAlam, FCPS (General Surgery), Registrar Surgery, Ibrahim Medical College and BIRDEM General Hospital, Shahbagh, Dhaka-1000, Bangladesh
3. Dr. Md. Abdul Karim, Resident Medical officer BIRDEM General Hospital, Shahbagh, Dhaka-1000, Bangladesh

Corresponding Author:

Dr. Md. Ezharul Haque Ratan, MS (General Surgery)
Associate professor, Surgery
Ibrahim Medical College and BIRDEM
Room no-445, BIRDEM General Hospital
Shahbagh, Dhaka-1000, Bangladesh
Phone : 01711172547
E-mail : ezhar65@gmail.com

Materials and methods:

From march 2008 to march 2017, 1500 patients underwent laparoscopic cholecystectomy for gall stone disease in a surgical unit of BIRDEM general hospital, Dhaka, Bangladesh. Eight of them (0.53%) were found intraoperatively to have cholecystoduodenal fistula, abnormal communication between gall bladder and the first part of the duodenum.We, retrospectively, reviewed the medical records of eight patients of cholecystoduodenal fistula. All the patients history were recorded and underwent physical examination, ultrasonography (USG), and biochemical tests to establish a preoperative diagnosis. USG revealed, fibrosed, contracted, thick walled gallbladder with stones in all cases. In each case laboratory findings were unremarkable. Data were collected on patients' age, sex, preoperative diagnosis, operative methods, morbidity and length of stay in hospital. Surgery was performed under general anesthesia using standard four ports technique. Cholecystoduodenal fistula was clearly demonstrated after careful blunt and sharp dissection. (Figure-1) Gall bladder end of the fistula tract was sealed with metal clip and the duodenal end was closed with a transfixation ligature and a simple ligature proximal to that. The cholecystoduodenal fistula was divided between ligature and clip. Duodenal end of the tract was inverted by three interrupted intracorporeal stitch within the duodenal wall in transverse fashion. Rest of the surgery was completed in usual manner of laparoscopic cholecystectomy. Oral diet was resumed 48 hours after surgery. Patients were followed up in the outpatient clinic 7 days and one month after surgery.

Results:

Cholecystoduodenal fistulas were diagnosed in 8 of 1500 patients (0.53%) over the last 9 years by a single surgeon. Five were male and three were female patients with age ranging from 54 to 69 years (mean 63 years). They had gall stones detected by abdominal Ultrasonography. Cholecystoduodenal fistula was found during operative treatment of gall stones. All the cases were managed laparoscopically. Cholecystoduodenal fistula was completely mobilized with a combination of blunt and sharp dissection and divided after application of metal clip at gall bladder end and intracorporeal transfixation ligature and simple ligature. Duodenal end was inverted by intracorporeal interrupted seromuscular suture of duodenal wall in a transverse manner. After that, laparoscopic cholecystectomy was completed. There were no intraopeprative complications in any of the patients. None of the cholecystoduodenal fistula was caused by malignancy. All eight patients had uneventful post-operative course. The hospital stay of eight patients ranged from 4 to 7 days (mean 5days). Follow up was scheduled at 7th post-operative day and at one month with an advice to report in need. None returned with a complication.

Discussion:

According to international publications ,cholecystoenteric fistulas are more common in female geriatric population[6]. Contrary to this, in our study, elderly male predominate over females (5 vs. 3). There were no specific symptoms suggestive of cholecystoduodenal fistula, rather chronic dyspeptic symptoms are indistinguishable from those of non-complicated calculus chronic cholecystitis. Thus, the diagnosis is made intraoperatively unless ultrasonography shows pneumobillia or there is an indication for more advanced diagnostic exercise like CT scan, MRCP or ERCP. In pre-laparoscopic era the standard treatment for this condition was open cholecystectomy with closure of the fistula with excision. With the advancement in video laparoscopic surgery many reports have described laparoscopic approach for cholecystoduodenal fistula [6]. The strategy and techniques used in open surgery are also applicable in laparoscopic operations. Prompt recognition is crucial along with meticulous preparation of the fistula site to demonstrate surrounding anatomy. The endoscopic stapling device appeared to be easy to use and effective in closure of cholecystoduodenal fistula. But it is expensive and not available in resource constrained areas where it is needed for an incidental occasion. Ligation of the fistula with an endoloop is another option. Though unreliable and loss of control over divided fistula stump may create a technical difficulty during application [2, 9]. Making a simple ligation either intracorporeally or extracorporeally is time consuming and cannot secure fistula closure [9]. An alternative is applying laparoscopic intracorporeal interrupted or continuous suture closure of the fistula. Similar to those in open procedure, again there is risk of loss of control outside the laparoscopic field of view. We solved the problem by combining, a transfixation ligature and holding it for control, a simple ligature proximal to it to avoid leak though needle prick for transfixation followed by simple interrupted seromuscular inversion suture and finally ends of transfixation ligature were cut. This technique is technically demanding but safe and effective.

Conclusion:

The standard treatment of cholecystoduodenal non-malignant fistula was open cholecystectomy and suture closure of fistula in pre-laparoscopic era. With increasing expertise contraindications of laparoscopic surgery in such rare complications of gall stone that are discovered at operation are decreasing. A little modification of technique of open surgery have been used successfully in laparoscopic surgery without intraoperative and postoperative complications with all the advantages that minimally invasive surgery offers using traditional instruments. Thus keeping the expenditure no more than laparoscopic cholecystectomy alone.

References:

1. Cuschieri A, Dubois F, Movie J, Mouret P, Becker H, Buess G, et al. The European experience with laparoscopic cholecystectomy. Am J surg 1991; 161:385-7.

2. Successful laparoscopic management of four cases of cholecystoduodenal fistula. MJAFI2012; 68:88-9.

3. AzraL,Ferid L,Mirela D, Josip S, DarkoK, Samir D. Successful laparoscopic treatement of cholecystoduodenal fistula. MED ARH 2010; 649(6):379-80.

4. Gentileschi P, Forlini A, Rossi P, Zaffoli M, Gentileschi E. Laparoscopic approach to cholecystocolic fistula: report of a case. J laparoendosc Surg,1995;5:413-7

5. Mervyn FSC, Dilip PAK, Swati VN, Jean-louis ASM. Colecystocolic fistula: a diagnostic enigma. The Saudi journal of gastroenterology 2009;15 (1): 42-4

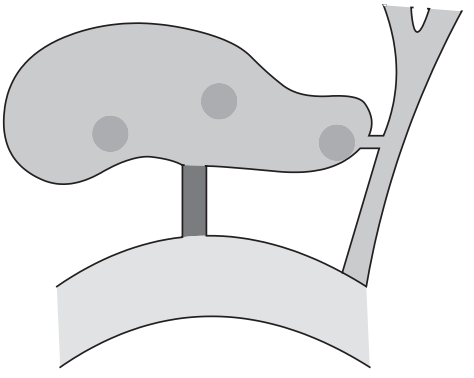
6. L Angrisani, F Coricione, ATartaglia, A Tricarico, F Rendano, R Vincenti et al. Cholecystoenteric fistula is not a contraindication for laparoscopic surgery. SurgEndosc 2001; 15:1038-41.

7. Sharm A, Sullivan M, English H, Folwy R. Laparoscopic repair of cholecystoduodenal fistula. SurglaparoscEndosc 1994; 4:433-5.

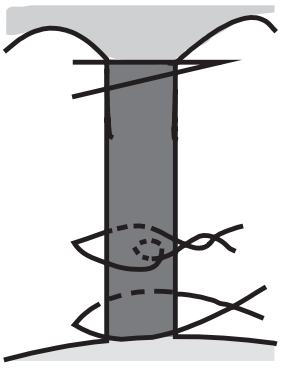
8. Moreno Ruiz F J,del Rey Moreno A, Suescun Garcia RM, Martinez Ferriz JA, Hidalgo Garrido JM, EspadasPadial B, et al. Treatment of cholecystoduodenal fistula in the era of laparoscopy. Rev EspEnferum Dig.2001 Nov; 93 (11); 715-20.

9. Wang WK, Yeh CN, Jan YY. Successful laparoscopic management for cholecystoenteric fistula. World J gastroenterol 2006; 12 (5):772-5.

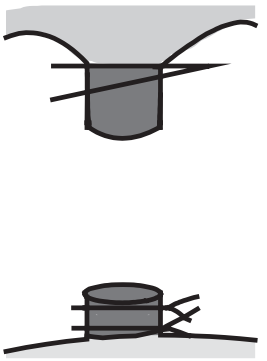
Figure I:
1-Anatomy of cholecystoduodenal fistula
2-Metal clip ligation at gall bladder end, intracorporeal transfixation ligature and simple ligature at duodenal end
3-Fistula transection after ligature placement
4-Duodenal end inverted by intracorporeal interrupted seromascular suture

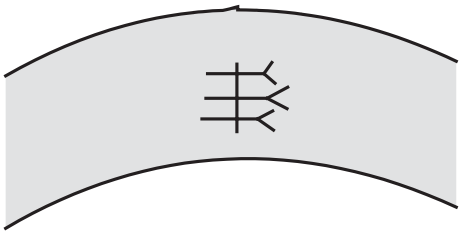


1



2





Bangladesh Crit Care J September 2017; 5 (2): 113-121

Review Article

Feeding adequacy among Critically Ill Patients in the Intensive Care Unit and Its Association with Clinical Outcomes: A Narrative Review

Zheng-Yii Lee[1], Mohd-Yusof Barakatun-Nisak[2], Ibrahim Noor Airini[3]*

Abstract

The Intensive Care Unit (ICU) is one of the disciplines in the hospital that provides close monitoring to the seriously ill or injured patients, also known as the critically ill patients. Critically ill patients in the ICU are usually unable to maintain volitional oral nutrition intake and therefore require nutritional therapy. Nutritional therapy can be delivered via the enteral or parenteral route. Optimal nutrition adequacy (i.e. neither underfeeding nor overfeeding) is very important for better clinical outcome. However, the problem of suboptimal feeding adequacy continues to be reported over the years. This article attempts to give an overview of the literature on feeding adequacy and the relationship of feeding adequacy with clinical outcomes among the critically ill patients in the ICU.

Keywords: *Critical Illness, Intensive Care Unit, Nutritional therapy, Feeding Adequacy*

Introduction

The Intensive Care Unit (ICU) is one of the disciplines in the hospital that provides close monitoring to the seriously ill or injured patients,[1] also known as the critically ill patients. Critically ill patients are often unconscious and may not be able to breathe adequately by themselves. Their respiratory function is often compromised and presents with low blood pressure, leading to poor oxygen perfusion to the vital organs.[2] Therefore, they are usually intubated and mechanically ventilated, given inotropes and vasopressors (drugs to support their blood pressure) and sedated. Their hemodynamic status is frequently unstable. Such conditions commonly predispose to multiorgan dysfunction as a complication, with a higher mortality rate seen in those with a higher number of organ failure.[3]

Critical illness is defined as "A life-threatening process…that ultimately involves respiratory, cardiovascular and neurological compromise".[4] Oral intake is almost always impossible in these patients,[5] necessitating the provision of artificial nutrition (i.e. feeding). Feeding the critically ill patients was previously regarded as adjunctive care (known as nutritional support). However, feeding is now regarded as nutritional therapy that may help to attenuate stress response, prevent oxidative cellular injury and favorably modulate immune responses.[6]

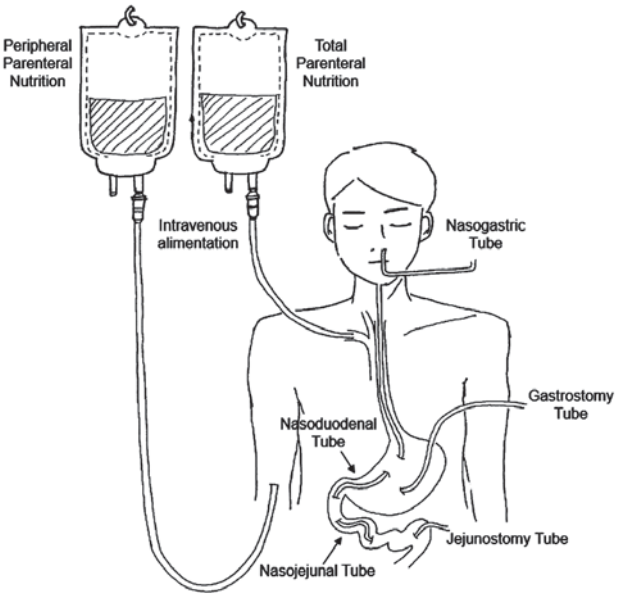


Figure-1: Enteral and Parenteral Nutrition

Enteral nutrition delivers nutrients into the gastrointestinal tract via a feeding tube. Depending on where the tube ends and how the tube is inserted into the gastrointestinal tract, enteral nutrition can be in the form of nasogastric tube, nasoduodenal tube, nasojejunal tube, gastrostomy tube and jejunostomy tube. Parenteral nutrition, also known as intravenous alimentation, delivers nutrients directly into the bloodstream. Total parenteral nutrition and peripheral parenteral nutrition delivers nutrients via the central and peripheral line, respectively.

1. Zheng Yii Lee, MSc, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. Email: zheng_yii@hotmail.com

2. Mohd-Yusof Barakatun-Nisak, PhD, Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. Email: bnisak@upm.edu.my

3. Dr. Ibrahim Noor Airini, MBBS, MMed, EDIC, Anaesthesiology Unit, Department of Surgery, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. Email: airini@upm.edu.my

Corresponding Author:

Dr. Ibrahim Noor Airini
MBBS, MMed, EDIC
Anaesthesiology Unit, Department of Surgery
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia.
Email: airini@upm.edu.my

Nutritional therapy can be delivered via the enteral or parenteral routes (Figure 1). Enteral nutrition (EN) delivers nutrients into the gastrointestinal tract via a feeding tube for patients who are unable to maintain volitional intake. Parenteral nutrition (PN) delivers nutrients directly into the bloodstream, via central or peripheral line. Compare to PN, EN has additional benefits of maintaining gut structural and functional integrity, modulating metabolic response, and attenuating oxidative stress and the inflammatory response while supporting the humoral immune system.[7] Therefore, EN (i.e. tube feeding) acts as the first line nutritional therapy in mechanically ventilated critically ill patients who are unable to maintain volitional intake.

While the rational of initiating feeding to patients who are unable to maintain oral intake is justified, the effort to ensure patients are fed optimally based on nutrition prescription are often neglected. Studies have reported that critically ill patients receiving inadequate energy and protein are presented with poor clinical outcomes such as increased risk of infections, length of mechanical ventilations, morbidities and mortality.[7] Although the definition of underfeeding differs in various studies, but it was generally recognized that 80% of prescribed energy and protein represent adequate feeding.[8] It may be more important to ensure protein adequacy as studies have shown that improvement of clinical outcomes is associated with adequate protein intake, even after adjustment for energy adequacy.[9,10]. However, caution also need to be taken to avoid overfeeding patients, which is usually defined as feeding over 110% of energy prescribed,[11] as it is associated with complications such as hyperglycemia, azotemia, hypertriglyceridemia, electrolyte imbalance, immunosuppression, alteration in hydration status, hepatic steatosis, and difficulty waning from mechanical ventilation.[12]

Over the years, suboptimal feeding continues to be a major concern in the critically ill patient population [8,13] despite various studies reporting on the relationship between nutritional adequacy and clinical outcomes. Factors associated with suboptimal feeding need to be investigated and action is needed to address this issue. This paper aims to review the literature that reported on feeding adequacy and studies that investigated on the relationship between feeding adequacy and clinical outcomes.

Methods

The literature search was conducted in electronic databases i.e. PubMed and Google Scholars up to December 2016, limited to articles published in English language. Studies included in this narrative review are adult (≥18 years old), critically ill patients who were admitted into the ICU, and nutritional therapy (EN or PN) initiated during the ICU stay.

For prevalence of underfeeding, studies must report energy and/or protein adequacy; while for studies reporting on the relationship between nutritional adequacy and clinical outcomes, at least one of the important clinical outcomes such as mortality, infectious complications, length of ICU and/or hospital stay or duration of mechanical ventilation must be reported. Studies in non-critically ill patients were excluded. In addition, studies that investigated on PN route and timing were also excluded.

Results

Feeding Adequacy in the World, Asia & Malaysia

Several single-center studies had reported the energy and/or protein adequacy among critically ill patients (Table 1). McClave et al[13] showed that ICU patients (n=44) received about 51.6% of their targeted calorie requirement, while De Jonghe and colleagues[14] found that 71% of calorie requirement was effectively delivered by both EN and PN route. On the other hand, Binnekade et al[15] reported on average about 66% and 54% of energy and protein respectively was delivered among the 403 critically ill patients investigated.

On the global level, two international, prospective, observational study was conducted in year 2007 and 2008. In 2007, 158 ICUs from 20 countries with 2946 mechanically ventilated patients who stayed in ICU for at least 72 hours showed that average nutritional adequacy across sites was 59% (range, 20.5%-94.4%) for energy and 60.3% (range, 18.6%-152.5%) for protein.[16] In year 2008, the second study involved 179 ICU from 18 countries with the same patient population (n=2956) showed that the average energy adequacy across sites was 56.2% (range, 20.3%-90.1%).[17]

The most recent international multi-center observational study across 6 different geographic regions (Europe & South Africa, Canada, Australia & New Zealand, Latin America, Asia & USA) from 26 countries, 201 ICUs and 3390 patients showed that on average, patients receive 61.2% ± 29.4% and 57.6% ± 29.6% of prescribed energy and protein, respectively, with a mean energy balance of - 695 ± 532 kcal/day.[8] When zoomed into Asia, a result lower than the international average was seen. On average, patients received 53.5% ± 28.0% and 51.9% ± 30.1% of prescribed energy and protein, respectively, with a mean energy balance of -736 ± 480 kcal/day. The prevalence of iatrogenic underfeeding (defined as received <80% of prescribed energy) was 74% at the international level, and 82% for Asia region.[8]

In Malaysia, three single-center studies had been conducted to investigate feeding adequacy among critically ill patients. A small cross-sectional study in Hospital Selayang among critically ill patients on total enteral nutrition (n=67) presented by Mageswary et al[18] showed that before appropriate feeding protocol was implemented, about 69.0% of patients achieved goal calorie (>70% of prescribed calorie) on day 5 after feeding initiation. Yip et al[19] showed that 66% of patients achieved 80% of prescribed energy within 3 days of admission at Universiti Malaya Medical Center. Lee et al[20] in their preliminary study in a Malaysian public hospital showed that the average energy and protein adequacy was 71.8% and 62.4%; while patients with high nutrition risk had lower adequacy, with average adequacy of 67.9% and 60.3% for energy and protein, respectively.

In summary, critically ill patients received approximately 50-70% of their energy and protein requirements.

Table 1: Studies investigated feeding adequacy among critically ill patients

First Author, year (country)	Population	Sample Size	Route	ER and/or PR	Energy and/or Protein delivered
McClave et al., 1999[13] (USA)	Mixed ICU	44	EN	ER: 25-35 kcal/kg/d	51% of ER
De Jonghe et al., 2001[14] (France)	Medical ICU	51	EN (12%), PN (28.3%), or Mixed (58.7%)	ER: Harris-Benedict Equation	71% of ER
Binnekade et al., 2005[15] (Netherlands)	Medical ICU	403	EN	ER: 25 kcal/kg/d PR: 1.5 g/kg/d	66% of ER 54% of PR
Cahill et al., 2010[16] (20 countries)	Mixed ICU	2946	EN (61.7%), PN (11.8%), or Mixed (6.7%)	Determined by attending healthcare professionals	59% of ER 60.3% of PR
Heyland et al., 2010[17] (18 countries)	Mixed ICU	2956	EN (71.6%), PN (6.0%), or Mixed (14.0%)	Determined by attending healthcare professionals	56.2% of ER
Heyland et al., 2014[8] (26 countries)	Mixed ICU	3390	EN (77%), PN (6%), Mixed (15%)	Determined by attending healthcare professionals	61.2% of ER 57.6% of PR Asia: 53.5% of ER 51.9% of PR
Malaysia					
Mageswary et al., 2013[18] (Malaysia)	N.R	67	EN	Determined by attending dietitian	69.0% of ICU patients achieved 70% of ER on day 5 after feeding initiation
Yip et al., 2014[19] (Malaysia)	Mixed	77	EN	ER: 25 kcal/kg/d	66% of patients achieved 80% of ER within 3 days of ICU admission
Lee et al., 2016[20] (Malaysia)	Mixed	25	EN	ER: 25 kcal/kg/d PR: 1.2 g/kg/d	78.2% of ER 62.4% of PR High nutrition risk: 67.9% of ER 60.3% of PR

ICU: Intensive Care Unit, EN: Enteral Nutrition, PN: Parenteral Nutrition, ER: Energy Requirement, PR: Protein Requirement

Feeding adequacy and its implication to clinical outcomes

Inadequate feeding among critically ill patients is associated with poorer clinical outcomes such as increased infectious complication, length of ICU and hospital stay, duration of mechanical ventilation, and mortality, although such association was not consistently demonstrated in recent studies. The association between feeding adequacy and clinical outcomes are reviewed.

Small observational studies

About eight small observational studies (Table 2) among critically ill patients conducted in various countries demonstrated the association between underfeeding and poorer clinical outcome. In 2005, Villet et al[21] conducted a prospective observational study on 48 surgical patients who stayed in ICU for ≥5 days. It was shown that negative energy balance correlated with increase length of stay (p=0.0001), infections (p=0.0042) and length of mechanical ventilation (p=0.0002). Rubinson et al[22] studied 138 medical ICU patients who was nil by mouth for ≥96 hours and showed that after adjustment for potential confounders, patients who received ≥25% of recommended calories was associated with a significantly lower risk of bloodstream infection [relative hazard 0.27, 95% confidence interval (CI), 0.11-0.68]. Dvir et al (2006) in a prospective study of 50 ICU patients also found that patients with negative energy balance of >4000 kcal has strong association with complications such as respiratory distress syndrome (p=0.0003), sepsis (p=0.0035) and renal failure (p=0.0001).

In a retrospective study of 295 patients, Tsai et al[23] demonstrated that patients receiving lower energy delivery was 2.43 times at risk of ICU mortality than high energy

Table 2: Observational Studies investigating the relationship between feeding adequacy and clinical outcomes.

First Author, year (country)	Study Design	Population	Sample Size	Main Findings
Small Observational Studies				
Rubinson et al. 2004[22] (USA)	Prospective	Medical ICU	138	Patients who received ≥25% of ER compared with <25% of ER had significant lower risk of bloodstream infection after adjustment for SAPS II
Villet et al., 2005[21] (Switzerland)	Prospective	Surgical ICU	48	Cumulated energy deficit after 7 days correlated with both total and infectious complications
Petros et al., 2006[41] (Germany)	Prospective	Medical ICU	61	Patients who took longer time to achieve target ER (≥4 days) compared with shorter time (<4 days) had significant higher mortality rate (73.3% vs 26.1%)
Dvir et al., 2006[42] (Israel)	Prospective	Mixed ICU	50	Maximum negative energy balance is associated with ARDS, sepsis, renal failure, pressure sores, need for surgery and total complications rate
Faisy et al., 2009[43] (France)	Retrospective	Medical ICU	38	Patients with mean energy deficit ≥1200 kcal/d had a higher ICU mortality rate than patients with lower deficit after the 14th ICU day
Tsai et al., 2011[23] (Taiwan)	Retrospective	Medical ICU	295	Patients who received <60% of ER had 2.43 times higher ICU mortality than ≥ 60% of ER
Heyland et al., 2011[24] (Canada)	Prospective	Mixed ICU	207	Increase 1000 kcal/d of energy and 30g/d of protein is associated with lower risk of developing at least 1 probable infection after >96 h of ICU admission
Allingstrup et at., (Denmark)	Prospective	Mixed ICU	113	Increased protein provision was associated with significant 2012[9] decrease hazard ratio of death, even after adjusted for baseline APACHE II, SOFA and age
Large Observational Studies				
Alberda et al., 2009[25] (37 countries)	Prospective	Mixed ICU	2772	Increased 1000 kcal/d of energy and 30g/day of protein is associated with significant reduced 60-d mortality and increased ventilator-free days. This association is only present in patients with BMI <25 and ≥35
Arabi et al., 2010[29] (Saudi Arabia)	Prospective	Mixed ICU	523	A dose-effect relationship between increasing calorie intake and higher hospital mortality, risk of ICU-acquired infections, ventilator-associated pneumonia, duration of mechanical ventilation, and length of stay in ICU and hospital.
Heyland et al., 2011[30] (33 countries)	Prospective	Mixed ICU	7872	After excluding days after permanent progression to oral intake and number of evaluable days, achieving approximate 80% of ER is associated with significant reduction in mortality in patients who stay >96 h in ICU
Elke et al., 2014[26] (33 countries)	Prospective	Mixed ICU	2270	In ICU patients with sepsis and/or pneumonia, increased 1000 kcal/d of energy and 30g/day of protein is associated with significant reduced 60-d mortality and increased ventilator-free days.
Wei et al., 2015[27] (ICUs in Canada, Europe and US)	Secondary analysis of a prospective RCT	Mixed ICU	475	- Survival time was significantly shorter in patients with low than high nutritional adequacy - At 3-month follow-up, every 25% increase in nutritional adequacy was associated with improvement of physical functioning and role physical score
Nicolo et al., 2015[10] (202 ICUs from INS 2013)	Prospective	Mixed ICU	2828	≥80% of prescribed protein intake was associated with reduced mortality. ≥80% of prescribed protein intake was associated with shorter time-to-discharge alive in adjusted 12-day sample

ICU: Intensive Care Unit, ER: Energy requirement, PR: Protein requirement, d: day, h: hour, SAPS II: Simplified Acute Physiology Score II, APACHE II: Acute Physiology and Chronic Health Evaluation II, SOFA: Sequential Organ-failure Assessment, INS: International Nutrition Survey

delivery after adjusting for confounders (p=0.020). Furthermore, a study in 3 medical/surgical ICUs among mechanically ventilated patients who stayed in the ICU for more than 72 hours and received EN showed that successful EN may be associated with reduction in infectious complications, particularly after 96 hour of ICU admission.[24] For protein, Allingstrup et al[9] also found that increased protein provision was associated with significant decrease in hazard ratio of death, even after adjusted for baseline prognostic factors.

Large Multicenter observational studies

Large multicenter observational studies (Table 2) was conducted since the commencement of the International Nutrition Survey (INS) in year 2007. Since then, about 5 analyses were conducted based on the international sample.

In year 2009, a large international observational study on 2772 mechanical ventilated patients by Alberda et al[25] showed an increase of 1000 kcal and 30 g protein per day was associated with reduced 60-days mortality [odds ratio (OR) 0.76, 95% CI 0.61-0.95, p=0.014] and an increased in number of ventilator free days (VFD) (3.5 VFD, 95% CI 1.2-5.9, p=0.003). Elke et al[26] selected a sample of 2270 ICU patients with sepsis and/or pneumonia from the database of the INS from year 2007 to 2011 also showed that an increase of 1000 kcal and 30 g protein per day was associated with reduced 60-day mortality (OR 0.61, 95% CI 0.48-0.77, p<0.001), and more ventilator-free days (2.81 days, 95% CI 0.53-5.08, p=0.02).

The relationship between nutritional adequacy and long-term outcome was also investigated. In a large sample (n=475) of patients who were mechanical ventilated for >8 days in ICU and had at least 2 organ failures related to their acute illness, survival time with low nutritional adequacy was significantly shorter than high nutritional adequacy (Hazard Ratio 1.7, 95% CI 1.1-2.6) and health-related quality of life was significantly higher with every 25% increase nutritional adequacy at 3 month follow up.[27]

On the contrary, Krishnan et al[28] showed that lower adequacy was associated with better outcomes than higher levels of calorie intake. Arabi et al[29] also showed that there was a dose-effect relationship between increasing calorie intake and higher hospital mortality, risk of ICU-acquired infections, rate of ventilator-associated pneumonia (VAP), increase duration of mechanical ventilation and length of stay in hospital and ICU. However, these associations were shown to be influenced by the statistical methodology used. Heyland et al[30] found that analyses that do not account for the progression to oral intake and the number of ICU days used in the calculation of the proportion calories received will lead to a potentially erroneous finding whereby higher calories intake is associated with increased mortality, whereas analyses that account for these key factors showed that better fed patients have reduced mortality.

In fact, Heyland et al[30] in the same study of an international sample of 7872 mechanically ventilated, critically ill patients who remained in the ICU for at least 96 hours showed that the overall association between percentage of the caloric prescription received and mortality is highly statistically significant with increasing calories associated with decreasing mortality (p<0.0001), and it appears that approximating goal of 80% of prescribed calories (and not more than 100% of prescribed calories) is associated with the best survival, regardless of body mass index. Similar results for protein was also demonstrated by Nicolo et al[10] among 2828 patients in ICU for at least 4 days, whereby patients who received ≥80% of prescribed protein had reduced mortality and shorter time-to-discharge alive, after adjusted for covariates and energy intake.

Randomized controlled trial (RCT)

Beside observational studies, several RCTs had been conducted in recent years (Table 3). Rice et al conducted the EDEN pilot (2011, n=200)[31] and multicenter RCT (2012, n=1000)[32] to investigate the effect of initial lower volume trophic or full enteral feeding for the first 6 days since ICU admission among patients with acute lung injury. Both studies achieved significant difference in calories and protein intake between the full and trophic feeding groups. The pilot study showed that the VFD to day-28, hospital mortality rate and ICU-free days were similar between groups. The multicenter RCT confirmed the results of the pilot study and showed no significant different between groups on VFD to day-28, 60-day mortality, development of infections and organ failure-free days.

The TICACOS study[33] is currently the only RCT that uses indirect calorimetry to calculate energy requirement, shows that there is a trend towards reduction of hospital mortality (p=0.058) and significant lower organ failure score at day 3 (p=0.027) in the intervention group who received significantly more calories and protein than the control group. However, the control group had a significant lower length of mechanical ventilation (p=0.03), length of stay in ICU (p=0.04), and trend towards reduce VAP (p=0.08) and infectious complications (p=0.05). These contradicting results is most probably due to calorie overfeeding as the study investigators did not consider intravenous non-nutrition energy intake (such as dextrose-containing fluids and propofol), which corresponds to an additional 10-15% calories.[34] Similar problem exists in a trial by Braunschweig et al[35] which showed 5.67 times higher hospital mortality in the full feeding group. The possibility of overfeeding is noted in their figure 2 that from day 5 onwards patients consistently received ≥100% of their energy prescription and almost reaching 120% on day 13 and day 14, probably contributing to the high mortality of the full feeding group.

In year 2014, Peake et al[36] randomized patients to receive isonitrogenous enteral formula with caloric density 1.5 kcal/ml and 1.0 kcal/ml. It was found that the 1.5 kcal/ml group who received significantly more calories had trend toward improved duration of survival (p=0.057), although there was no difference on VFD to day-28 and ICU & hospital length of stay. In the same year, Petros et al[37] also found that patients who are fed more adequately had reduced nosocomial infection, despite no difference in mortality rate.

Table 3: Randomized controlled trials comparing clinical outcomes between full feeding and underfeeding

First Author, year (country)	Population	Sample Size	Energy (E) and Protein (P) received		Outcome (Full feeding compare with underfeeding)
			Full feeding group	Underfeeding group	
Taylor et al., 1999[44] (UK)	Head injured and MV	82	E: 59.21% P: 68.7%	E: 36.8% P: 37.9%	- Good neurologic outcome at 3 months: ↑ trend (p=0.08) - At least 1 infection: ↓ - At least 1 complication: =
Desachy et al.,	Mixed ICU	100	E: 1715 ± 331 kcal/d P: unknown	E: 1297 ± 331 kcal/d P: unknown	- ICU LOS: = - Hospital LOS: = - ICU mortality: = - Hospital mortality: =
Arabi et al., 2011[38] (Saudi Arabia)	Mixed ICU	240	E: 1251.7 ± 432.5 kcal/d (71.4 ± 22.8%) P: 43.6 ± 18.9 g/d (63.7 ± 25.0%)	E: 1066.6 ± 306.1 kcal/d (59.0 ± 16.1%) P: 47.5 ± 21.2 g/d (65.2 ± 25.7%)	- ICU LOS: ↑ trend (p=0.09) - Hospital LOS:= - MV duration: ↑ trend (p=0.10) - 28-d mortality: = - 180-d mortality: ↑ trend (p=0.07) - ICU mortality: = - Hospital mortality: ↑
Singer et al., 2011[33] (Israel)^	Mixed ICU	130	E: 2086 ± 460 kcal/d P: 76 ± 16 g/d	E: 1480 ± 356 kcal/d P: 53 ± 16 g/d	- Length of MV: ↑ - ICU LOS: ↑ - Hospital LOS: = - ICU mortality: = - VAP: ↑ trend (p=0.08) - Infectious complications: ↑ trend (p=0.05) - Hospital Mortality: ↓ trend (p=0.058) - SOFA at Day 3: ↓
Rice et al., 2011[31] (USA)	Acute Lung Injury	200	E: 1418 ± 868 kcal/d (74.8 ± 38.5%) P: 54.4 ± 3.2g/d	E: 300 ± 149 kcal/d (15.8 ± 11.0%) P: 10.9 ± 6.8g/d	- VFD to d-28: = - Hospital Mortality: = - ICU-free day: = - Hospital-free day: =
Rice et al., 2012[32] (USA)	Acute Lung Injury	1000	E: ~1300 kcal/d (~80%) P: Unknown	E: ~400 kcal/d (~25%) P: Unknown	- VFD to d-28: = - 60-d Mortality: = - VAP: = - Infections: =
Charles et al., 2014[46] (USA)	Surgical ICU	83	E: 1338 ± 92 kcal/d (17.1 ± 1.1 kcal/kg) P: 83 ± 6 g/d (1.1 ± 0.1 g/kg)	E: 982 ± 61 kcal/d (12.3 ± 0.7 kcal/kg) P: 86 ± 6 g/d (1.1 ± 0.1 g/kg)	- Total no. of infections: = - ICU LOS: = - Hospital LOS: = - Mortality: =
Petros et al., 2014[37] (Germany)	Medical ICU	100	E: 19.7 ± 5.7 kcal/kg (75.5%) P: ~0.8 g/kg	E: 11.3 ± 3.1 kcal/kg (42.2%) P: ~0.5 g/kg	- Nosocomial infection: ↓ - ICU mortality: = - Hospital mortality: = - 28-d mortality: =
Peake et al., 2014[36] 0(Australia)	Mixed ICU	112	E: 2040 ± 578 kcal/d P: 70 ± 20 g/d	E: 1504 ± 573 kcal/g P: 74 ± 30 g/d	- VFD to d-28: = - ICU LOS: = - Hospital LOS: = - ICU mortality: = - Hospital Mortality: = - 90-d mortality: ↓ trend (p=0.057)

Arabi et al., 2015[39] (Saudi Arabia & Canada)	Mixed ICU	894	E: 1299 ± 467 kcal/d (71 ± 22%) P: 59 ± 25 g/d (69 ± 25%)	E: 835 ± 297 kcal/d (46 ± 14%) P: 57 ± 24 g/d (68±24%)	- ICU mortality: = - Hospital mortality: = - 28-d, 90-d, 180-d mortality: = - Incident of RRT: ↑
Braunschweig et al., 2015[35] (USA)	Mixed ICU	78	E: 1798 ± 509 kcal/d (84.7 ± 22%) P: 82 ± 23 g/d (76.1%)	E: 1221 ± 423 kcal/g (55.4 ± 19%) P: 60.4 ± 24 g/d (54.4%)	- Nosocomial infections: = - Length of MV: = - ICU LOS: = - Hospital LOS: = - Hospital mortality: ↑

^The intention-to-treat results were presented for Singer et al., 2011
MV: Mechanically-ventilated, ICU: Intensive Care Unit, LOS: Length of stay, d: day, VFD: ventilator-free day, SOFA: sequential organ failure assessment, VAP: ventilator-associated pneumonia. =: No significant difference, ↑: significantly increased, ↓: significantly reduced

Arabi et al[38] in year 2011 found that the full feeding group in their study had higher hospital mortality, and trend towards longer ICU length of stay, duration of mechanical ventilation as well as higher 180-d mortality. However, it must be noted that the absolute caloric intake between group were small (~184 kcal/d) despite reaching statistical difference, and the protein intake of the underfeeding group was higher than the full feeding group. Therefore, it is hard to attribute the poorer clinical outcome in the full feeding group to greater nutritional intake. The same authors in year 2015 conducted the PERMIT multicenter trial[39] which randomized patients to receive permissive underfeeding (40-60% of caloric requirement) or full-feeding (70-100% of caloric requirement) with similar protein intake. It was shown that there was no significant difference in all important clinical outcomes (mortality, length of stay, VAP) except that the permissive underfeeding group had a lower incident of renal replacement therapy (p=0.04).

In a nutshell, results from RCTs tend to show there is no significant difference in clinical outcomes between patients who received more calorie and/or protein, although some of them did show a trend towards better survival in patients who received more nutrition. Findings from RCTs combined with the signal of improved clinical outcomes in better fed patients shown in various multicenter prospective observational studies should allow us to conclude that optimal calories and protein provided to critically ill patients may improve patients' outcomes, provided overfeeding is avoided. The use of nutritional screening tools such as the NUTRIC score[40] in stratifying patients who require full or hypocaloric feeding is an important consideration but is out of the scope of this review.

Recommendation and Conclusion

The relationship between optimal feeding adequacy (neither underfeeding nor overfeeding) and better clinical outcomes (improved survival, reduced length of stay and infectious complications) is shown in many observational studies, while some RCTs showed reduced infections and mortality with better feeding adequacy. Despite this relationship, feeding adequacy was suboptimal, which warrants further investigation on the contributing factors so that a more informed action can be taken to address this issue.

In Malaysia, data regarding feeding adequacy and the factors associated with suboptimal feeding adequacy among the critically ill patients are still lacking. It is suggested that these factors are investigated in future research. This is because it is imperative to first discover the scope of the problem and factors associated with poor feeding practices, which then acts as a 'stepping stone' for the implementation of effective solution to improve nutritional delivery and status, ultimately leading to better overall clinical outcome and cost-saving in the Malaysian ICU.

Acknowledgement

We would like to thank Ms Chan Mui Shien for drawing Figure 1. We have no conflict of interest to declare. This study is not funded.

References

1. Vincent J-L. Critical care – where have we been and where are we going? *Crit Care*. 2013;17(Suppl 1):S2. doi:10.1186/cc11500.
2. Sakka SG. Hemodynamic Monitoring in the Critically Ill Patient - Current Status and Perspective. *Front Med*. 2015;2(August):44. doi:10.3389/fmed.2015.00044.
3. Bilevicius E, Dragosavac D, Dragosavac S, Araújo S, Falcão ALE, Terzi RGG. Multiple Organ Failure in Septic Patients. *Braz J Infect Dis*. 2001;5(3):103-110. doi:10.1590/S1413-86702001000300001.
4. Robertson LC, Al-Haddad M. Recognizing the critically ill patient. *Anaesth Intensive Care Med*. 2013;14(1):11-14. doi:10.1016/j.mpaic.2012.11.010.
5. Kreymann KG, Berger MM, Deutz NEP, et al. ESPEN Guidelines on Enteral Nutrition: Intensive care. *Clin Nutr*. 2006;25(2):210-223. doi:10.1016/j.clnu.2006.01.021.
6. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the

Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enter Nutr*. 2016;40(2):159-211. doi:10.1177/0148607115621863.

7. McClave, Martindale RG, Rice TW, Heyland DK. Feeding the Critically Ill Patient. *Crit Care Med*. 2014. doi:10.1097/CCM.0000000000000654.

8. Heyland DK, Dhaliwal R, Wang M, Day AG. The prevalence of iatrogenic underfeeding in the nutritionally "at-risk" critically ill patient: Results of an international, multicenter, prospective study. *Clin Nutr*. 2014. doi:10.1016/j.clnu.2014.07.008.

9. Allingstrup MJ, Esmailzadeh N, Wilkens Knudsen A, et al. Provision of protein and energy in relation to measured requirements in intensive care patients. *Clin Nutr*. 2012;31(4):462-468. doi:10.1016/j.clnu.2011.12.006.

10. Nicolo M, Heyland DK, Chittams J, Sammarco T, Compher C. Clinical Outcomes Related to Protein Delivery in a Critically Ill Population: A Multicenter, Multinational Observation Study. *JPEN J Parenter Enter Nutr*. 2015. doi:10.1177/0148607115583675.

11. Reid C. Frequency of under- and overfeeding in mechanically ventilated ICU patients: causes and possible consequences. *J Hum Nutr Diet*. 2006;19:13-22.

12. Schlein KM, Coulter SP. Best Practices for Determining Resting Energy Expenditure in Critically Ill Adults. *Nutr Clin Pr*. 2014;29(1):44-55. doi:10.1177/0884533613515002.

13. Mcclave SA, Sexton LK, Spain DA, et al. Enteral tube feeding in the intensive care unit: Factors impeding adequate delivery. *Crit Care Med*. 1999;27(7):1252-1256.

14. De Jonghe B, Appere-De-Vechi C, Fournier M, et al. A prospective survey of nutritional support practices in intensive care unit patients: What is prescribed? What is delivered? *Crit Care Med*. 2001;29(1):8-12.

15. Binnekade J, Tepaske R, Bruynzeel P, Mathus-vliegen E, de Haan R. Daily enteral feeding practice on the ICU : attainment of goals and interfering factors. *Crit Care*. 2005;9(3):R218-R225. doi:10.1186/cc3504.

16. Cahill NE, Dhaliwal R, Day AG, Jiang X, Heyland DK. Nutrition therapy in the critical care setting: What is "best achievable" practice? An international multicenter observational study. *Crit Care Med*. 2010;38(2):395-401. doi:10.1097/CCM.0b013e3181c0263d.

17. Heyland DK, Heyland RD, Cahill NE, et al. Creating a Culture of Clinical Excellence in Critical Care Nutrition: The 2008 Best of the Best'' Award. *JPEN J Parenter Enter Nutr*. 2010;34(6):707-715. doi:10.1177/0148607110361901.

18. Mageswary LL, Adlin Natasya MS, Fathiyah Noor O, Lee Fang T, Sing Ean T. Improving Enteral Nutrition Support Practice Among ICU Patietns at Hospital Selayang. 2013:29. http://www.slideshare.net/lionelchewvunliung/l-mageswary-lapchmanan-improving-nutrition-support-practices-among-intensive-care-unit-patients-at-selayang-hospital.

19. Yip KF, Rai V, Wong KK. Evaluation of delivery of enteral nutrition in mechanically ventilated Malaysian ICU patients. *BMC Anesthesiol*. 2014;14(1):127. doi:10.1186/1471-2253-14-127.

20. Lee ZY, Barakatun-nisak MY, Airini IN. Enteral Nutrition Feeding Adequacy among Mechanically Ventilated Critically Ill Patients with High Nutrition Risk in a selected Public Hospital in Malaysia : A preliminary study. *Bangladesh Crit Care J*. 2016;4(1):9-13.

21. Villet S, Chiolero L, Bollmann MD, et al. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. *Clin Nutr*. 2005;24:502-509. doi:10.1016/j.clnu.2005.03.006.

22. Rubinson L, Diette GB, Song X, Brower RG, Krishnan J a. Low caloric intake is associated with nosocomial bloodstream infections in patients in the medical intensive care unit. *Crit Care Med*. 2004;32(2):350-357. doi:10.1097/01.CCM.0000089641.06306.68.

23. Tsai J, Chang W, Sheu C, et al. Inadequate energy delivery during early critical illness correlates with increased risk of mortality in patients who survive at least seven days: A retrospective study. *Clin Nutr*. 2011;30:209-214. doi:10.1016/j.clnu.2010.09.003.

24. Heyland DK, Stephens KE, Day AG, McClave SA. The success of enteral nutrition and ICU-acquired infections : A multicenter observational study. *Clin Nutr*. 2011;30(2):148-155. doi:10.1016/j.clnu.2010.09.011.

25. Alberda C, Gramlich L, Jones NE, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients : results of an international multicenter observational study. *Intensive Care Med*. 2009;35:1728-1737. doi:10.1007/s00134-009-1567-4.

26. Elke G, Wang M, Weiler N, Day AG, Heyland DK. Close to recommended caloric and protein intake by enteral nutrition is associated with better clinical outcome of critically ill septic patients: secondary analysis of a large international nutrition database. *Crit Care*. 2014;18(1):R29. doi:10.1186/cc13720.

27. Wei X, Day AG, Ouelette-Kuntz H, Heyland DK. The Association Between Nutritional Adequacy and Long-Term Outcomes in Critically Ill Patients Requiring Prolonged Mechanical Ventilation: A Multicenter Cohort Study. *Crit Care Med*. 2015. doi:10.1097/CCM.0000000000001000.

28. Krishnan JA, Parce PB, Martinez A, Diette GB, Brower RG. Caloric Intake in Medical ICU Patients : Consistency of Care With Guidelines and Relationship to Clinical Outcomes Caloric Intake in Medical ICU Patients. *Chest*. 2003;124(1):297-305. doi:10.1378/chest.124.1.297.

29. Arabi YM, Haddad SH, Tamim HM, et al. Near-Target Caloric Intake in Critically III Medical-Surgical Patients Is Associated With Adverse Outcomes. *JPEN J Parenter Enter Nutr*. 2010;34(3):280-288. doi:10.1177/0148607109353439.

30. Heyland DK, Cahill N, Day AG. Optimal amount of calories for critically ill patients: Depends on how you slice the cake! *Crit Care Med*. 2011;39(12):1. doi:10.1097/CCM.0b013e318226641d.

31. Rice TW, Mogan S, Hays MA, Bernard GR, Jensen GL, Wheeler AP. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. *Crit Care Med*. 2011;39(5):967-974. doi:10.1097/CCM.0b013e31820a905a.

32. Rice TW, Wheeler AP, Thompson BT, et al. Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury: The EDEN Randomized Trial. *JAMA*. 2012;307(8):795-803. doi:10.1001/jama.2012.137.

33. Singer P, Anbar R, Cohen J, et al. The tight calorie control study (TICACOS): A prospective, randomized, controlled pilot study of nutritional support in critically ill patients. *Intensive Care Med*. 2011;37(4):601-609. doi:10.1007/s00134-011-2146-z.

34. Berger MM, Pichard C. Understanding the causes of death in INTACT by Braunschweig et al. *JPEN J Parenter Enter Nutr*. 2015;39(2):144. doi:10.1177/0148607114542831.

35. Braunschweig CA, Sheean PM, Peterson SJ, et al. Intensive nutrition in acute lung injury: a clinical trial (INTACT). *JPEN J Parenter Enter Nutr*. 2015;39(1):13-20. doi:10.1177/0148607114528541.

36. Peake SL, Davies AR, Deane AM, et al. Use of a concentrated enteral nutrition solution to increase calorie delivery to critically ill

patients: a randomized, double-blind, clinical trial. *Am J Clin Nutr*. 2014;100:616-625. doi:10.3945/ajcn.114.086322.

37. Petros S, Horbach M, Seidel F, Weidhase L. Hypocaloric vs Normocaloric Nutrition in Critically Ill Patients: A Prospective Randomized Pilot Trial. *JPEN J Parenter Enter Nutr*. 2014. doi:10.1177/0148607114528980.
38. Arabi YM, Tamim HM, Dhar GS, et al. Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial. *Am J Clin Nutr*. 2011;93:569-577. doi:10.3945/ajcn.110.005074.
39. Arabi YM, Aldawood AS, Haddad SH, et al. Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults (supp). *N Engl J Med*. 2015;372(25):2398-2408. doi:10.1056/NEJMoa1502826.
40. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care*. 2011;15(6):R268. doi:10.1186/cc10546.
41. Petros S, Engelmann L. Enteral nutrition delivery and energy expenditure in medical intensive care patients. *Clin Nutr*. 2006;25(1):51-59. doi:10.1016/j.clnu.2005.08.013.
42. Dvir D, Cohen J, Singer P. Computerized energy balance and complications in critically ill patients: An observational study. *Clin Nutr*. 2006;25:37-44. doi:10.1016/j.clnu.2005.10.010.
43. Faisy C, Lerolle N, Dachraoui F, et al. Impact of energy deficit calculated by a predictive method on outcome in medical patients requiring prolonged acute mechanical ventilation. *Br J Nutr*. 2009;101:1079-1087. doi:10.1017/S0007114508055669.
44. Taylor SJ, Fettes SB, Jewkes C, Nelson RJ. Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. *Crit Care Med*. 1999;27(11):2252-2531.
45. Desachy A, Clavel M, Vuagnat A, Normand S, Gissot V, Francois B. Initial efficacy and tolerability of early enteral nutrition with immediate or gradual introduction in intubated patients. *Intensive Care Med*. 2008;34:1054-1059. doi:10.1007/s00134-007-0983-6.
46. Charles EJ, Petroze RT, Metzger R, et al. Hypocaloric compared with eucaloric nutritional support and its effect on infection rates in a surgical intensive care unit: a randomized controlled trial. *Am J Clin Nutr*. 2014;100(5):1337-1343. doi:10.3945/ajcn.114.088609.1.

Bangladesh Crit Care J September 2017; 5 (2): 122-125

Review Article

Combined pulmonary fibrosis and emphysema (CPFE)

Rawshan Arra Khanam

Abstract

Combined pulmonary fibrosis and emphysema (CPFE) is rare but increasingly recognized condition characterized by simultaneous coexistence of both upper lobe predominant emphysema and diffuse pulmonary fibrosis mainly in lower lobe. Patients with CPFE are usually heavy smokers or former smokers. HRCT has a pivotal role in diagnosis. Pulmonary function test showed relatively preserved lung volumes and reduced diffusing capacity of the lung for carbon monoxide (DLCO). Development of pulmonary hypertension (PH) is largely attributed to morbidity in patients with CPFE which is the principal prognostic factor for this condition. However more studies are needed to establish natural history of the disease & treatment option. In this review, we will discuss the current knowledge of the pathogenesis, clinical characteristics, treatment options and prognostic factors of CPFE.

Keywords: *Combined pulmonary fibrosis and emphysema (CPFE), pulmonary arterial hypertension (PAH), forced expiratory volume in 1 second (FEV1).*

Introduction:

Combined pulmonary fibrosis and emphysema (CPFE) is a radiologically defined syndrome characterized by simultaneous coexistence of both upper lobe emphysema and lower lobe pulmonary fibrosis.[1]With the advent of HRCT, the combination of these two conditions has been increasingly described and has been proven to be a prevalent and distinct entity rather than a rare coincidence. Initially the association of Interstitial Pulmonary Fibrosis (IPF) and emphysema was described by Wiggins et al in 1990.[2] But the term CPFE was first used in 2005 by Cottin et al who described a group of patients with CT findings of emphysema in the upper zones and interstitial lung disease (ILD) with pulmonary fibrosis in the lower lobes.[1] In 2005,Grubstein et al. reported an association of fibrosis with emphysema in eight patients, their clinical and functional findings being similar to those of the aforementioned study. The authors also found moderate to severe pulmonary arterial hypertension (PAH) and postulated that smoking is an important factor linking emphysema, pulmonary fibrosis, and pulmonary vascular disease.[3] When CPFE was first described, patients with ILDs other than interstitial pulmonary fibrosis(IPF) were excluded from the study.[1]Later on, CPFE was described in patients with other ILDs, such as connective tissue disease (CTD) associated ILD,[4-7]as well as in patients with microscopic polyangiitis.[8]

1. Dr. Rawshan Arra Khanam, MD (Chest Diseases), Jr. Consultant, Dept. of Resp. Medicine United Hospital Ltd, Gulshan 2, Dhaka, Bangladesh. Email: rawshan.dr@gmail .com

Corresponding Author:

Dr. Rawshan Arra Khanam
MD (Chest Diseases),
Jr. Consultant, Dept. of Resp. Medicine
United Hospital Ltd,
Gulshan 2, Dhaka , Bangladesh.
Email: rawshan.dr@gmail .com
Phone : 01843 894436

The fact that IPF has the worst prognosis in relation to other chronic lung fibrotic diseases, it is important to establish the interstitial lung disease that constitutes the fibrotic component of CPFE. Patients with CPFE are predominantly male, with a history of heavy tobacco exposure, and usually present with severe breathlessness and cough. Physical examination reveals "Velcro" crackles at the lung bases and digital clubbing.[1,9]Pulmonary hypertension is a hallmark of the syndrome and determines poor prognosis.[9]Studies have shown that patients with CPFE associated with CTDs (e.g. rheumatoid arthritis and systemic sclerosis) are significantly younger than their idiopathic CPFE counterparts, are predominantly female, and have less DLCO impairment.[4]

Pathogenesis:

The exact pathogenetic mechanisms that lead to the development of CPFE has yet to be elucidated. Smoking is believed to play a major role as almost all (about 98 %) of CPFE patients are current or former smokers .Tobacco smoke-induced oxidative and nitrative stress in the lungs may amplify inflammation due to reduced histone deacetylase activity that may contribute pathogenetically to both emphysema and fibrosis.[10]Smoking may also contribute to both emphysema and fibrosis by over expression of tumor necrosis factor-α and platelet-derived growth factor-β(PDGF-β).[11,12] Exposure to agrochemical substances has also been described as risk factor for CPFE.[13] Diaz CleLeon *et al*. demonstrated evidence of emphysema in 20% of telomerase mutation carriers with idiopathic pulmonary fibrosis(IPF).[14] Cottin *et al*. reported a dominant mutation 173T in the surfactant protein C gene in a patient with CPFE.[15]

Lung Function in CPFE :

In patients with CPFE, spirometry can be normal or show mild abnormalities. They typically present with preserved or slightly reduced lung volumes in relation to the extent of fibrotic changes in the lungs. Forced vital capacity (FVC), FEV_1 , and Total lung capacity(TLC) values usually within normal limits or slightly reduced. The ratio FEV1/FVC can be normal or reduced (<70 %)and is lower compared to patients

with IPF alone.[16]One possible explanation for normal or subnormal spirometry results despite severe impairment in DLCO is that hyperinflation and greater lung compliance as a result of loss of elasticity in the areas of emphysema can compensate for the losses in volume and lung compliance caused by fibrosis. Another plausible explanation is that fibrosis prevents the early small airway closure observed in patients with emphysema. However, both processes cause damage to the alveolar-capillary membrane resulting in a disproportionately reduced DLCO.[1,17-19] In patients with CPFE, arterial oxygen tension (PaO2) and arterial oxygen saturation (SaO2) at rest, and SaO2 and PaO2 at exercise are significantly decreased.[20,21] Hypercarbia is usually not observed.[1,22] Patients with fibrosis adopt a rapid/ shallow pattern of breathing which increases alveolar ventilation and thus reduces the levels of alveolar and blood pCO2. Exertional dyspnea is the most common presenting symptom in patients with CPFE. on examination, end-inspiratory fine 'velcro' crackles mainly in basal regions are the predominant findings and digital clubbing may also be seen in many of these patients.[22]

Imaging studies in CPFE:

The diagnosis of the CPFE syndrome is based on findings on High-Resolution Computed Tomography (HRCT) of the chest.[1] HRCT scans typically show centrilobular or paraseptal emphysema in the upper lobes, as well as reticular opacities, traction bronchiectasis, septal thickening, ground-glass opacities, and honeycombing in the lower lobes. (Figures 1). Although Usual Interstitial Pneumonia (UIP) is the most common CT pattern, some patients have ground-glass opacities that are more extensive than expected for a UIP pattern and are therefore suggestive of nonspecific interstitial pneumonia, Respiratory Bronchiolitis Interstitial Lung Disease (RB-ILD), and even Desquamative Interstitial Pneumonia (DIP).[1]

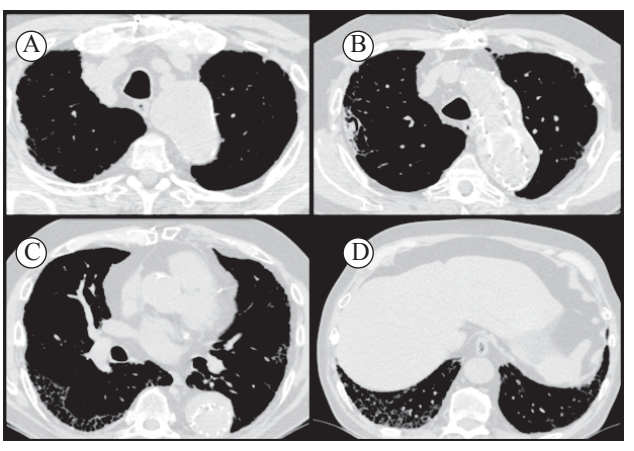


Figure 1 : shows CT scan of the chest of a 67-year-old female patient with combined pulmonary fibrosis and emphysema, showing centrilobular and paraseptal emphysema in the upper lobes (A and B), as well as ground-glass opacities, traction bronchiectasis, and honeycombing in the lower lobes (C and D). Note an aspergilloma in one of the paraseptal bullae in the right upper lobe (white arrow, in B)

Paraseptal emphysema seems to be more common in the CPFE population than in patients with COPD. In the study by Cottin et al. [1] it was observed in 93 % of patients and was suggested to be a hallmark of CPFE. The increased prevalence of paraseptal emphysema in CPFE was also observed in another study. Furthermore, the presence of paraseptal emphysema has been associated with a higher extent of fibrosis in comparison to centrilobular emphysema.[23]

The coexistence of emphysema and fibrosis makes the estimation of the extent of fibrosis really difficult. In the transition zone of the emphysematic to the fibrotic areas it is very tricky to make the appropriate distinction. Brillet et al. [24.] identified three HRCT patterns in 61 patients with CPFE: i) progressive transition (38%) with diffuse emphysema (centrilobular and/or bullous) and zone of transition between bullae and honeycombing, ii) paraseptal emphysema (21 %) with predominant subpleural bullae of enlarging size at the bases and iii) separate processes (23 %) with independent areas of fibrosis and emphysema.

CPFE and pulmonary hypertension (PH):

The prevalence of PAH is exceedingly high in patients with CPFE, and PAH correlates with worse survival.[1,24,25] The prevalence of PAH in CPFE patients varies from 47% to 90%, being considerably higher than that in patients with COPD or IPF alone.[26] Transthoracic echocardiography used to measure pulmonary artery pressure (Ppa) is an operator dependent imaging examination. Furthermore, the presence of emphysema can add further difficulties in the accurate estimation of right ventricular systolic pressure (RVSP). Right heart catheterization (RHC) remains the gold standard for the diagnosis of PAH. Cottin et al. retrospectively estimated the prevalence of PAH in 40 CPFE patients with RHC.[24] Out of them 27 patients (68 %), the mean Ppa was >35 mmHg.

The increased prevalence of PAH in CPFE is probably explained by the coexistence of emphysema and fibrosis. Both cause destruction of the pulmonary vasculature bed and of the lung parenchyma. The destruction of pulmonary vasculature reduces the total cross sectional area. Furthermore, as mentioned CPFE patients are usually hypoxemic due to V/Q mismatching caused by the coexisting emphysema and pulmonary fibrosis. The induced hypoxic pulmonary vasoconstriction is also an important cause of elevated pulmonary arterial pressure. If other pathogenic pathways are implicated, then the development of "out of proportion" PAH remains to be clarified. From a clinical point of view the physician should be vigilant in looking for underlying intermittent nocturnal and exercise induced intermittent hypoxia.[27-29]

Novel noninvasive methods for the diagnosis and quantification of PAH in CPFE patients have been proposed, including time-resolved Magnetic Resonance Angiography (MRA), which allows anatomic imaging of the pulmonary vasculature and evaluation of hemodynamic parameters. Using this technique, Sergiacomi et al. prospectively studied

18 CPFE patients using pulmonary arterial mean transit time and time to peak enhancement as surrogate parameters for hemodynamic data (mean pulmonary artery pressure and pulmonary vascular resistance), which were obtained through right heart catheterization performed three days before time-resolved MRA was performed. Pulmonary arterial mean transit time and time to peak enhancement showed good correlation with the invasive parameters.[30]

Patient Management & Prognosis :

Therapeutic options for patients with CPFE are limited. According to the most recent international guidelines, there are no data on which to make recommendations for treatment of emphysema in the setting of IPF.[31] Smoking cessation is an obvious objective. Oxygen therapy is appropriate for the management of hypoxemia. Inhaled bronchodilators are often prescribed. Currently, there are two approved drugs for the treatment of IPF, pirfenidone and nintedanib.[32] They slowed disease progression by reducing the annual rate of FVC decline independent of the presence of emphysema at baseline.[33] The main concern is not whether pirfenidone and nintedanib are efficacious in CPFE, but whether the rate of FVC decline underestimates their efficacy in this specific subpopulation.

The presence of emphysema and abnormal pulmonary pathology in patients with CPFE and pulmonary hypertension may be associated with an imbalance in the ventilation / perfusion ratio (V/Q), as hypoxic vasoconstriction is one of the main mechanisms to avoid worsening arterial oxygenation. Vasodilator drugs can worsen hypoxemia by inhibiting this mechanism.[34] Specific therapies approved for treating pulmonary arterial hypertension in appropriately designed trials are also necessary to study the effect of these drugs in CPFE patients.[35]

Patients with CPFE seem to be at greater risk for developing lung cancer. Thus, increased vigilance is required for early detection of such lesions. Management of lung cancer in CPFE patients should follow current guidelines.[36] Stem cell therapy is a promising approach for COPD and IPF. Conducting clinical trials of stem cell therapy in CPFE is an intriguing project that could shed further light in the areas of pathogenesis and treatment.[37]

In IPF patients the follow up and response to therapy are based on the measurement of FVC and DLCO. However, CPFE patients tend to exhibit a delay in the reduction of FVC and DLCO which reduces their utility as surrogate markers for disease progression[17, 38]. In addition, a decline in DLCO should be viewed cautiously, as it could be the result of development/progression of pulmonary hypertension which is commonly encountered in CPFE. The annual decrease of the ratio FEV1/ FVC in CPFE seems to be significantly higher compared to IPF.[17, 19]

In a study by Schimdt et al., mortality in CPFE patient was better predicted by the decline in FEV1, while changes in FVC, DLCO and Composite Physiological Index (CPI) were not predictive at 12 months follow-up and only FVC was predictive at 6 months[38]. The prognostic validity of FEV1 increased with increasing severity of emphysema in a dose-dependent fashion. On the other hand, FEV1 had no prognostic role in patients with IPF and with no emphysema.

Conclusion:

CPFE is a recently recognized entity with unique features. It is more frequent (30%) than previously believed and may have a worse prognosis than IPF alone, with PAH being the major determinant of morbidity and mortality. The rate of FEV1 decline is the strongest predictor of mortality.

It is obvious that many aspects of the CPFE syndrome still remain to be explored. Further studies are needed to ascertain the aetiology, morbidity, mortality and management of CPFE, with or without PH, and also to delineate more precisely the boundaries between IPF and patients with CPFE syndrome. Further research is essential to understand etiology, pathophysiology, and management of this distinct clinical entity.

References:

1. CottinV, Nunes H, Brillet PY, Delaval P, Devouassoux G, Tillie-Leblond I, *et al*. Combined pulmonary fibrosis and emphysema: a distinct under recognized entity. Eur Respir J 2005;26:586-93.
2. WigginsJ, Strickland B, Turner-Warwick M. Combined cryptogenic fibrosing alveolitis and emphysema a: the value of high resolution computed tomography in assessment. RespirMed.1990;84(5):365-9.
3. GrubsteinA, BendayanD, SchactmanI, CohenM, ShitritD, KramerMR. Concomitant upper-lobe bullous emphysema, lower-lobe interstitial fibrosis and pulmonary hypertension in heavy smokers: report of eight cases and review of the literature. Respir Med. 2005;99(8):948-54.
4. CottinV, NunesH, MouthonL, GamondesD, LazorR, HachullaE, etal. Combined pulmonary fibrosis and emphysema syndrome in connective tissue disease. Arthritis Rheum.2011;63(1):295-304.
5. LubattiC, ZeniS, IngegnoliF. Combined pulmonary fibrosis and emphysema syndrome in systemic sclerosis. Int J Rheum Dis. 2012;15(5):122-3.
6. CottinV, FreymondN, CabaneJ, CordierJF. Combined pulmonary fibrosis and emphysema syndrome ina patient age 28years with severe systemic sclerosis. J Rheumatol. 2011;38(9):2082-3.
7. CottinV, CordierJF. Combined pulmonary fibrosis and emphysema in connective tissue disease. Curr Opin Pulm Med. 2012;18(5):418-27.
8. Tzouvelekis A, Zacharis G, Oikonomou A, Koulelidis A, Steiropoulos P, Froudarakis M, et al. Combined pulmonary fibrosis and emphysema associated with microscopic polyangiitis. EurRespir J. 2012;40(2):505-7.
9. KishabaT, ShimaokaY, Fukuyama H, YoshidaK, TanakaM, Yamashiro S, etal. A cohort study of mortality predictors and characteristics of patients with combined pulmonary fibrosis and emphysema. BMJ Open.2012;15:2(3).
10. Barnes PJ , AdcockI M, Ito K. Histone acetylation and deacetylation : Importance in inflammatory lung diseases. EurRespirJ 2005;25:552-63.
11. LundbladLK, Thompson- FigueroaJ, LeclairT, SullivanMJ, PoynterME, IrvinCG, *etal.* Tumor necrosis factor-alpha over expression in lung disease :A single cause behind a complex phenotype. Am J Respir Crit Care Med 2005;171:1363-70.

12. HoyleGW, LiJ, FinkelsteinJB, EisenbergT, LiuJY, LaskyJA, *etal.* Emphysematous lesions, inflammation, and fibrosis in the lungs of transgenic mice over expressing platelet-derived growth factor. Am J Pathol 1999;154:1763-75.

13. DaniilZ, Koutsokera A, GourgoulianisK,. Combined pulmonary fibrosis and emphysema in patients exposed to agrochemical compounds. Eur Respir J 2006;27:434.

14. Diazde LeonA, CronkhiteJT, KatzensteinAL, GodwinJD, RaghuG, GlazerCS, *et al* .Telomere lengths, pulmonary fibrosis and telomerase (TERT) mutations. PLoS One 2010;5:e10680.

15. CottinV, ReixP, KhouatraC, Thivolet-BéjuiF, FeldmannD, CordierJF. Combined pulmonary fibrosis and emphysema syndrome associated with familial SFTPC mutation. Thorax 2011;66:918-9.

16. Strickland NH, Hughes JM, Hart DA, et al. Cause of regional ventilation- perfusion mismatching in patients with idiopathic pulmonary fibrosis: a combined CT and scintigraphic study. Am J Roentgenol. 1993;161(4):719–25.

17. AkagiT, MatsumotoT, HaradaT, etal. Coexistent emphysema delays the decrease of vital capacity in idiopathic pulmonary fibrosis.RespirMed.2009;103(8):1209–15.

18. Jankowich MD, Rounds S. Combined pulmonary fibrosis and emphysema alters physiology but has similar mortality to pulmonary fibrosis without emphysema. Lung.2010;188:365–73.

19. KimYJ, Shin SH, Park JW, Kyung SY,Kang SM,Lee SP, etal. Annual Change in Pulmonary Function and Clinical Characteristics of Combined Pulmonary Fibrosis and Emphysema and Idiopathic Pulmonary Fibrosis:Overa3-Year Follow-up. Tuberc Respir Dis.2014;77(1):18–23.

20. Oikonomou A, Mintzopoulou P, Tzouvelekis A, etal. Pulmonary fibrosis and emphysema: Is the emphysema type associated with the pattern of fibrosis? World JRadiol.2015;7(9):294–30

21. Hubbard R, Venn A, Lewis S, Britton J. Lung cancer and cryptogenic fibrosing alveolitis a population-based cohort study. Am J Respir Crit Care Med.2000;161(1):5

22. KitaguchiY, FujimotoK, Hanaoka M, KawakamiS, HondaT ,Kubo K. Clinical characteristics of combined pulmonary fibrosis and emphysema. Respirology.2010;15(2):265–71

23. BrilletPY, CottinV. Letoumelin Petal., Combined apical emphysema and basal fibrosis syndrome (emphysema /fibrosis syndrome):CT imaging features and pulmonary function tests. JRadiol.2009;90 (1Pt1):43–51.

24. CottinV, Le PavecJ, PrévotG, MalH, HumbertM, SimonneauG, et al. Pulmonary hypertension in patients with combined pulmonary fibrosis and emphysema syndrome. EurRespirJ.2010;35(1):105-11.

25. MejíaM, CarrilloG, Rojas-SerranoJ, EstradaA, SuárezT, Alonso D,et al. Idiopathic pulmonary fibrosis and emphysema :decreased survival associated with severe pulmonary arterial hypertension. Chest. 2009;136(1):10-5.

26. Portillo CarrozK, Roldán Sánchez J, Morera PratJ. 18.Combined pulmonary fibrosis and emphysema [Article in Spanish].Arch Bronco neumol.2010;46(12):646-51

27. Corte TJ, WortSJ, GatzoulisMA, etal. Pulmonary vascular resistance predicts early mortality in patients with diffuse fibrotic lung disease and suspected pulmonary hypertension. Thorax.2009;64:883–8.

28. HamadaK, Nagai S, Tanaka S, et al. Significance of pulmonary arterial pressure and diffusion capacity of the lung as prognosticator in patients with idiopathic pulmonary fibrosis.Chest.2007;131:650–6.

29. LettieriCJ , Nathan SD, Barnett SD, etal. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. Chest.2006;129:746–52.

30. Sergiacomi G, Bolacchi F, CadioliM, AngeliML, Fucci F, CruscoS, et al. Combined pulmonary fibrosis and emphysema: 3Dtime-resolved MR angiographic evaluation of pulmonary arterial mean transit time and time to peak enhancement. Radiology. 2010;254(2):601-8.

31. Raghu G, Collard HR, Egan JJ, etal .An official ATS/ERS/JRS/ ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. AmJ Respir Crit Care Med2011;183:788–824.

32. RicheldiL, duBoisRM ,Raghu G.etal; INPULSIS Trial Investigators. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis.NEnglJMed.2014;370:2071–82.

33. Pfeifer M et al. Effect of baseline emphysema on reduction in FVC decline within tedanib int heINPULSIStrials. Pneumologie.2015;69:P254.

34. Portillo K, MoreraJ. Combined pulmonary fibrosis and emphy sema syndrome: a new phenotype within the spectrum of smoking-related interstitial lung disease. Pulm Med 2012;2012:

35. CottinV. Treatment of pulmonary hypertension in interstitial lung disease: do not throw the baby with the bath water. Eur Respir J2013;41:781–783.

36. Detterbeck FC, Lewis SZ, Diekemper R, et al. Executive Summary: Diagnosis and management of lung cancer, 3rded: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013; 143(5Suppl):7S–37S

37. TzilasV, BourosD et al. Prospective phase1open clinical trial to study the safety of adipose derived mesenchymal stem cells (ADMSCs) in COPD and combined pulmonary fibrosis and emphysema (CPFE).ERJ.2015, 46 (suppl59).

38. Schmidt SL, Nambiar AM, Tayob N, et al. Pulmonary function measures predict mortality differently in IPF versus combined pulmonary fibrosis and emphysema. Eur Respir J. 2011;38(1):176–83.

33. KwakN, Park CM, LeeJ, etal. Lung cancer risk among patients with combined pulmonary fibrosis and emphysema. RespirMed. 2014;108:524e30.

34. UsuiK,TanaiC,Tanaka Y,NodaH,Ishihara T.The prevalence of pulmonary fibrosis combined with emphyse main patients with lung cancer. Respirology. 2011;16:326–31.

Bangladesh Crit Care J September 2017; 5 (2): 126-128

Brief Communication

Association of Reduced Lung Function With Major Depressive Disorder

Khandaker Nadia Afreen[1], Masud Imtiaz[2], Mahadi Abdur Rouf[3], Rono Mollika[4] ,Lutfun Nahar[5], Richmond Ronald Gomes[6]

Abstract

Background: *Major Depressive Disorder (MDD) is associated with reduced lung function.*

Objectives: *To observe & compare $FEF_{25\%-75\%}$ in Major Depressive Disorder patients with control group.*

Methods: *This prospective study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January to December, 2014 to assess the lung function status in newly diagnosed MDD patients. For this, 30 newly diagnosed female MDD patients (group B), aged 20 to 50 years were enrolled from the Department of Psychiatry of BSMMU. For control (group A) age, BMI, and occupation matched 30 apparently healthy females were randomly selected by personal contact. $FEF_{25\%-75\%}$ of all subjects were assessed by a portable digital spirometer (PONY FX, Cosmed, Italy). For statistical analysis, ANOVA, Independent sample 't' test were done and p value ≤0.05 was considered as level of significance.*

Results: *$FEF_{25\%-75\%}$was significantly lower (p≤0.001) in all MDD patients than control.*

Conclusion: *From this study it may be concluded that the ventilatory lung function is significantly reduced in newly diagnosed MDD patients.*

Key words: *Major Depressive Disorder (MDD), Forced Expiratory flow ($FEF_{25-75\%}$).*

Introduction:

Depression is the most common chronic condition next to hypertension in general medical practice. Out of ten patients visiting psychiatric outpatient department, one patient is suffering from major depression.[1]

Major Depressive Disorder (MDD) is defined by depressed mood or loss of interest in nearly all activities or both for at least two weeks, accompanied by a minimum of three or four of the following symptoms (for a total of at least five symptoms altogether) such as insomnia or hypersomnia, feeling of worthlessness or excessive guilt, fatigue or loss of energy, diminished ability to think or concentrate, substantial change in appetite or weight, psychomotor agitation or retardation and recurrent thoughts of death or suicide.[1]

1. Dr. Khandaker Nadia Afreen, Assistant Professor, Department of Physiology, Z H Sikder Women's Medical College Hospital, Dhaka.
2. Dr. Masud Imtiaz, Associate Professor, Department of Physiology, Khulna City Medical College, Khulna.
3. Dr. Mahadi Abdur Rouf, Assistant Professor, Department of Physiology, Northern International Medical College, Dhaka.
4. Dr. Rono Mollika, Assistant Professor, Department of Physiology, Enam Medical College, Dhaka.
5. Dr. Lutfun Nahar, Assistant Professor, Department of Physiology, Z H Sikder Women's Medical College Hospital, Dhaka.
6. Dr. Richmond Ronald Gomes, Assistant Professor, Department of Medicine, Ad-din Sakina Medical College, Jessore.

Corresponding Author:

Dr. Khandaker Nadia Afreen
Assistant Professor
Department of Physiology
Z H Sikder Women's Medical College Hospital, Dhaka.
Email: drnadiaafreen@ yahoo.com.
Phone: +8801715566868

Introduction:

Depression is a major cause of morbidity worldwide. The WHO ranks depression as the fourth leading cause of disability worldwide and by 2020, it will be the second leading cause. Population studies have consistently shown major depression is about twice as common in women as in men, although the underlying cause and factor is unclear. Old age people are more affected. People are most likely to suffer their first depressive episode at about 25.7 years in high income and 24 years in low to middle income country[2].

Depression may affect almost all the organs of the body and is responsible for different diseases such as myocardial infarction (MI), other coronary artery diseases, stroke, diabetes, kidney diseases, arthritis, Parkinson's disease and other autoimmune diseases[3].

Researchers found depressed lung function in depressive illness patients which is more in MDD[4]. Carroll D et al found that MDD was associated with lower FEV_1[5]. Whereas Calikoglu et al. found no difference in lung function in MDD patients in comparison to control[6].

Methods

This study was carried out in the Department of Physiology of BSMMU, Dhaka, between January to December 2014. Thirty female newly diagnosed Major Depressive Disorder patients aged 20 to 50 years constituted study group (Group B). Thirty age, sex, BMI matched healthy subjects were taken as control (Group A). Study protocol was approved by Institutional Review Board (IRB) of BSMMU, Shahabag, Dhaka, Bangladesh. Patients were randomly selected from the OPD of Psychiatry Department of BSMMU, Dhaka. Subjects with pregnancy and lactation and evidence of lung diseases, coronary heart disease, diabetes mellitus, neurological disorders, smokers were excluded from the study. An informed written consent was taken from the willing participants. A detail personal, medical, family, socioeconomic, occupational and drug history were recorded in a preformed questionnaire and thorough physical examinations were done and documented. For this assessment of lung function $FEF_{25\%-75\%}$ of all the subjects were recorded by a digital spirometer. Data were expressed as mean ± SE (Standard Error) and also in frequency percent. Independent sample't' test was done to compare between the groups by using SPSS (Windows version 16). In the interpretation of results, p value < 0.05 was accepted as level of significance.

Result

The mean ± SE of age, BMI & Systolic Blood Pressure (SBP) & Diastolic Blood Pressure (DBP) of all the subjects was almost similar in all the subjects & these values where non-significant between 2 groups (Table I).

Table I: Age, BMI and BP in different groups (n=60)

Groups	Age (years)	BMI (Kg/m2)	SBP (mmHg)	DBP (mmHg)
A (n=30)	34.40±1.72 (20-50)	27.03±0.64 (20.2-33.7)	121±1.79 (100-140)	80.83±1.66 (60-95)
B (n=30)	34.13±1.49 (22-50)	27.51±0.56 (20.16-32.2)	120±1.86 (100-140)	79.00±1.73 (60-90)

Statistical analysis

p value Groups	Age	BMI	SBP	DBP
A vs. B	0.907^{ns}	0.574^{ns}	0.654^{ns}	0.449^{ns}

BMI= Body Mass Index, SBP= Systolic Blood Pressure, DBP=Diastolic Blood Pressure

Group A: Apparently healthy subjects (control)

Group B: Newly diagnosed MDD patients before medication

ns = Nonsignifiant (p>0.05), n= Number

The percentage of predicted values of $FEF_{25\%-75\%}$ was significantly lower (P< 0.000) in study group than that of control (Table II).

Table II: Percentage of predicted values of $FEF_{25\%-75\%}$ in different groups

Parameters	Group A (n=30)	Group B (n=30)	P value
$FEF_{25\%}$	71.63±3.42 (29-101)	41.33±4.24 (10-90)	0.000***
$FEF_{50\%}$	71.13±3.69 (26-102)	36.20±4.54 (4-95)	0.000***
$FEF_{75\%}$	65.86±4.72 (78-97)	33.56±4.32 (4-88)	0.001***

Group A: Apparently healthy subjects (control)

Group B: Newly diagnosed MDD patients before medication

***= Significant (p≤0.001)

n= Number

Discussion

The present study has been undertaken to observe pulmonary functions in 30 newly diagnosed female MDD patients. Pulmonary functions were assessed by measuring $FEF_{25\%-75\%}$ with a portable micro spirometer. $FEF_{25-75\%}$ actually represents Force Expiratory Flow in the middle half of FVC. Different studies were done to see different effects on others parameters like FVC, FEV_1, PEFR of lung function status. But very few studies were done to see different effects on Force Expiratory Flow in the middle half of FVC. This variable were also studied initially in 30 apparently healthy subjects for comparison. All data in the healthy subjects were normally distributed. In this study, value of all the lung function variable of healthy subjects were within physiological limit [7,8]. Again, both the groups (control and study) were comparable in their biological characteristics as there was no significant difference in the confounding variables such as age, BMI and occupation. However, to exclude the effect of age and BMI on the measured values of ventilatory variables, measured values as the percentage of predicted values were used for analysis. Different researchers found that pulmonary functions are significantly reduced in patients with depressive illness especially in major depressive disorder patients. Islam and his colleagues investigated lung function by spirometry in depressive disorder patients and found lung function parameters were significantly lower in depressive disorder patients in comparison to healthy subjects[4]. Another study was done on US soldiers experience to find out association between MDD with lung function. But they did not found any significant association between MDD and poor lung function[5]. Calikoglu and his colleagues investigated lung function test by spirometry in 30 female MDD patients[6]. After comparing with control group, they found that dyspnea was higher in MDD. The apparent effect of depression on poor lung function in MDD patients may be explained by the reduced psychomotor activity along with poor respiratory muscle strength in depressive illness [9].

Conclusion

The result of this study may be concluded that ventilatory function of lung are significantly reduced in MDD patients.

References :

1. Whooley, MA and Simon, GE. Managing depression in medical science. *N Engl J Med*. 2000;. 343: 1942-50.
2. Bromet E, Andrade LH, Hwang I, Sampson, NA, Alonso J, Girolamo Gd, et. al (2011). Cross national epidemiology of DSM IV major depressive episode, *BMC Medicine.*9:90.
3. Goldberg, S . Goldberg, S depression scale. *Ann of Biol Res*. 2012;3(9): 4564-73.
4. Islam, S, Jahan, N, sultana, N, Akhter, R.FVC, FEV1 and FEV1/FVC% in patients with depressive illness and their relationships with the level of depression. *J Bangladesh soc Physiol* 2010*;* 5(2): 94-100.
5. Carroll, D, Phillips, AC, Gale, CR, Batty, GD .Generalized anxiety disorder is associated with reduced lung function in the Vietnam experience study. *Psychosom med.* 2011;73:716-20.
6. Calikoglu, M, Sahin, G, Yazici, AE, Yazici, K and Ozisik, S .Pulmonary muscle strength, pulmonary function tests and dyspnea in women with major depression. *J women health.2004;13* (1):1-7.
7. American Thoracic Society. Medical sections of the American Lung Association. *Am Rev Respir Dis.* 1991;144: 1202-18.
8. Global Initiative for Chronic obstructive Lung Disease. Spirometry for Health Care Providers 2010; [internet sited by May 23, 2013] available from *http//www. Goldcopd. Org.*
9. Kupfer, DJ, Weiss, BL, Foster, FG, Detre, TP, Delgado, Portland, RM . Psychomotor activity in affective states. *Arch Gen Psy*.1974; 30(6): 765-8.

Bangladesh Crit Care J September 2017; 5 (2): 129-131

Case Report

Guillain-Barré Syndrome Masquerading As Cervical Myelopathy

Uzzwal Kumar Mallick[1], Badrul Alam[2], Mohammad Asaduzzaman[3]

Abstract

Guillain-Barré syndrome (GBS) is an acute inflammatory demyelinating polyneuropathy. In typical cases, the first symptoms of GBS are pain, numbness, paresthesia, weakness in the limbs. Autonomic involvement is common and causes urinary retention and ileus. Most of these symptoms overlap with those of cervical myelopathy. Therefore, correct diagnosis of GBS in a patient with symptomatic cervical myelopathy or in a patient with atypical manifestations of GBS can be difficult, especially early in the course of GBS.

We report a 60-year-old man who was admitted to the neurosurgery department with worsening neck pain, numbness and weakness in the hands initially thought to be secondary to progressive cervical myelopathy. However, his symptoms rapidly progressed to flaccid areflexic quadriparesis and respiratory difficulty within few days and shifted to ICU for ventilator support. Electrophysiological studies and cerebrospinal fluid analysis were consistent with an acquired demyelinating polyradiculoneuropathy. We planned for immunotherapy with intravenous immunoglobulin , but his condition was improving day by day with conservative treatment , so immunotherapy with intravenous immunoglobulin was not initiated. Any patient presenting as unexplain Cervical myelopathy, GBS should be kept in mind before planning any surgical intervention.

Keywords: *Guillain-Barré syndrome (GBS); cervical myelopathy, Nerve conduction study (NCS)*

Introduction:

Guillain-Barré syndrome (GBS)-Acute Inflammatory Demyelinating Polyradiculoneuropathy, (AIDP) is an acute polyneuropathy that commonly manifests with areflexic flaccid paralysis associated with variable sensory and autonomic disturbances.[1] Albuminocytologic dissociation; elevated cerebrospinal fluid (CSF) protein without pleocytosis is a typical finding in GBS.[1, 2] GBS is a neurological emergency that affects 1:100,000 person-years in the Western World .[1,3] Symptoms progress over a period of up to 4 weeks. During and after the acute phase of GBS, the prognosis is extremely variable, nearly 25% of patients develop respiratory impairment, 20% remain severely disabled, and 5% may die, despite immunotherapy[1].

1. Dr. Uzzwal Kumar Mallick, Registrar, Dept. of Critical Care Medicine, National Institute of Neurosciences and Hospital, Dhaka.
2. Dr. Badrul Alam, Professor of neurology, National Institute of Neurosciences and Hospital, Dhaka.
3. Dr. Mohammad Asaduzzaman, Assistant registrar, Dept. of CCM, National Institute of Neurosciences and Hospital, Dhaka

All authors had equal contribution in writing the manuscript.

Corresponding Author:

Dr. Uzzwal Kumar Mallick
Registrar
Dept. of Critical Care Medicine
National Institute of Neurosciences and Hospital
Dhaka, Bangladesh
Cell: 01712715180
E-mail: ukm1980@gmail.com.

Cervical myelopathy is one of the most common causes of spinal cord dysfunction in older persons[4]. The aging process results in degenerative changes in the cervical spine that in advanced stages can cause compression of the spinal cord[4]. On the other hand, GBS and Cervical myelopathy both may present as subacute progressive paraparesis or quadriparesis[5]. Patients with GBS typically have reduced or absent reflexes and may have cranial nerve involvement[1]. While patients with cervical myelopathy are usually present with neck and arm pain with weakness and hyperreflexia and do not have cranial nerve involvement[4]. However, these clinical signs could be absent early at the time of the presentation. Therefore, neuroimaging and electrophysiological studies are often required in solving the diagnostic complexity[5].

Here, we present a case to report of GBS in a patient with chronic cervical myelopathy. We encourage detailed neurologic assessment in patients with cervical myelopathy especially in atypical presentation before consideration for surgical intervention.

CASE REPORT

A 60-year-old man, hypertensive, shop-keeper, admitted in the neuro-surgery department in National Institute of Neurosciences and Hospital, Dhaka, with the complaints of neck pain for five months. There was no history of bulbar dysfunction, sphincter abnormality, or autonomic symptoms. He had no history of preceding upper respiratory tract or gastrointestinal infection. Neurological examination revealed no cranial nerve dysfunction or generalized hypotonia,

Plantar responses were flexor on both sides, sensory and cerebellar examinations were normal.

Whole cervical spine MRI showed multilevel degenerative changes with moderate cord compression, most prominent at the C4-C5 level (Figure 1). The initial working diagnosis was Cervical myelopathy with subacute worsening (compression of the spinal cord). On the 4th day of admission, in neurosurgery dept. the patient's condition became progressively worse; he developed moderate flaccid quadriplegia (power grade 3/5), absent deep tendon reflexes, and swallowing difficulty.

Gradually he developed breathing difficulty and he was transferred to the intensive care unit (ICU).

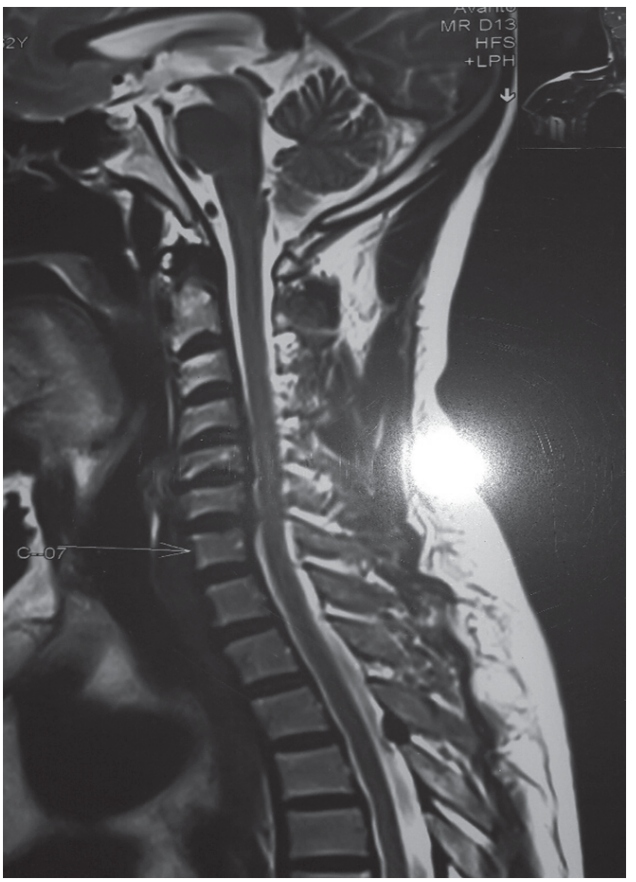


Fig-1: Shows the non-compressive lesion of the cervical cord with signal change on C5/6.

Two days after admission in ICU his respiratory function further deteriorated. ABG (arterial blood gas) showed type-II respiratory failure, then endotracheal intubation was done and patient was kept on mechanical ventilation. During this time Nerve conduction study (NCS) was done and it showed AIDP variety. CSF report showed protein 60 mg/dl, Glucose 3.42 mmol/L, Cells 4/HPF. He was planned to have immunotherapy with intravenous immunoglobulin (IVIG) but from the 7th day of ICU admission, the patient's condition was gradually improving. After weaning we did tracheostomy on 11th day of mechanical ventilation. He was transferred to the HDU on next day. After seven days of staying in HDU, he showed marked improvement and was able to swallow normally, and his muscle strength improved both in the upper and lower extremities. He was discharged home with closure of tracheostomy tube. His hematological and routine metabolic workup were normal. He was discharged in a stable condition, and was advised to get daily physiotherapy. He was advised to come for follow-up for myelopathy. After six months he came for follow-up and we found that he fully recovered and he could walk independently without any helping aid.

Discussion

Acute myelopathy due to spinal cord compression can be clinically confused with GBS since the deep tendon reflexes may be depressed in these condition[4]. However, early bowel and bladder dysfunction and a sensory level point to myelopathy that is usually supported by finding a focal lesion in the MRI of the spine[4,5].

When our patient was admitted to the neurosurgery department, he had neck pain and numbness in the fingers that were thought to be due to the progression of cervical myelopathy. Neck pain is not common symptoms of GBS; it is more prevalent in cervical myelopathy. However, neck pain has been rarely reported in the pharyngeal-cervical-brachial variant, which accounts for approximately 3% of total GBS cases[2]. Our case may represent this variant that would also explain why he developed bulbar weakness soon after admission. Alternatively, his disease could have started with axial and neck hypotonia that had aggravated her preexisting cervical roots compression. The rapid progression of her upper limbs weakness followed by acute quadriplegia and arreflexia high suspicion of AIDP.

The diagnostic challenge, in this case, is that his cervical MRI was abnormal when he attended the ED, showing cervical myelopathy confirmed by signal changes within the cervical spinal cord at the C5 level (Fig-1). In this case, the diagnosis of GBS was confirmed by the electrophysiological study that demonstrated slowing of the nerve conduction velocities, partial motor conduction block that are not typical findings of cervical myelopathy[6] . High protein level in CSF may be observed early in GBS course, although, protein level may not yet be prominent until 1-2 weeks after the onset of weakness, rarely they do remain persistently normal[1,2] . In this case, we diagnosed acute polyradiculoneuropathy superimposing a chronic cervical myelopathy. In reviewing the literature, we found no association between GBS and cervical myelopathy. Only one case similar to our case was reported previously by Abai et al., a 39-year-old lady developed progressive lower and upper limbs weakness and her MRI neck demonstrated cervical spondylosis with cord compression at C5/C6[5]. The diagnosis was confirmed by electrophysiological studies. The authors assumed that the patient developed GBS followed by cervical myelopathy while our case is known to have cervical myelopathy followed by GBS. Considering this case and the previously reported one, variable development of symptoms of GBS may coexist in a patient with cervical myelopathy

highlighting the importance of the making appropriate diagnosis especially in patients considered for surgery.

Conclusion

GBS and cervical myelopathy may coexist. The clinicians should suspect GBS in a patient with cervical myelopathy who present with symptoms like neck pain, numbness and weakness in the hands with diminish or loss of reflexes that cannot be explained by cervical cord compression alone.

Conflict of Interest

None

Consent for Manuscript and Figure

The patient and his wife gave written consent for the use of personal and medical information for the publication of this case report and accompanying images.

References:

1. Yuki N, Hartung HP (2012) Guillain-Barré syndrome. N Engl J Med 366: 2294-304.
2. Dimachkie MM, Barohn RJ (2013) Guillain-Barré syndrome and variants. NeurolClin 31: 491-510.
3. Alter M (1990) The epidemiology of Guillain-Barré syndrome. Ann Neurol 27: S7-12.
4. Wu JC, Ko CC, Yen YS, Huang WC, Chen YC, et al. (2013) Epidemiology of cervical spondylotic myelopathy and its risk of causing spinal cord injury: a national cohort study. Neurosurg Focus 35: E10.
5. Abai S, Kim SB, Kim JP, Lim YJ (2010) Guillain-barré syndrome combined with acute cervical myelopathy. J Korean NeurosurgSoc 48: 298-300.
6. Hadden RD, Cornblath DR, Hughes RA, Zielasek J, Hartung HP, et al. (1998) Electrophysiological classification of Guillain-Barré syndrome: clinical associations and outcome. Plasma Exchange/SandoglobulinGuillain-Barré Syndrome Trial Group. Ann Neurol 44: 780-8.

Bangladesh Crit Care J September 2017; 5 (2): 132-134

Case Report

Lightning Injury

Rajib Hasan[1], Md. Motiul Islam[2], ARM Nooruzzaman[3] , Mohiuddin Ahmed[3], Mohammad Rabiul Halim[1], Muhammad Mahbubur Rahman Bhuiyan[1], Muhammad Moshiur Rahman[1], Kazi Nuruddin Ahmed[1], Tapash Chandra Roy[4]

Abstract

Lightning injuries are injuries caused by lightning strikes. Lightning delivers a massive electrical pulse over a fraction of a millisecond. It can kill a person by instantaneously short-circuiting the heart. Lightning injuries have been the second most common cause of storm-related death in the United States[1,2,3]. Far more injuries and deaths occur in tropical and subtropical countries. Here we present the case report of a 45 year old Bangladeshi lady who was struck by lightning. Patient presented with immediate loss of consciousness and some superficial skin burn about 1 hour following the event. Over the next few days she was found to have intracerebral haemorrhage and infarct, tympanic membrane rupture and bilateral cataract. Surprisingly patient did not suffer from any cardiac or renal injury. All lightning strike victims should receive emergency medical support on site of injury and be treated in intensive care units (ICU) equipped with multiple organ support facility.

Introduction

For most thunderstorms, 90% of lightning strikes from cloud to cloud. From 10-30% of lightning can be cloud to ground, depending on the storm. Lightning strikes the earth more than 100 times each second and 8 million times per day. Worldwide, approximately 50,000 thunderstorms occur per day that may result in forest fires, injury to animals and people and damage to electrical and communications lines and electronics[4]. Since lightning is caused by common meteorological conditions, anyone is a potential victim.

Case Report

Mrs. X, a 45 years old non-diabetic, normotensive previously healthy lady hailing from Enayetpur, Sirajgonj got admitted to the medical ICU of a tertiary care hospital through Emergency Room (ER) with the complaints of unconsciousness, labored breathing, feeble pulse, unrecordable blood pressure & superficial burn injury over face, scalp, chest and thigh following hit by a lightning strike during a thunderstorm about 1 hour back. Patient got struck by a lightning bolt one hour back while she was sitting beside a pond. Following the strike patient fell from sitting position and did not sustain any injury due to fall. There was no history of vomiting or convulsion. There were four people altogether at the site of the lightning strike; two children, one young lady and the discussed patient. The two children were dead on spot but the young lady suffered mild physical trauma with rupture of tympanic membrane.

After admission in ICU patient was thoroughly evaluated. She was unconscious with GCS scoring of 5/15 (E_1,V_2,M_2), pupils were bilateral 4.5 mm and sluggishly reacting to light, planter response were bilaterally extensor. She was hemodynamically unstable with heart rate of 100 bpm, sinus rhythm and BP of 80/60 mm of Hg. Respiration was labored with SpO_2 of 80% with 5L O_2 through face mask. Arterial blood gas analysis showed features of type I respiratory failure. Patient was having profuse vomiting. On physical examination she was noted to have multiple superficial burn injury over face, neck, chest and lateral part of right thigh. ENT examination was normal with intact tympanic membranes and ophthalmological examination also revealed no abnormalities.

After initial assessment immediate attempts were made for resuscitation of the patient by endotracheal intubation and putting on mechanical ventilator support to correct hypoxia. Intravenous pressors were started after adequate fluid resuscitation to achieve hemodynamic stability. All supportive care were established according to the standard ICU protocol. All baseline investigations were sent.

Following initial resuscitative measures patient got stabilized hemodynamically with pressor support, hypoxia was corrected, urine output was adequate. Blood reports showed neutrophilic leukocytosis with mildly raised troponin I and moderately raised creatine phosphokinase (CPK). Liver function, kidney function and other reports were within normal limits. Bedside echo was normal with no regional wall motion abnormalities with LVEF of 60%.

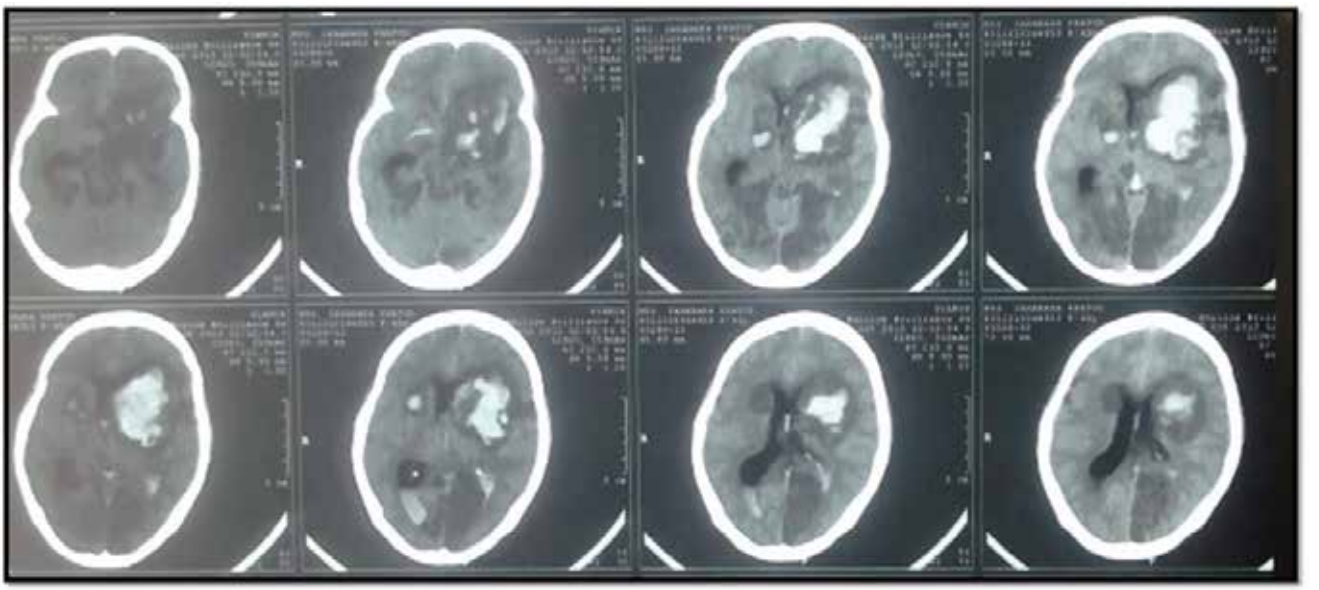
On the second day during her stay in ICU, patient's vitals became more stabilized. BP was stable without any pressor support, urine output remained adequate. Lab reports also showed improvement with down going troponin I and CPK.

1. Senior Clinical Staff, ICU, Asgar Ali Hospital 111/1/A, Distillery Road, Gandaria, Dhaka-1204, Bangladesh.
2. Associate Consultant, Medical ICU, Asgar Ali Hospital, 111/1/A, Distillery Road, Gandaria, Dhaka-1204, Bangladesh.
3. Consultant, Internal Medicine & ICU, Asgar Ali Hospital, 111/1/A, Distillery Road, Gandaria, Dhaka-1204, Bangladesh.
4. Resident Medical Officer, ICU, Asgar Ali Hospital, 111/1/A, Distillery Road, Gandaria, Dhaka-1204, Bangladesh.

Corresponding Author:

Dr. Rajib Hasan (MBBS, FICM)
Senior Clinical Staff, ICU,
Asgar Ali Hospital, 111/1/A, Distillery Road, Gandaria,
Dhaka-1204, Bangladesh.
Email: dr.rajib.icu@gmail.com

But there was bloody discharge from the right auditory canal. Otoscope examination revealed ruptured tympanic membrane. Patient's pupils were also becoming increasingly non-reacting to light. Ophthalmological examination revealed development of bilateral cataract. Patient's level of consciousness however remained unchanged at GCS 5/15. She was still on mechanical ventilator support though oxygen requirement was gradually decreasing.



On the third day, as the patient was not improving neurologically, a CT scan of brain and brainstem was done which revealed "Bilateral capsulo basalganglionic acute haematoma with intraventricular extension with acute occipital and brainstem infarct". Patient's management was headed by an intensivist and special support was taken from internist, cardiologist, general surgeon, ophthalmologist, ENT surgeon and neurosurgeon. Neurosurgical intervention was advised but patient's next of kin denied any surgical treatment although her clinical condition including possible poor prognosis was discussed in details with her relatives. The following day, patient was transferred to a different facility against our medical advice and eventually we lost contact with the patient.

Discussion

Two-thirds of lightning-associated deaths occur within one hour of injury and are generally due to a fatal arrhythmia or respiratory failure[5]. Approximately 30 percent of those struck by lightning die and up to 74 percent of survivors may have permanent disabilities[6].

Lightning injury is caused by a DC current exposure that lasts from 1/10 to 1/1000 of a second, but often has voltages that exceed 10 million volts. Peak temperature within a bolt of lightning rises within milliseconds to 30,000 Kelvin (five times hotter than the sun), generating a shock wave of up to 20 atmospheres induced by the rapid heating of the surrounding air [7,8,9]. This shock wave then can be transmitted through the body and result in mechanical trauma. Injuries due to electricity occur by three mechanisms [10]:

- Direct effect of electrical current on body tissues
- Conversion of electrical energy to thermal energy, resulting in deep and superficial burns
- Blunt mechanical injury from lightning strike, muscle contraction, or as a complication of a fall after electrocution.

Serious lightning injuries are likely to primarily cause cardiac and neurologic injury. Otologic injury and cutaneous burns have also been noted as frequent sequelae of these events. Cataract formation resulting from lightning injury typically occurs within days to weeks of injury, as was the case in our patient.

American Heart Association recommends, prolonged cardiopulmonary resuscitation (CPR) should be undertaken following electrical injury regardless of the initial rhythm, since most victims are young and good outcomes have been noted even among patients with asystole[11]. The treatment for particular arrhythmias is unchanged. Patients can have spontaneous cardiac activity but paralysis of the respiratory muscles. Prompt restoration of gas exchange via a secure airway may prevent secondary cardiac and neurologic dysfunction or death. However, in our patient there was no cardiac involvement or arrhythmia and cardiac resuscitation was not needed.

The person who suffers a serious lightning strike has sustained significant trauma. Appropriate trauma resuscitation should be performed, beginning with a rapid assessment of the airway and cardiopulmonary status. Cervical spine immobilization is necessary, and tetanus prophylaxis should be administered.

Neurologic complications after lightning consist of: 1) immediate and transient variety presenting with the symptomatology which includes loss of consciousness, amnesia, confusion, headache, paresthesia, and weakness; 2) immediate and prolonged or permanent variety which

includes post-hypoxic-ischemic encephalopathy, intracranial hemorrhages, cerebral infarction and cerebellar syndromes; 3) delayed presentation after weeks to months including motor system disease and movement disorders and 4) destructive injuries secondary to falls[12]. Our patient's neurological complications fall in the second category as she had bilateral basal ganglia haemorrhage with occipital and brainstem infarct.

Intracranial hemorrhages in lightning-strike patients often appear in basal ganglia[13-16]. Studies suggest that current may enter via orifices (eyes, nose, ears) and travel caudally from neocortex toward the basal ganglia and brainstem[12]. Blood vessels and neural tissue have been found to carry more current per unit area than the other tissues and to become damaged before the surrounding tissues, in an animal model. Preferential conduction along Virchow-Robin spaces in the anterior perforated substance has been a proposed mechanism of bleed after a lightning strike[14]. However, this mechanism does not explain the predilection for basal ganglia, as was the case in our patient.

Patients with soft tissue injuries from a severe electrical exposure require aggressive IV fluid replacement, especially if there are signs of muscle necrosis. The approach to fluid resuscitation in lightening is similar to that used for the prevention of acute kidney injury from rhabdomyolysis. Our patient had no muscle injury as evidenced by mildly raised CPK.

In general, wounds in lightening injury patients are treated in a similar manner to flame or other thermal burns. Patients with burns may require transfer to a burn unit and treatment with fasciotomy, escharotomy, extensive skin reconstruction, or limb amputation. Our patient only sustained superficial skin burns which was treated by topical antibiotics and frequent dressing.

After stabilization, careful otologic and audiometric examinations may reveal injuries that are amenable to delayed repair. Ophthalmologic evaluation is warranted because of the potential for delayed development of cataracts, particularly following lightning injury. Cataracts generally develop several days after injury, though there may be a lag of up to two years. Our patient developed bilateral cataract and ruptured tympanic membrane on the second day after injury.

In case of patients who recover from the various types of injury sustained by lightning attack, early institution of physical therapy may prevent deterioration in functional status, and psychiatric consultation may be required for patients who develop behavioral disturbances or post-traumatic stress disorder.

References :

1. Centers for Disease Control and Prevention. Lightning-associated deaths-United States, 1980-1995. Morbidity Mortality Weekly Reports. 391-4. 1998.
2. Jensenius JS. A detailed analysis of recent lightning deaths in the United States. 23rd International Lightning Detection Conference; 2014.
3. Roeder WP. Lightning has fallen to third leading source of US storm deaths. National Weather Association Annual Meeting; 2012.
4. Okafor UV. Lightening and acute renal failure: A review. Ren Fail 2005; 27:129-34.
5. Blumenthal R. Lightening fatalities on the South African Highveld: a retrospective descriptive study for the period 1997-2000. Am J Forensic Med Pathol 2005; 26(1):66-9
6. Whitecomb D, Martinez J A, Daberkow D. Lightening injuries. South Med J 2002; 95:1331-4.
7. Bier M, Chen W, Bodnar E, Lee RC. Biophysical injury mechanisms associated with lightening injury. Neurorehabilitation 2005; 20(1):53-62.
8. Lee RC. Injury by electrical forces: Pathophysiology, manifestations, and therapy. Curr Probl Surg 1997; 34(9):677-764.
9. Lee RC, Zhang D, Hannig J. Biophysical injury mechanisms in electrical shock trauma. Annu Rev Biomed Eng 2000; 2:477-509.
10. Cooper MA. A fifth mechanism of Lightening injury. Acad Emerg Med 2002; 9(2):172-4
11. Anonymous. Part 8: advanced challenges in resuscitation. Section 3: special challenges in ECC. 3G: electric shock and lightning strikes. European Resuscitation Council. Resuscitation 2000; 46(1–3):297–9.
12. Cherington M. Neurologic manifestations of lightning strikes. Neurology. 2003;60:182–5
13. Carrera-Izquierdo E, Morán-Sánchez JC, Carrera-Izquierdo M, Jiménez-Corral C, Rodríguez-Recio FJ, Ocastegui-Candial JL. Intracranial haemorrhage secondary to a lightning strike: A case report. Rev Neurol.2004;39:530–2.
14. Ozgun B, Castillo M. Basal ganglia hemorrhage related to lightning strike. AJNR Am J Neuroradiol.1995;16:1370–1.
15. Stanley LD, Suss RA. Intracerebral hematoma secondary to lightning stroke: Case report and review of the literature. Neurosurgery. 1985;16:686–8.
16. Thomas M, Pillai M, Krishna Das KV. Intracranial haematoma resulting from lightning stroke. J Assoc Physicians India. 1991;39:421–2.

Bangladesh Crit Care J September 2017; 5 (2): 135-138

Case Report

A case of a recurrent GBS

Md. Mahabub Morshed[1], A. K. M. Ferdous Rahman[2], Syed Tariq Reza[3], Muhammad Asaduzzaman[4], Mohammad Selim[5], Mohammad Asrafuzzaman[6]

Abstract

Background: *Guillain-Barré syndrome is an acquired polyradiculo-neuropathy, often preceded by an antecedent event. It is a monophasic disease but a recurrence rate of 1–6 % is documented in a subset group of patients.*

Case presentation: *Thirty-five-years-old female with past history of near complete recovery following Guillain-Barré syndrome 17 years back presented with acute, ascending symmetrical flaccid quadriparasis extending to bulbar muscles and respiratory compromise needing mechanical ventilation. Nerve conduction study revealed AMAN variant of Guillain-Barré syndrome. Cerebrospinal fluid analysis done after 1 weeks during recurrent episode revealed albuminocytologic dissociation. She was treated with intravenous immunoglobulin resulting in a remarkable recovery.*

Conclusion: *Recurrence of Guillain-Barré syndrome can occur in a subset of patients with Guillain-Barré syndrome even after many years of asymptomatic period. Most patients with recurrent GBS respond favourably to treatment with plasmapheresis or IVIG.*

Keywords : *Recurrent Guillain-Barré syndrome (GBS), Acute motor axonal neuropathy(AMAN), Asymptomatic period.*

Background:

Guillain-Barré syndrome is an acquired polyradiculo-neuropathy, often preceded by an antecedent event[1,2,3]. It is a monophasic disease but a recurrence rate of 1–6 % is documented in a subset group of patients following an asymptomatic period of few months to years (4 months – 10 years)[3,4,5,6]. Guillain-Barré syndrome (GBS) is a heterogeneous group of disorders due to an immune-mediated inflammation and demyelination of the peripheral nervous system, following an antecedent illness in two thirds of the patients, commonly an infection[1,2,3]. It is a medical emergency which usually presents with acute onset, rapidly progressive symmetrical ascending flaccid paralysis of the limbs with accompanying absent or diminished deep tendon reflexes. It is often associated with sensory symptoms, cranial nerve involvement, less commonly autonomic dysfunction and respiratory compromise.

It is suggested by Kuitwaard et al. that there is a subset of patients with GBS who are susceptible for recurrence.Recurrent GBS (RGBS) is characterized by 2 or more attacks of acute inflammatory demyelinating neuropathy with an onset to peak time of 4 weeks or less, and having complete or near complete recovery[3,5]. Compared to non-recurrent GBS group recurrence is characterized by younger age (mean age, 34.2 vs. 46.9 years; 44% were <30 years vs. 22% of the non-recurrent group), milder course of disease and having Miller-Fisher variant of GBS during their first attack. The mean interval between attacks was 7 years (range, 2 months to 37 years)[7].

Literature revealed that the patients with recurrence had similar but more severe symptoms and signs in subsequent episodes while having similar or different antecedent event[3,6]. It is important to distinguish recurrent GBS from GBS with treatment related fluctuations (GBS-TRF) and chronic inflammatory demyelinating polyradiculo-neuropathy (CIDP) as the treatment regimens are different. Cerebrospinal fluid (CSF) shows albuminocytologic dissociation in 82–90% of the patients with GBS after 10–14 days from onset of the illness[8]. Electrophysiological studies and CSF analysis are taken to aid clinical diagnosis of GBS but normal CSF profile can be found in 10 % of GBS patients throughout the disease. Therefore normal values cannot rule out GBS[9].

We present a case of RGBS presenting after 17 years, adding to the limited number of cases with a long asymptomatic interval. Such reported cases from South-Asia are rare.

1. Dr. Md. Mahabub Morshed, MBBS- Post-graduate Student. MD. CCM (Thesis)
2. Dr. A. K. M. Ferdous Rahman, MBBS, MD (CCM)
3. Dr. Syed Tariq Reza, MBBS, MD (CCM)
4. Dr. Muhammad Asaduzzaman, MBBS, MD (CCM)
5. Dr. Mohammad Selim, MBBS, MCPS(Medicine), MD (CCM)
6. Dr. Mohammad Asrafuzzaman, MBBS- Post-graduate Student (CCM)

All the authors work in the Intensisive Care Unit of Dhaka Medical College Hospital, Dhaka, Bangladesh.

Corresponding Author:

Dr. Md. Mahabub Morshed
Post-graduate Student
MD. CCM (Thesis)
E-mail : mahasinmorshed@yahoo.com

Case Presentation:

Mrs Jannatul, 35 years old young lady presented with generalized weakness of four limbs for 2 days with a previous history of loose stool,On next day of admission her condition deteriorates & she has been shifted to ICU due to heaviness in chest with tingling sensation of face. After admission to ICU,patient developed respiratory distress & patient was intubated.Patient was diagnosed as a case of GBS on 2000 and was aided with mechanical ventilation at that time, She Improved with the course of treatment except some residual weakness in right lower limb. Since then she was on her previous health status until 2 days back when she developed loose motion and weakness. On examination upon arrival at ICU she was found conscious and oriented, pulse 80 bpm, BP was recorded 110/70 mm of Hg, afebrile and not dyspneic. On neurological examination higher mental functions were intact. Cranial Nerves including fundoscopy was normal, Bulk of muscles were normal, power was 1/5 in both upper limbs. and 0/5 in both lower limbs. All modalities of sensations were intact. All reflexes were absent and plantar was bilaterally absent. Gait couldn't be evaluated due to muscle weakness, cough reflex were poor. She was intubated on 5th day of illness needed mechanical ventilation and successfully extubated on 23rd day of her illness.

Investigations:

Unfortunately no investigation papers of patients 1st episodes of illness was found except the discharge paper.

CSF study of this episode:

Cerebrospinal fluid profile	Day 07
CSF Glucose (mmol/L)	4.2
Proteins (g/dL)	
(normal: 15 – 40 g/dL)	68
White blood cells/HPF	
(normal: 0 – 5 cells/HPF)	Nill
Neutrophils %	-
Lymphocytes %	-
Red blood cells/HPF	-
Random blood glucose tested at the time of lumbar puncture (mmol/L)	5.7

Sensory Nerve conduction Study:

Nerve	Region	Distal latency (ms)	Conduction velocity (m/s)	Amplitude (uV)
Median (Right)	Wrist	2.24	62.5	44.90 uV
Ulnar (right)	Wrist	1.88	63.8	47.6 uV
Sural(Left)	Wrist	2.18	55	20.50 uV

Motor Nerve conduction Study:

Nerve	Region	Distal latency (ms)	Conduction velocity (m/s)	Amplitude (mV)
Median (Right)	Palm	1.04	19.1 m/s	3.880 mV
	Wrist	4.70	53.3 m/s	2.680 mV
	Cub. fossa	9.20		2.230 mV
Ulnar (Right)	Wrist	4.20	27.7	1.170
	Below Elbow	11.42	22.4	940.0
	Above Elbow	14.10		450.0
Peroneal(left)	Ankle	-	0	-
	Fib Neck	-	0	-
	Popliteal fossa	-	-	-
Tibial (left)	Ankle	7.58	41.8 m/s	990.0 uV
	Pop fossa	16.90		610.0 uV

Discussion:

GBS is an acute, immune mediated inflammatory polyradiculo-neuropathy involving the peripheral nervous system. Onset is preceded by an antecedent event in two thirds of the patients, usually an upper respiratory tract infection or a diarrheal illness[1,2,3], where the causative agent is assumed to trigger an immune response against the gangliosides and glycolipids distributed along the myelin sheaths and peripheral nervous system. This results in marked inflammation of the peripheral nerves, resulting in demyelination and defective impulse propagation. It is a heterogeneous group of disorders which involves motor, sensory and autonomic nervous systems to varying degrees depending on the sub type; [1] Acute inflammatory demyelinating polyneuropathy, [2] Acute motor axonal neuropathy, [3] Acute motor sensory axonal neuropathy, [4] Miller Fisher syndrome, [5] Acute pan-autonomic neuropathy and [6] Pure sensory GBS.

GBS is a monophasic illness, with an annual incidence rate of 1.2–3 per 100 000 population[10]. Yet, recurrence of GBS is observed in 1–6 % of patients, where it is defined as 2 or more attacks of acute inflammatory demyelinating neuropathy with an onset to peak time of 4 weeks or less having complete or near complete recovery [3,4,5,6].

We do not know why a particular trigger will cause one person to develop GBS, while many others in the same situation have no neurological symptoms. Certainly there is an individual susceptibility to developing GBS. This was supported by a study by Dr. K. Geleijns and colleagues, published in 2004. The authors described 12 families of susceptible individuals in which at least two family members developed GBS over the preceding 15 years. The underlying host factors causing susceptibility for these families and for individuals with single-episode and recurring GBS, remain to be discovered. Patients who have residual weakness after GBS may experience excessive fatigue, or has weakness of muscles that were especially affected by the initial GBS. These muscles do not have normal reserve endurance under stress. Weakness may appear after vigorous or prolonged exercise, insufficient sleep, or an unrelated medical illness. This new weakness may be mistaken for a second attack of GBS. Also, decades after recovery from GBS patients may notice slowly increasing weakness in a muscle or limb that was weak during the GBS episode. The most comprehensive study, reported by Dr. R. H. Kennedy and colleagues at Mayo Clinic in 1978, retrospectively followed 40 GBS patients for up to 42 years after the first attack. In that study only one individual had a second episode of GBS, which occurred four years after the initial one[11].

The time lag between two episodes of GBS was 4 months to 10 years in a study done by Das et al. and a mean of 7 years with a range from 2 months to 37 years was described by Kuitwaard et al.[3,5]. Patients tend to get similar clinical presentations and shorter intervals in between subsequent episodes of GBS[3]. Results of the study by Kuitwaard also found that RGBS patients were younger, with milder disease and had Miller-Fisher variant of GBS at the initial episode. Patients with above characteristics on initial presentation of GBS are more prone for recurrences[3]. They also identified that there are similar presentations but more severe clinical deficit and residual effects with each recurrence[3,6]. Yet, there is limited literature addressing why only a certain subset of patients with GBS get recurrences of the disease. The indexed case, although young at presentation, patient had a more alarming disease initially with poor neck muscle power and limb power and did not have Miller-Fisher variant. This shows a deviation from the classically identified features favoring a recurrence of GBS. The time gap between the episodes was 17 years. During the episode of recurrence, she had rapid development of more severe disabling illness involving respiratory compromise needing mechanical ventilation. This episode had AMAN variant of GBS in electrophysiological study with similar initial presentations.

The RGBS patients with similar presentations during the subsequent episodes had different antecedent infections and this may point towards immunogenic and host factors as major determinants of the disease[3,5,6]. Yet, exact mechanism by which similar clinical manifestations occur during recurrence is not established. Our patient also had a GI tract infection preceding the recurrence of GBS.

It is important to distinguish RGBS from two clinical entities; (1) GBS with treatment related fluctuations (GBS-TRF), (2) Chronic inflammatory demyelinating polyneuropathy (CIDP). Since our patient had a long asymptomatic period, GBS-TRF is less likely but CIDP comes as a differential diagnosis. CIDP is suspected when progression of weakness lasts more than 8 weeks followed by a chronic course but it can be of steadily progressive, relapsing remitting or monophasic. The treatment differs as CIDP can be treated with either immunoglobulin or immunosuppressive therapy with a subsequent maintenance immunosuppressive drug treatment whereas GBS and GBS-TRF do not show a response to immunosuppressant therapy but has good response to immunoglobulin or plasmaparesis. GBS is a more likely diagnosis in our patient as there was a rapid onset of symptoms, subsequent complete or near complete recovery, high incidence of an antecedent illness, high CSF protein levels one week after the onset of a recurrence.

Conclusion: In conclusion, GBS rarely recurs. Only about 1–6 % of all former GBS patients will have a second episode.

Multiple recurrences are highly unlikely. Most patients with recurrent GBS respond favourably to treatment with plasmapheresis or IVIG. Former GBS patients who develop a new weakness or sensory symptoms should consult with their primary physician and neurologist before concluding that the cause is a new episode of GBS. Further research is needed to understand what makes some individuals susceptible to GBS in its various forms, and why a very small fraction of those who contract GBS do so more than once.

References

1. Winer JB, Hughes RAC, Anderson MJ, et al. A prospective study of acute idiopathic neuropathy. II Antecedent events. J Neurol Neurosurg Psychiatry. 1988;51:613–8.
2. Seneviratne U. Guillain-Barré syndrome. Postgrad Med J. 2000;76:774–82.
3. Kuitwaard K, Koningsveld RV, Ruts L, Jacobs BC, Doorn PAV. Recurrent Guillain–Barre syndrome. J Neurol Neurosurg Psychiatry. 2009;80:56–9.
4. Grand'Maison F, Feasby TE, Hahn AF, Koopman WJ. Recurrent guillain-barre syndrome. Clinical and laboratory features. Brain. 1992;115(4):1093–106.
5. Das A, Kalita J, Misra UK. Recurrent Guillain Barré syndrome. Electromyogr Clin Neurophysiol. 2004;44(2):95–102.
6. Hadden RDM. Deterioration after Guillain-Barré syndrome: recurrence, treatment-related fluctuation or CIDP. J Neurol Neurosurg Psychiatry. 2009;80(1):3
7. David C. Preston, MD reviewing *Kuitwaard K et al.* Recurrent Guillain-Barré Syndrome,*J Neurol Neurosurg Psychiatry 2009 Jan.*
8. Acute immune polyneuropathies: Neuromuscular. Washington University, 10Mar,2016. http://neuromuscular.wustl.edu/antibody/gbs.htm.
9. Sharma M, Kes P, et al. Guillain-Barré syndrome in a patient suffering acute myocardial infarction. Acta clin Croat. 2002;41(3):255–7.
10. Andary M, et al. Guillain-Barré syndrome: Medscape, 2016.
11. Toby A. Ferguson, M.D., Ph.D and Mark J. Brown, M.D. Does Guillain-Barré Syndrome Recur
Department of Neurology, University of Pennsylvania Medical Center, Philadelephia. PA.

Bangladesh Crit Care J September 2017; 5 (2): 139-140

Case Report

Cough – A Curious Case

Sanjith Saseedharan[1*], Edwin Pathrose[2], A.M. Argikar[3]

Abstract

Cough, as a symptom by default gets the focus of a physician towards the chest ruling out the causes could be of the same. However an incessant cough causing life threatening extra pulmonary complications is a rarity. We present a case of an elderly female who presented with a cough with expectoration but ended up requiring strict hemodynamic monitoring due to a rectus sheath hematoma.

Keywords: *Cough, rectus sheath hematoma (RSH), computed tomography (CT), hemodynamics.*

Introduction:

Rectus sheath hematoma (RSH) is one of the uncommon causes of abdominal pain. It is defined as a collection of blood in the sheath of the rectus abdominis muscle. The cause for this could be a tear of the epigatric vessels and/or branches or trauma to the abdomen. Clinical examination can cause a misdiagnosis of an abnormal growth, inflammatory bowel disease or acute abdomen.[1] Most common complaints of the patients on presentation were abdominal pain and/or palpable mass of the abdominal wall. Risk factors of RSH are sex (female), elderly, cough, abdominal trauma, anticoagulation agents, deranged coagulation profile etc.[2] Computed tomography (CT) scan of the abdomen and pelvis is a reliable diagnostic tool for confirmation of diagnosis.[1,2] The treatment of choice is managing conservatively i.e. ice packs, analgesics, bed rest, intravenous fluids +/- blood transfusion depending on size of hematoma and hemoglobin (Hb) of the patient.

Case Report

60 year old female, a known case of Diabetes Mellitus, Hypertension, Chronic Obstructive Pulmonary Disease, Ischemic Heart Disease and Hypothyroidism was transferred from another private hospital with history of breathlessness, cough with production of phlegm, fever on and off, increased frequency and urge to pass urine with a swollen abdomen, hyponatremia and loss of appetite since 7-8 days.

On arrival to the hospital, patient's Hb was around 9 gm/dl with a blood pressure of 110/90 mm of Hg and a pulse rate of 99/min. Next day she became unstable with a hypotension. Immediate resuscitation was started. On examination, a painful, firm, abdominal mass was felt on the abdominal wall. An immediate CT scan of the abdomen and pelvis was done along with ongoing resuscitation which revealed an anterior abdominal wall rectus sheath hematoma (Figure 1). Her basic coagulation tests were normal with no history of receiving any low molecular weight heparin (LMWH). The development of this hematoma was related to incessant cough which resulted in shearing forces disrupting the inferior epigastric vessels at the lower end of the rectus sheath.

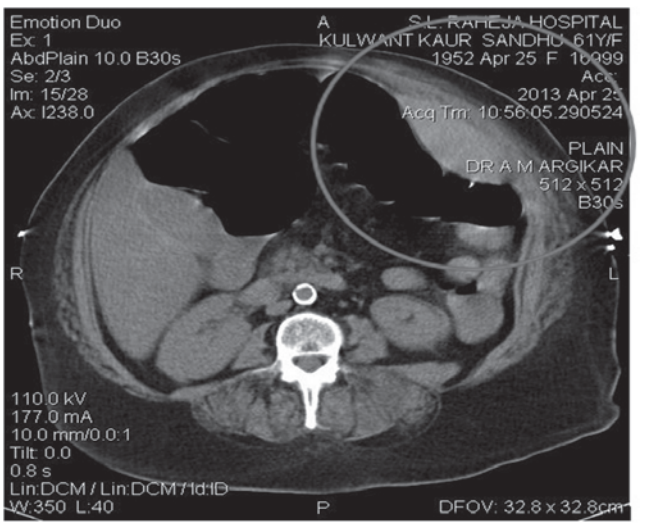


Figure : 1 CT Abdomen showing rectus sheath hematoma in anterior abdominal wall (Encircling mark)

Blood tranfusions were initiated as the Hb had dropped to 7 gm/dl. The interventional radiology team was placed on standby. Unfortunately she developed an anterior wall ST elevation myocardial infarction (STEMI) the same day with the ejection fraction dropping to 25%. In view of the large life threatening RSH, it was not possible to anticoagulate /thrombolyse or give antiplatelets to this patient and further management was purely based on hemodynamic optimization. She progressively became breathless with manifestations suggestive of left ventricular failure. She was

1 Dr. Sanjith Saseedharan, M.D. (Anaes), D.A. (Univ), D.A. (C.P.S.), I.D.C.C., F.N.N.C. (Israel), E.D.I.C. (Europe), FIMSA Consultant Critical Care Head-Intensive Care, S.L. Raheja Hospital (A Fortis Associate), Mumbai, Maharashtra, India

2 Dr. Edwin Pathrose, M.B.B.S. (Smolensk State Medical Academy, Russia) ICU Registrar, S.L. Raheja Hospital (A Fortis Associate), Mumbai, Maharashtra, India

3 Dr. A.M. Argikar, M.D. (Grant Medical College and Sir Jamshedjee Jeejeebhoy Group of Hospitals) Consultant, S.L. Raheja Hospital (A Fortis Associate), Mumbai, Maharashtra, India

Corresponding Author:

Dr. Sanjith Saseedharan
S.L. Raheja Hospital (A Fortis Associate),
Raheja Hospital Road, Mahim West, Mumbai-400016
Maharashtra, India
E-mail: sanjith@rahejahospital.com
Tel : +919004479549
Phone: +77-9841248584

intubated and placed on mechanical ventilator owing to unstable hemodynamics, marked respiratory distress and inability to treat the myocardial infarction by standard means. Extensive monitoring equipment including a cardiac output monitor was used.

Fluid challenges/boluses and inotropes were managed after correlating stroke volume variation, cardiac output and stroke volume and central venous pressure. Three days later, patient was extubated and three days post extubation patient was transferred to the general ward uneventfully.

Discussion

This case explains the dangers of a seemingly innocuous cough which resulted in near death of the patient due to the exsanguination caused by the RSH probably triggering the myocardial infarction.Diagnosis of rectus sheath hematoma is challenging since only 50% of patients will have a visible hematoma at the time of presentation.[3] As a result, RSHs are often confused with other causes of acute abdomen such as appendicitis, cholecystitis, incarcerated inguinal hernia, torsion of ovarian cyst, or acute pancreatitis. Nonspecific nature of symptoms combined with the low incidence (1-2%)[4,5] of the disorder lead to difficulty in considering this diagnosis. This case also highlights the importance of optimizing hemodynamics in the right patient with the right monitoring.

Conclusion

Rectus sheath hematoma should be considered as a differential diagnosis in a patient presenting with an acute abdomen to prevent misdiagnoses and unnecessary laparotomies. Although they are very rarely fatal, we should keep in mind the risk factors which includes cough.[2]CT scan helps in clinching the diagnosis. Conservative management is the mainstay treatment although it can modify depending on severity of the hematoma.

References

1. Kapan S, Turhan AN, Alis H, Kalayci MU, Hatipoglu S, Yigitbas H, et al. Rectus sheath hematoma: three case reports. Journal of medical case reports. 2008 Jan 25;2(1):1.
2. Cherry WB, Mueller PS. Rectus sheath hematoma: review of 126 cases at a single institution. Medicine. 2006 Mar 1;85(2):105-10.
3. James RF. Rectus sheath haematoma. Lancet. 2005 May 21-27;365(9473):1824. PubMed PMID: 15910957.
4. Klingler PJ, Wetscher G, Glaser K, Tschmelitsch J, Schmid T, Hinder RA. The use of ultrasound to differentiate rectus sheath hematoma from other acute abdominal disorders. SurgEndosc. 1999 Nov;13(11):1129-34. PubMed PMID: 10556453.
5. Edlow JA, Juang P, Margulies S, Burstein J. Rectus sheath hematoma. Ann Emerg Med. 1999 Nov;34(5):671-5. PubMed PMID: 10533018.

Bangladesh Crit Care J September 2017; 5 (2): 141-142

Case Report

Superior Mesenteric Artery occlusion presenting with severe acute abdomen and subsequent gangrenous small gut

Chishti Tanhar Bakth[1], Jamal Ahmed[2], Mrigen Kumar Das[3]

Abstract

Superior Mesenteric Artery occlusion is not very uncommon in developing world . It mimic clinically with many differential diagnosis.[2] There is a clinical scenario of 60 yrs male, smoker presented in Accident & Emergency (A&E) department with history of central abdominal pain for two days associated with vomiting. Pain was gradually increasing, abdomen became tense, tender and patient developed restlessness. Even after all sorts of conservative management, pain was not subsiding. Following day of admission laparotomy attempted with clinical vision of burst appendix and peritonitis. After exploration of abdomen the finding was thundering. The almost whole small gut was gangrenous , resection anastomosis had done. In this case the differential diagnosis was burst appendix and Intestinal obstruction . Possibility of Superior Mesenteric Artery occlusion should be kept in mind by this clinical ground .

Keywords: *Superior Mesenteric Artery, Laparotomy, Gangrene.*

Introduction:

Acute superior mesenteric artery occlusion which can result in an acute mesenteric ischaemia and can be a life threatening event related to the artery supplying the majority of small bowel and right side of colon[1]. An acute occlusion is an uncommon event that typically affects elderly patients who are at increased risk of other cardiovascular events. Because of the high rate of mortality and the difficulty of diagnosis, mesenteric ischaemia poses a substantial legal risk. This risk can be reduced by a high degree of clinical suspicion, early and aggressive diagnostic imaging and early surgical intervention with clear documentation of timing.

Case presentation:

A 60 years of male, smoker presented in A&E department with history of central abdominal pain for two days and associated with vomiting. Emmergency Medical Officer (EMO) had evaluated the patient. He had no comorbid illness or surgical history.

On examination, hemodynamics were stable, abdomen examination revealed tenderness in central abdomen with sluggish bowel sound. Pain intensity was increasing in timely fashion and abdomen became tense, tender with diminished bowel sound. Finally he developed severe agonizing pain for which he was unable to talk and breath normally. His pulse was >120 beat per minute and became very restless. His abdominal pain was not subsiding even with mixed analgesics.

Hematological investigations showed neutrophilic leukocytosis, urine routine examination revealed pus cell 6-10 per high power field (HPF), RBC 3-5/HPF, USG of whole abdomen showed fine floating echogenic debris in urinary bladder otherwise normal USG. Other relevant investigations (LFT, RFT, X-RAY, amylase, lipase, ECG) were normal.

Patient became very toxic with evidence of diffuse peritonitis, exploration of abdomen was planned and the findings were thundering. Almost the whole small gut was gangrenous (Figure), after resection of gangrenous gut, approximately 30 cm of gut could be saved. Tensionless jejuno-ileal anastomosis was made after examining for the evidence of gut viability. Total procedure took about 3 hours and 2 units of whole blood were transfused with infusion of about 3 liters of crystalloidal solution per-operatively. Patient was shifted to ICU in a orotracheally intubated state for close hemodynamic monitoring and ventilatory support. Though patient developed dys-electrolytaemia and acute lung injury on postoperative days but gradual improvment was there. on 8th post-operative day liquid diet was started orally, but there was evidence of anastomotic leakage on two drain tube sites. Patient again developed peritonitis and subsequent septicaemia. But unfortunately patient died on 18th post-operative day .

Discussion:

Acute Superior Mesenteric Artery occlusion is time dealing case[2]. Early prediction of disease, the damage would be the minimum. In late age with atypical presentation of abdomen with atypical clues of lab findings, mesenteric occlusion

1. Dr. Chishti Tanhar Bakth Choudhury, MS (Surg), MCPS (Surg), Consultant surgeon, Sylhet Womens Medical college Hospital
E-mail : chishtitanharbakthchoudhury@yahoo.com.
2. Dr. Jamal Ahmed Chowdhury, FCPS (Surg), Professor, Sylhet Womens Medical College Hospital,
E-mail : jamal_achowdhury@hotmail.com
3. Dr. Mrigen Kumar Das Chowdhury, FCPS (Surg), Professor, Sylhet Womens Medical College Hospital,
E-mail : dr.mrigen.chowdhury@gmail.com

Corresponding Author:

Dr. Chishti Tanhar Bakth Choudhury
MS (Surg), MCPS (Surg), Consultant surgeon
Sylhet Womens Medical College Hospital
E-mail : chishtitanharbakthchoudhury@yahoo.com
Phone: +8801717026037

should be kept in mind as a important differential diagnosis. Differential diagnosis comes from intense history taking, clinical and abdominal findings and laboratory support.

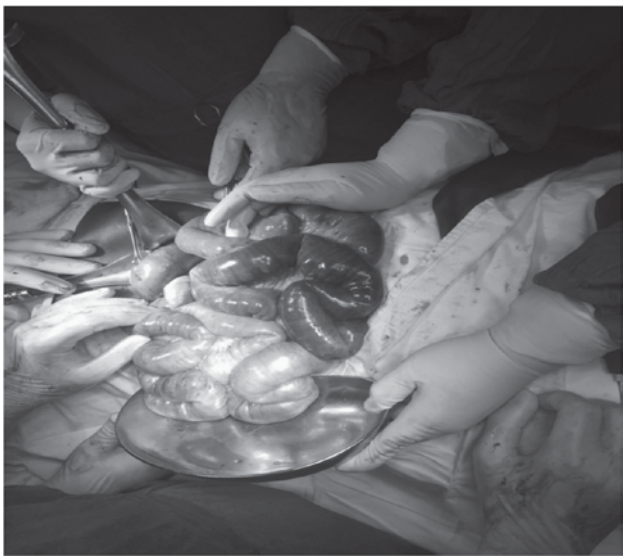


Fig : Per-opearative infarcted small gut

Mesenteric occlusion causes impairment of gut viability. Early exploration of abdomen and thrombectomy can minimize the damage of gut. CT or MR angiogram can diagnose the disease early as well as combined vascular and general surgeon should start the work. Mesenteric occlusion is a life threatening, more than 80% mortality even in all facilitated place.

Conclusion:

Clinicians need to have high suspicion of Acute Superior Mesenteric Artery occlusion in their dfferentials when dealing with such presentation in a elderly morbid patient.

Learning Points

a. Emergency exploration as early as possible can minimize damage.

b. Both end of gut exteriorization can minimize the leakage rate although fluid and electrolytes management is challenging.

c. CT or MR angiogram needed to localize the thrombus and for resection.

d. It is a multidisciplinary approach involvement process and should need to involve multiple faculties including intensivist.

e. Intraluminal papaverine has contribution in occlusion.

f. Predisposing factors are old age ,smoking, prothrombotic tendency , vascular, cardiac cause (mechanical heart valve, atrial fibrillation, acute MI).

Consent:

Verbal consent has been obtained from patient attendance to participate in this case report.

References:

1. Bradbury AW, et al. Br J Surg 1995; 82: 1446-59 .
2. Brandt LJ, Feuerstadt P. Intestinal ischaemia . In: Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger and Fordtrans Gastrointestinal and liver disease . 10th ed. Philadelphia, PA: Elsevier saunders; 2016: chapt 118.
3. Bergan j.j. : Recognition and treatment of intestinal ischaemia . surg. Clin.N . Amer. , 147: 109, 1967.
4. Hauser SC. Vascular disease of the gastrointestinal tract. IN: Goldman L, Schafer Al, eds. Goldmanscecil Medicine. 25th ed. Philadelphia, PA: Elsevier Saunders; 2016 :chapt 143.
5. Jackson , B.B. : Occlusion of the superior mesenteric artery. springfield, Illinois, charles C Thomas, 1963, P. 40.

Bangladesh Crit Care J September 2017; 5 (2): 143-146

Case Report

Takotsubo Cardiomyopathy in Traumatic Brain Injury: A Case Report

Rajib Hasan[1], Mohiuddin Ahmed[3], ARM Nooruzzaman[3], Md. Motiul Islam[2], Mohammad Rabiul Halim[1], Kazi Sami Saleh Abdullah[1], Muhammad Mahbubur Rahman Bhuiyan[1], Muhammad Mashiur Rahman[1], Kazi Nuruddin Ahmed[1], Md. Hafizur Rahman[1]

Abstract

Background: *Takotsubo cardiomyopathy (TC) is a well-known complication of severe brain insult but has been rarely described in patients with traumatic brain injury (TBI).*

Methods: *Case report and review of literature.*

Results: *We report a 25-year-old lady with moderate traumatic brain injury (TBI) developing circulatory shock. Takotsubo cardiomyopathy (TC) was diagnosed by repeated echocardiography. Cardiovascular support by pressor agents led to hemodynamic stabilization after initiation of noradrenaline. Cardiac function fully recovered within 2 weeks. We performed an in-depth literature review and identified 17 reported patients with TBI and TC. Clinical course and characteristics are discussed in the context of our patient.*

Conclusion: *TC is rarely diagnosed after TBI and may lead to poor outcome if not addressed in time.*

Introduction:

Takotsubo cardiomyopathy (TC) is a transient cardiac syndrome that involves left ventricular akinesis and mimics acute coronary syndrome (ACS). It was first described in Japan in 1990 by Sato et al [1, 2]. Although the exact etiology of TCM is still unknown, the syndrome appears to be triggered by a significant emotional or physical stress [3]. It has been widely described after severe brain insult like subarachnoid hemorrhage (SAH, 1.2–28 %) [4–6]; however, it rarely occurs in patients with intracerebral hemorrhage, ischemic stroke, and traumatic brain injury (TBI) [7]. Here, we report a case of moderate TBI presenting with severe TC and provide a comprehensive review of all reported TBI cases [8–20].

Case Report

A previously healthy 25 years old Bangladeshi young lady got admitted to the general intensive care unit (GICU) of a tertiary care hospital through ER with moderate traumatic brain injury (TBI) three hours following a RTA.

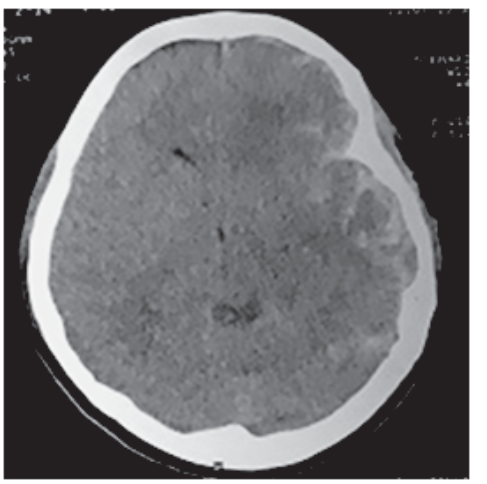


Fig 1: CT scan of head on admission

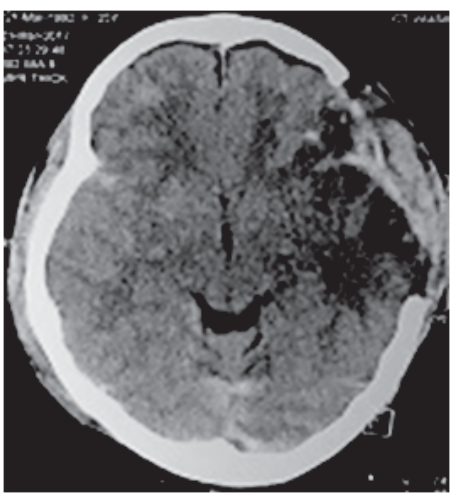


Fig 2: CT scan of head on 3rd POD

1. Senior Clinical Staff, Medical ICU, Asgar Ali Hospital, 111/1/A, Distillery Road, Gandaria, Dhaka-1204, Bangladesh.
2. Associate Consultant, Medical ICU, Asgar Ali Hospital, 111/1/A, Distillery Road, Gandaria, Dhaka-1204, Bangladesh.
3. Consultant, Internal Medicine & ICU, Asgar Ali Hospital, 111/1/A, Distillery Road, Gandaria, Dhaka-1204, Bangladesh.

Corresponding Author:

Dr. Rajib Hasan
Email: dr.rajib.icu@gmail.com

On presentation, she was disoriented and had a Glasgow Coma Scale (GCS) score of 11 ($E_2V_3M_6$). No focal neurological deficit was present and her vital signs were stable with BP 110/70 mm of Hg, HR 76bpm, regular. She vomited twice since the RTA and had no H/O any convulsion. Patient had multiple lacerations over her head and bleeding from right ear. There were no signs of trauma in any other parts of the body. CT scan of the head showed left fronto-temporal acute subdural haematoma with temporal contusion (Fig 1). Cervical spine screening was negative for any injury. All laboratory workups were normal except for some mild electrolyte imbalance. Initial ECG findings were also within normal limit. The following day patient developed hypotension associated with tachycardia (HR>130). All possible causes of hypotension including any concealed hemorrhage, acute MI or septic foci were ruled out. As patient remained hypotensive after adequate volume resuscitation, pressor support was required (Noradrenaline 0.4 mcg/kg/min). About 4 to 5 hours afterwards her GCS also dropped significantly from 11 to 9. At this time she was intubated and put on mechanical ventilator support for airway

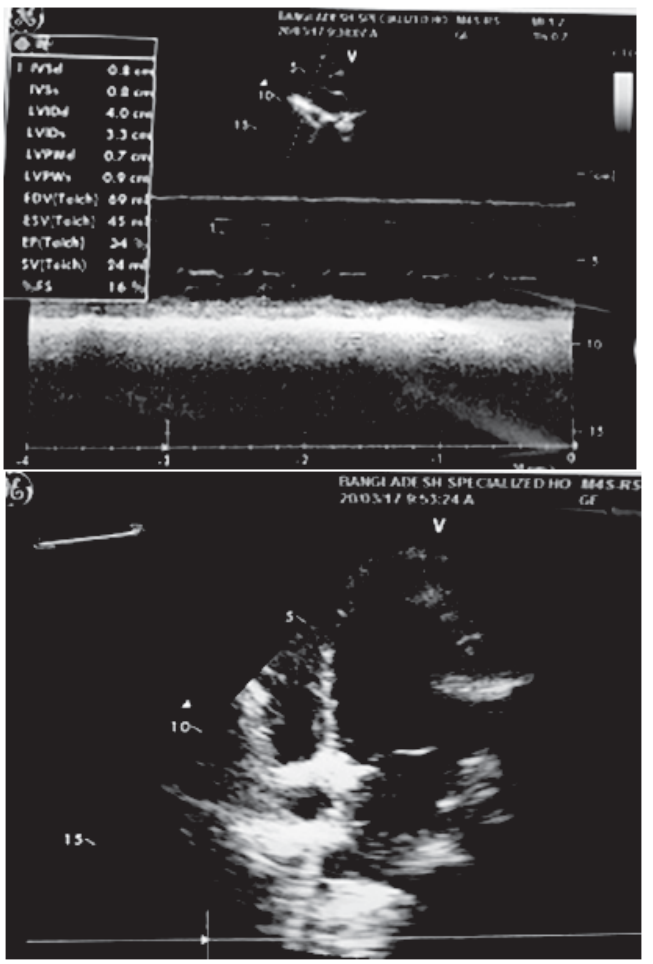


Fig 3: First ECHO on 2nd POD with EF 32%

protection. Patient underwent decompressive craniectomy (Fig 2) on that day and was kept sedated under mechanical ventilator support in the post-operative period. Patient was otherwise stable but remained in shock requiring noradrenaline support. On the 2nd POD a bedside transthoracic echocardiography was done which showed global hypokinesia of septal, anterior, lateral and post-inferior LV with an EF of 31% (Fig 3). On the 3rd POD, patient's BP gradually increased requiring less noradrenaline support. Bedside echo was repeated which showed an increase in EF up to 42% (Fig 4). Patient was eventually extubated on the 4th POD when she was on minimum pressor support and was gradually weaned off noradrenaline on the 7th POD without any significant drop in BP. Patient was transferred out of GICU to cabin on the 9th POD with GCS 15/15, stable hemodynamics and in an afebrile condition. A bedside transthoracic echo done 2 weeks after the RTA showed no RWMA with an EF of 68% (Fig 5).

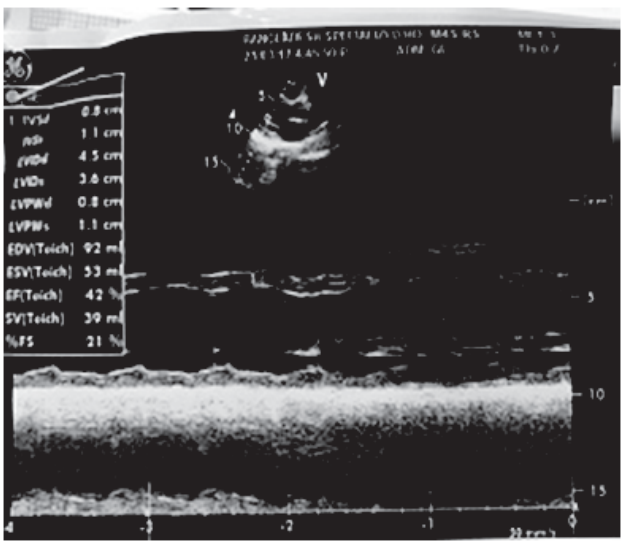


Fig 4: 2nd ECHO on 3rd POD with EF 42%

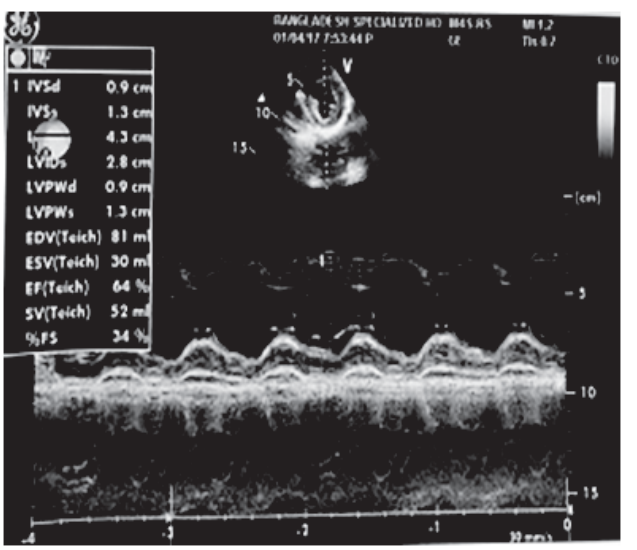


Fig 5: Normal ECHO 2 weeks after RTA

Review of Literature

Method

We performed a comprehensive literature search using the search terms 'Takotsubo cardiomyopathy,' 'Tako-tsubo cardiomyopathy,' 'stress cardiomyopathy,' 'stunned myocardium,' 'Broken heart syndrome,' 'transient-left-ventricular ballooning syndrome,' 'apical ballooning syndrome,' 'myocardial dysfunction' or 'heart failure' together with 'traumatic brain injury,' 'head injury,' and 'polytrauma.' Only articles in English language were included.

Results

Overall we identified 14 published articles involving 17 TBI patients with TC [8–21]. Among them, 14 were adults, all except two patients presented with loss of consciousness requiring endotracheal intubation and mechanical ventilation for airway protection. The brain injury pattern was variable including contusional hematoma, epidural hemorrhage (EDH), subdural hemorrhage (SDH), and traumatic SAH, 6 patients underwent neurosurgical intervention. TC was diagnosed within first day after admission in most patients. In 4 patients, coronary angiography was performed and confirmed TC. Electrocardiography abnormalities were found in 9/17 patients including ST segment and T wave changes, and 11/17 had elevated serum troponin level. Treatment differed; however, most received inotropic support using dobutamine. In addition, various drugs were used to sustain adequate blood pressure including adrenaline, noradrenaline, and vasopressin. In two patients, levosimendan was used. Echocardiography revealed abnormal results in all patients (100 %) and was reversible in the majority of patients within 7 days except in 3 patients where complete cardiac recovery took place after 12days, 17 days and 21 days respectively.

Discussion

Cardiovascular complications are common after brain injury and associated with increased morbidity and mortality. TC represents a serious manifestation of myocardial dysfunction and is defined as an acute, transient, and reversible heart failure syndrome due to regional wall abnormalities of the ventricular myocardium with associated new electrocardiography changes and elevation of myocardial biomarkers in the absence of culprit atherosclerotic coronary artery disease or cardiac condition causing the temporary ventricular dysfunction [22.23]. Underlying pathophysiologic mechanisms are still incompletely understood. Most investigations suggest an interconnected cascade of neuronal injury causing sympathetic overstimulation and direct catecholamine toxicity to the heart [24]. Damage to the insula and hypothalamus also initiates a complex cascade of events, including activation followed by dysfunction of the autonomic nervous systems and an intense inflammatory response, which have major adverse effects on the heart (Fig 6) [25].

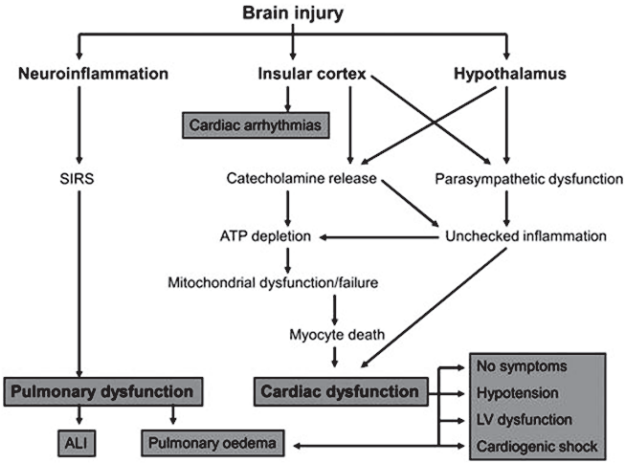


Fig 6: The pathophysiology of cardiovascular complications after brain injury.

SIRS, systemic inflammatory syndrome; ATP, adenosine triphosphate; ALI, acute lung injury

Our patient had full recovery of cardiac function 2 weeks after trauma. Even though transient and reversible in nature, some reports suggest recovery even up to 12-week post injury. Improving cardiac function in patients with TC may be achieved by using dobutamine, noradrenaline and other pharmacological or nonpharmacological treatment including extracorporeal life support [26]. Our patient improved after starting noradrenaline. Recently, the use of levosimendan has been reported in patients with aneurysmal SAH where other inotropes were found ineffective [27].

Conclusion

Takotsubo cardiomyopathy is an underdiagnosed disorder especially in patients suffering from traumatic brain injury. It is a reversible condition associated with good overall prognosis. Supportive management is the mainstay of treatment for this condition.

References :

1. Sato H, Tateishi H, Uchida T, et al. Kodama K, Haze K, Hon M, eds. Clinical Aspect of Myocardial Injury: From Ischaemia to Heart Failure. Tokyo: Kagakuhyouronsya; 1990. 56-64.
2. Kurisu S, Kihara Y. Clinical management of takotsubo cardiomyopathy. Circ J. 2014. 78 (7):1559-66. [Medline].
3. Boland TA, Lee VH, Bleck TP. Stress-induced cardiomyopathy. Crit Care Med. 2015 Mar. 43 (3):686-93. [Medline].
4. Lee VH, Connolly HM, Fulgham JR, Manno EM, Brown RD Jr, Wijdicks EFM. Tako-tsubo cardiomyopathy in aneurysmal subarachnoid hemorrhage: an under appreciated ventricular dysfunction. J Neurosurg. 2006;105:264–70.
5. Kilbourn KJ, Levy S, Staff I, Kureshi I, McCullough L. Clinical characteristics and outcomes of neurogenic stress cardiomyopathy in aneurysmal subarachnoid hemorrhage. Clin Neurol Neurosurg. 2013;115:909–14.
6. Banki N, Kopelnik A, Tung P. Prospective analysis of prevalence, distribution, and rate of recovery of left ventricular systolic dysfunction in patients with subarachnoid hemorrhage. J Neurosurg. 2006;105:15–20.

7. Finsterer J, Wahbi K. CNS disease triggering Takotsubo stress cardiomyopathy: review. Int J Cardiol. 2014;177:322–9.

8. Palac RT, Sumner G, Laird R, O'Rourke DJ. Reversible myocardial dysfunction after traumatic brain injury: mechanisms and implications for heart transplantation. Prog Transplant. 2003;13:42–6.

9. Krishnamoorthy V, Sharma D, Prathep S, Vavilala MS. Myocardial dysfunction in acute traumatic brain injury relieved by surgical decompression. Case Rep Anaesthesiol. 2013;13: 1–4.

10. Divekar A, Shah S, Joshi C. Neurogenic stunned myocardium and transient severe tricuspid regurgitation in a child following nonaccidental head trauma. Pediatr Cardiol. 2006;27(3):376–7.

11. Deleu D, Kettern MA, Hanssens Y, Kumar S, Salim K, Miyares F. Neurogenic stunned myocardium following hemorrhagic cerebral contusion. Saudi Med J. 2007;28(2):283–5.

12. Wippermann J, Bennink G, Wittwer T, Madershahian N, Ortmann C, Wahlers T. Reversal of myocardial dysfunction due to brain injury. Asian Cardiovasc Thorac Ann. 2008;16(3):30–1.

13. Mare´chaux S, Goldstein P, Girardie P, Ennezat PV. Contractile pattern of inverted takotsubo cardiomyopathy: illustration by two-dimensional strain. Eur J Echocardiogr. 2009;10(2):332–3.

14. Vergez M, Pirracchio R, Mateo J, Payen D, Cholley B. Takotsubo cardiomyopathy in a patient with multiple trauma. Resuscitation. 2009;80(9):1074–7.

15. Riera M, Llompart-Pou JA, Carillo A, Blanco C. Head injury and inverted takotsubo cardiomyopathy. J Trauma. 2010;68: 13–5.

16. Samol A, Grude M, Stypmann J, et al. Acute global cardiac decompensation due to inverted takotsubo cardiomyopathy after skull-brain trauma- a case report. Injury Extra. 2011;42(5):54–7.

17. Santoro F, Ieva R, Ferraretti A, et al. Safety and feasibility of levosimendan administration in takotsubo cardiomyopathy: a case series. Cardiovasc Ther. 2013;31(6):133–7.

18. Krpata DM, Barksdle EM Jr. Trauma induced left ventricular apical ballooning syndrome in a 15 year-old: a rare case of takotsubo cardiomyopathy. J Pediatr Surg. 2013;48:876–9.

19. Bonacchi M, Vannini A, Harmelin G, et al. Inverted-takotsubo cardiomyopathy: severe refractory heart failure in poly-trauma patients saved by emergency extracorporeal life support. Interact Cardiovasc Thorac Surg. 2015;20(3):365–71.

20. Hong J, Glater-Welt LB, Siegel LB. Takotsubo cardiomyopathy in a 23 months-old following traumatic brain injury. Ann Pediatr Child Health. 2014;2(4):1029.

21. Cheah, C.F., Kofler, M., Schiefecker, A.J. et al. Takotsubo Cardiomyopathy in Traumatic Brain Injury. Neurocrit Care (2017) 26: 284-91.

22. Lyon AR, Bossone E, Schneider B, et al. Current state of knowledge on Takotsubo syndrome: a position statement from the taskforce on Takotsubo syndrome of the heart failure association of the European society of cardiology. Eur J Heart Fail. 2016;18(1):8–27.

23. Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of Takotsubo (stress) cardiomyopathy. N Engl J Med. 2015;373(10):929–38.

24. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med. 2005;352(6):539–48.

25. Nguyen H, Zaroff JG. Neurogenic stunned myocardium, Curr Neurol Neurosci Rep , 2009, vol. 9 486-91.

26. Lyon AR, Bossone E, Schneider B, et al. Current state of knowledge on Takotsubo syndrome: a position statement from the taskforce on Takotsubo syndrome of the heart failure association of the European society of cardiology. Eur J Heart Fail. 2016;18(1):8–27.

27. Taccone FS, Brasseur A, Vincent JL, De Backer D. Levosimendan for the treatment of subarachnoid haemorrhage-related cardiogenic shock. Intensive Care Med. 2013;39(8):1497–8.

Bangladesh Crit Care J September 2017; 5 (2): 147-148

Clinical Image

Pulsatile neck mass

Mohammad Omar Faruq[1], Sabria Islam[2]

A 60 years old non-diabetic, hypertensive female patient from Dhaka was admitted to the ICU with the complaints of drowsiness and breathlessness for a couple of hours following postponement of haemodialysis owing to low blood pressure. She also had a high grade intermittent fever for 7 days. The fever had followed an intra-articular steroid injection given to the left knee for osteoarthritis. She was diagnosed with hypertension 20 years back and was on antihypertensives but not on regular follow up. 8 years prior to admission she was diagnosed with CKD and was on MHD twice weekly for 7 years via a brachiocephalic arteriovenous fistula in the right cubital fossa. For the last 6 years, after having the AV fistula, she developed a gradually growing pulsatile swelling on her right neck, which according to her attendants did not cause any problem other than a cosmetic one and for which they did not seek any medical attention. A similar but smaller swelling developed on the left. There was no history of trauma to the neck or upper limbs. On examination, patient was drowsy and disoriented. She was moderately anemic, dehydrated and had bilateral leg edema. Her neck veins on the right were engorged more than on the left and there was a pulsatile swelling along the right side of the neck (Fig 1). It had a palpable thrill and had a systolic flow murmur heard over it. The AV fistula in the right cubital fossa was active. There was a similar but smaller pulsatile swelling on the left side of the neck.Pulses were diminished in left upper limb, left anterior tibial artery and arteria dorsalis pedis pulses were absent in both lower limbs. She was hypotensive and tachycardic. Breath sound was vesicular with bilateral basal creps. Chest findings were otherwise normal.

Investigations showed anemia, a low WBC count and thrombocytopenia with a markedly raised CRP, uremia and electrolyte imbalance. Sonography of abdomen revealed splenomegaly with ascites and pleural effusion and features consistent with CKD. Bedside echocardiography showed moderate concentric LVH with preserved systolic function

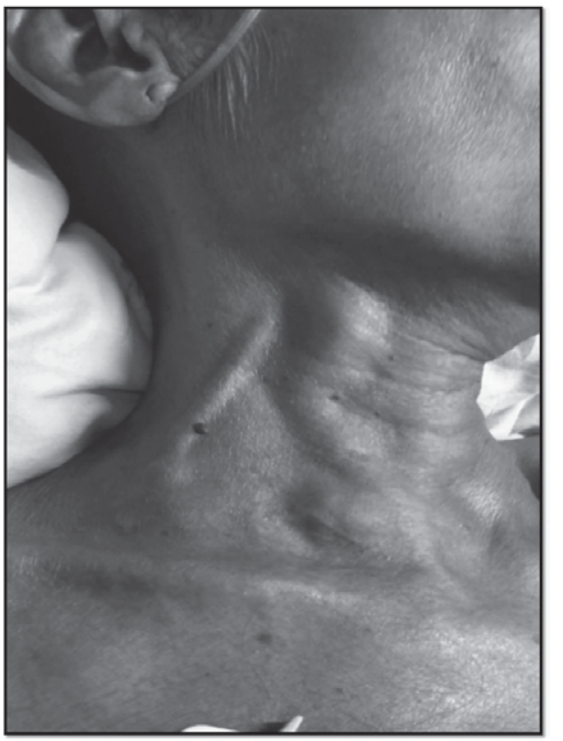


Fig 1

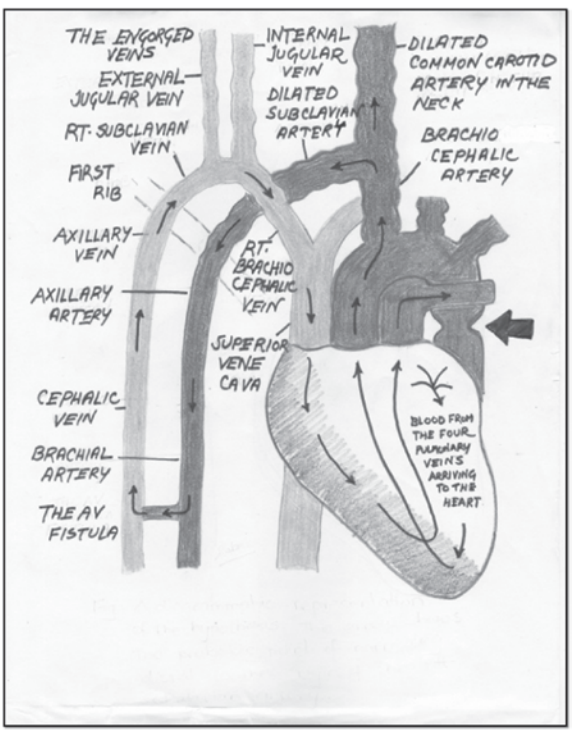


Fig 2

1 Prof. Mohammad Omar Faruq, MD, FACP, FACEP, FCCM, FCPS. Prof. of Critical care Medicine, Ibn Sina Hospital, Dhaka 1209 Bangladesh.

2 Dr. Sabria Islam, MBBS, Honorary Medical Officer, Department of Medicine, Dhaka Medical College Hospital, Dhaka-1209, Bangladesh.

Corresponding Author:

Prof. Mohammad Omar Faruq
MD, FACP, FACEP, FCCM, FCPS.
Prof. of Critical Care Medicine,
Ibn Sina Hospital, Dhaka-1209, Bangladesh.
E mail : faruqmo@yahoo.com

and no regional wall motion abnormality. There was mild MR with SAM, mild TR with PASP of 31 mmHg and mild pericardial effusion. CT showed pneumonitis with mild pleural effusion but no other abnormality including that of the mediastinum. Duplex study showed moderate dilatation of the brachiocephalic trunk and its two divisions, the left common carotid artery and the left subclavian artery. The right upper limb had a well functioning fistula with a normal artery system. The left ulnar artery was occluded with scanty flow. The lower limbs revealed occluded right and left posterior tibial artery and stenosis in left anterior tibial artery.She was treated for septicemia but went into a septic shock and later died from multiorgan failure.

DISCUSSION

A case series of nine pulsatile neck masses reported by Takeuchi Y et al[1] diagnosed using Color Doppler revealed 7 vascular masses, 3 of which were due to tortuosity of the common carotid, two of the brachiocephalic artery, one a pseudoaneurysm and one a traumatic AV fistula.The others were a neurofibroma and a metastatic lymph node.

A review article by Calderelli C et al[2] elaborating on acquired AV fistulas involving the carotid artery and internal jugular vein described features very similar to the ones in this patient, viz. a pulsatile neck swelling, systolic murmur, palpable thrill, and dilated superficial veins. This is the result of hemodynamic alteration caused by sudden diversion of blood flow from the arterial circuit into the venous one. Physiologic effects of this rearrangement of blood flow are affected by general factors, such as concomitance of pre-existing cardiac diseases and factors related to fistula itself, such as its size, the volume of flow through it, the calibre of the vessel involved, and the proximity to the heart. A proportion of these cases were iatrogenic due to a history of placement of a CV line in the internal jugular vein and the rest were traumatic. But no such history was known by this patient's attendants. Aneurysms of arteries and veins at the site of fistula for haemodialysis have been reported to be up to 5-6% of cases by Stolic[3] though none of these studies mention any effect on the feeding arteries away from the site. Hence we currently are unable to provide any evidence that the AV fistula was directly responsible for the dilatation of the arteries.

Known contributors of carotid artery aneurysm and/or dissection[4,5] include congenital defects, heritable connective tissue disorders, oral contraceptives, smoking, hypertension, and atherosclerosis, the last two of which were present in this patient.

One hypothesis that can be considered is that there was an undiagnosed coarctation of aorta distal to the left subclavian artery, or narrowing of that part of the artery due to other reasons such as atherosclerosis (Fig 2). The impediment to blood flow combined with the hyperdynamic circulation within that circuit following the making of the AV fistula caused the arteries to dilate. Upon expiry of the patient, further investigations could not be carried out. Hence the true reason will remain unknown until another similar case with a thorough investigation including a CT or MR angiography becomes available.

References

1. Takeuchi Y, Numata T, Suzuki H, Konno A, Kaneko T. Differential Diagnosis of Pulsatile Neck Masses by Doppler Colour Flow Imaging. Ann Otol Rhinol Lryngol. 1995 Aug; 104(8): 633-8.
2. Caldarelli C,Biricotti M, Materazzi G, Spinelli C, and SpisniR. Acquired Carotid-Jugular Fistula: Its Changing History and Management.ISRN Vascular Medicine. 2013 Apr; vol. 2013.
3. Stolic R. Most Important Chronic Complications of Arteriovenous Fistulas for Haemodialysis. Med Princ Pract 2013; 22: 220-8.
4. Garg K, Rockman CB, Lee V, Maldonado TS, Jacobowitz GR, Adelman MA et al. Presentation and management of carotid artery aneurysms and pseudoaneurysms. Journal of Vascular Surgery. 2012 June; 55(6): 1618-22.
5. Zohrabian D. Carotid Artery Dissection. Medscape. Updated 2016 Dec