ISSN 2521-3113 (Online)
ISSN 1024-8714 (Print)

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# BANGLADESH HEART JOURNAL

VOL. 38 NO. 2 JULY 2023

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Official Journal of
Bangladesh Cardiac Society

# BANGLADESH HEART JOURNAL

Vol. 38, No. 2, July 2023





***Published by :***
Prof. M.G. Azam
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***Printed by :***
Asian Colour Printing
130, DIT Extension Road
Fakirerpool, Dhaka-1000
Phone : 49357726, 58313186
E-mail: asianclr@gmail.com

# *We gratefully acknowledge the contribution of the reviewers of this issue of Bangladesh Heart Journal*

**Vol. 38, No. 2, JULY 2023**

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# INSTRUCTION TO AUTHORS

## A. Introduction

Bangladesh Heart Journal is the official journal of Bangladesh Cardiac Society, and accepts articles for publication from home and abroad. This is a biannual, peer-reviewed journal and aims to publish work of the highest quality from all sub-specialties of cardiology and cardiovascular surgery. The aim of the publication is to promote research in Bangladesh and serve as platform for dissemination of scientific information in cardiology.

## B. Categories of Articles

The journal accepts original research, review articles, case reports, cardiovascular images and letters to the editor, for publication.

*Original Research:*

Original, in-depth research article that represents new and significant contributions to medical science. Each manuscript should be accompanied by a structured abstract of up to 250 words using the following headings: Objective, Methods, Results, and Conclusions. Three to 5 keywords to facilitate indexing should be provided in alphabetical order below the abstract. The text should be arranged in sections on INTRODUCTION, METHODS, RESULTS and DISCUSSION. The typical text length for such contributions is up to 3000 words (including title page, abstract, tables, figures, acknowledgments and key messages). Numberof references should be limited to 50.

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Generally review articles are by invitation only. But unsolicited reviews will be considered for publication on merit basis. Following types of articles can be submitted under this category: Newer drugs, new technologies and review of a current concept.The manuscript should not exceed 5000 words (including tables and figures). A review article should include an abstract of up to 250 words describing the need and purpose of review,methods used for locating, selecting, extracting and synthesizing data, and main conclusions. The number of references should be limited to 50.

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Only case reports of exceptional quality will be published in the case report format. The text should not exceed 1500 words and is arranged as introduction, case report and discussion. Include a brief abstract of about 150 words. Number of tables/figures should be limited to 3. Include up to 10 most recent references. The patient's written consent, or that of the legal guardian, to publication must be obtained.

*Cardiovascular Images:*

Only clinical photographs with or without accompanying skiagrams, pathological images, echocardiographic images, angiographic images etc. are considered for publication. Image should clearly identify the condition and have the classical characteristics of the clinical condition. Clinical photographs of condition which are very common, where diagnosis is obvious, or where diagnosis is not at all possible on images alone would not be considered. Photographs should be of high quality, usually 127 × 173 mm (5 × 7 in) but no larger than 203 × 254 mm (8 × 10 in). A short text of up to 250 words depicting the condition is needed. Figures should be placed exactly at a logical place in the manuscript. The submitted images should be of high resolution (>300 dpi). The following file types are acceptable: JEPG and TIFF. The number of authors should not exceed 3. The authors should ensure that images of similar nature have not been published earlier. Authors must obtain signed informed consent from the patient, or the legal guardian.

*Letter to the Editor:*

Letters commenting upon recent articles in Bangladesh Heart Journal are welcome.Such letters should be received within 16 weeks of the article's publication. Letters should be up to 250 words; should contain no more than 1 figure/table and upto 5 most recent references. The text need not be divided into sections. The number of authors should not exceed 3.

## C. Criteria for Acceptance

All manuscripts should meet the following criteria: the material is original, study methods areappropriate, data are sound, conclusions are reasonable and supported by the data, and the information is important; the topic has general cardiology interest; and that the article is written in reasonably good English. Manuscripts which do not follow the guidelines of Bangladesh Heart Journal are likely to be sent back to authors without initiating the peer-review process. All accepted manuscripts are subject to editorial modifications to suit the language and style of Bangladesh Heart Journal and suggestions may be made to the authors by the Editorial Board to improve the scientific value of the journal.

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The Bangladesh Heart Journal commits to high ethical and scientific standards. Submitted manuscripts are considered with the understanding that they have not been published previously in print or electronic format

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**E. Cover Letter**

The cover letter should outline the importance and uniqueness of the work. It should include the signed declaration from all authors on:

1. Category of manuscript (original research, review article, case report, cardiovascular image, letter to the Editor)
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6. Sources of research support, if any, including funding, equipment, and drugs.

The cover letter should also include the mailing address, telephone and fax numbers, and e-mail address of the corresponding author.

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The manuscripts should comply with the prescribed guidelines. It should be well organized and written in simple and correct English under appropriate headings. The abbreviations and acronyms should be spelled out when they occur first time.

The Introduction should address the subject of the paper. The Methods section should describe in adequate detail the laboratory or study methods followed and state the statistical procedures employed in the research. This section should also identify the ethical guidelines followed by the investigators with regard to the population, patient samples or animal specimens used. A statement should be made, where applicable, that their study conforms to widely accepted ethical principles guiding human research (such as the Declaration of Helsinki) AND also that their study has been approved by a local ethics committee.The Results section should be concise and include pertinent findings and necessary tables and figures.The Discussion should contain conclusions based on the major findings of the study, a review of the relevant literature, clinical application of the conclusions and future research implications. Following the Discussion, Acknowledgements of important contributors and funding agencies may be given.

*a. Title page information*

- Title. Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations where possible.
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- Corresponding author. Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.

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A concise and factual abstract is required. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. References should be avoided. Also, non-standard or uncommon abbreviations should be

avoided, but if essential they must be defined at their first mention in the abstract itself.

*c. Keywords*

Immediately after the abstract, provide a maximum of 5 keywords. Keywords should be the listed terms in the Medical Subject's Headings (MeSH) of the National Library of Medicine (NLM), available at https://www.nlm.nih.gov/mesh.

*d. Abbreviations*

Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

*e. Acknowledgements*

Collate acknowledgements in a separate section at the end of the article before the references. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

*f. Units*

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*h. Tables*

Tables should be placed next to the relevant text in the article.

- Number tables consecutively in accordance with their appearance in the text. Each table should be cited in the text in Arabic numerals.
- Titles should be brief and a short or abbreviated heading for each column should be given.
- Explanatory matter should be placed in footnotes and not in the heading.
- Abbreviations in each table should be explained in footnotes.
- The data presented in a table should not be repeated in the text or figure.

*i. References*

References should follow the standards summarized in the NLM's International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals (ICMJE recommendations), available at: http://www.icmje.org/recommendations/. The titles of journals should be abbreviated according to the style used for MEDLINE (www.ncbi.nlm.nih.gov/nlmcatalog/journals). Journals that are not indexed should be written in full.

- References should be numbered consecutively in the order in which they are first mentioned in the text.
- References in text, tables and legends should be identified by superscript Arabic numerals at the end of the sentence outside any punctuation. If several different studies or papers are cited within one sentence, the number should be placed where it will accurately identify the correct study.
- The names of authors in the text should concur with the reference list.
- References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration.
- Abstracts as references may be used; "unpublished observations" and "personal communications" may not be used as references, although references to written, not oral, communications may be inserted (in parentheses) in the text.
- Papers accepted but not yet published may be included as references by adding "In press" after the journal name. Information from manuscripts submitted but not yet accepted should be cited in the text as "unpublished observations" (in parentheses).
- In general: All authors/editors should be listed unless the number exceeds six, when you should give six followed by "et al."

Examples of correct forms of references are given below:

**Articles in Journals** (see also *Journal article on the Internet*)

1. *Standard journal article*

List the first six authors followed by et al.

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV-infected patients. N Engl J Med. 2002 Jul 25;347(4):284-7.

More than six authors:

Rose ME, Huerbin MB, Melick J, Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.

2. *Organization as author*

Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance.Hypertension. 2002;40(5): 679-86.

3. *Both personal authors and organization as author* (List all as they appear in the byline.)

Vallancien G, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1,274 European men suffering from lower urinary tract symptoms. J Urol. 2003;169(6):2257-61.

4. *Volume with supplement*

Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. Headache. 2002;42Suppl 2:S93-9.

5. *Issue with supplement*

Glauser TA. Integrating clinical trial data into clinical practice.Neurology. 2002;58(12 Suppl 7):S6-12.

6. *Type of article indicated as needed*

Tor M, Turker H. International approaches to the prescription of long-term oxygen therapy [letter]. Eur Respir J. 2002;20(1):242.

Lofwall MR, Strain EC, Brooner RK, Kindbom KA, Bigelow GE. Characteristics of older methadone maintenance (MM) patients [abstract]. Drug Alcohol Depend. 2002;66Suppl 1:S105.

7. *Article published electronically ahead of the print version*

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells. Blood. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

**Books and Other Monographs**

1. *Personal author(s)*

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

2. *Editor(s), compiler(s) as author*

Gilstrap LC 3rd, Cunningham FG, VanDorsten JP, editors. Operative obstetrics. 2nd ed. New York: McGraw-Hill; 2002.

3. *Organization(s) as author*

Advanced Life Support Group. Acute medical emergencies: the practical approach. London: BMJ Books; 2001. 454 p.

4. *Chapter in a book*

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

5. *Conference proceedings*

Harnden P, Joffe JK, Jones WG, editors.Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer; 2002.

6. *Dissertation or thesis*

Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

**Other Published Material**

*Newspaper article*

Tynan T. Medical improvements lower homicide rate: study sees drop in assault rate. The Washington Post. 2002 Aug 12;Sect. A:2 (col. 4).

**Unpublished Material**

*In press or Forthcoming*

Tian D, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. ProcNatlAcadSci U S A. Forthcoming 2002.

**Electronic Material**

1. *Journal article on the Internet*

Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs. 2002 Jun [cited 2002 Aug 12];102(6):[about 1 p.]. Available from: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm Article

Article published electronically ahead of the print version:

Yu WM, Hawley TS, Hawley RG, Qu CK. Immortalization of yolk sac-derived precursor cells.Blood. 2002 Nov 15;100(10):3828-31. Epub 2002 Jul 5.

Article with document number in place of traditional pagination:

Williams JS, Brown SM, Conlin PR. Videos in clinical medicine.Blood-pressure measurement. N Engl J Med. 2009 Jan 29;360(5):e6. PubMed PMID: 19179309.

Article with a Digital Object Identifier (DOI):

Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. BMJ. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752. PubMed PMID: 19129307; PubMed Central PMCID: PMC2615549.

2. *Monograph on the Internet*

Foley KM, Gelband H, editors. Improving palliative care for cancer [Internet]. Washington: National Academy Press; 2001 [cited 2002 Jul 9]. Available from: http://www.nap.edu/books/0309074029/html/.

3. *Homepage/Web site*

Cancer-Pain.org [Internet]. New York: Association of Cancer Online Resources, Inc.; c2000-01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: http://www.cancer-pain.org/.

**G. 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.

1. The submission has not been previously published elsewhere, is original and has been written by the stated authors.
2. The article is not currently being considered for publication by any other journal and will not be submitted for such review while under review by the Bangladesh Heart Journal.
3. The submission file is in Microsoft Word file format, and the figures are in JEPG or TIFF format.
4. The text is single-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.
5. The text adheres to the stylistic and bibliographic requirements outlined in the Instruction to Authors. Make sure that the references have been written according to the ICMJE Recommendations Style.
6. Spell and grammar checks have been performed.
7. All authors have read the manuscript and agree to publish it.

**H. Submission**

Papers should be submitted to the Editor. Three copies of manuscript should be submitted duly signed by all authors with a copy of CD, to:

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Papers can also be submitted via the email using the following address:

Email: bangladeshheartj@yahoo.com

Vol. 38, No.2, - July 2023 Heart J.

*Original Article*

# Determination of Values of the Tricuspid Annular Plane Systolic Excursion (TAPSE) in Bangladeshi Adult Patient with or without LV Dysfunction

R J Tamanna [1], S J Hoque[2], F M Pasha[3]

**Abstract:**

**Background: Tricuspid annular plane systolic excursion (TAPSE) is an Echocardiographic measure that allows us to assess right ventricular systolic function and it correlates well with reference techniques like Cardiac Magnetic Resonance Imaging. TAPSE measurement is common in adults.**

**Objective: Our objective was to determine values of TAPSE in Bangladeshi adults with or without LV systolic dysfunction and to determine the relationship of these values with age, sex, RVIDd, LVEF & EPSS.**

**Method: This was an prospective observational study in patients undergoing comprehensive transthoracic echocardiography for any indication. From April 2022 to April 2023 we prospectively enrolled 100 adult (from 30 to age 80 years) of both sexes who presented to the Cardiology Clinic of LABAID Cardiac Hospital. We performed a complete transthoracic echocardiography study. We measured TAPSE in 2-dimensional M-mode echocardiograms from the apical 4- chamber view, positioning the cursor on the lateral tricuspid annulus near the free RV wall and aligning it as close as possible to the apex of the heart . The mean values were taken by at least 2 measurements for reducing interobserver and intraobserver variability's. Patients with confirmed congenital & valvular heart disease were excluded.**

**Results: Mean TAPSE values were 19.15±3.87cm irrespective of LVEF, with no significant differences between sexes, 18.45±3.801 in male , 19.94±3.853 in female (P=.056). TAPSE value was 22.00±1.581 in person with normal LVEF & 16.77±2.455 in person with reduced LVEF ( P<.001) A statistically significant positive correlation of LVEF (r=.813) and significant negative correlation of EPSS (r=-.639) were observed with TAPSE (p<0.001). But no significant correlation of TAPSE was found between age (r=-.185)). ), gender (r=.192) & RVIDd (r= -.063) (p >0.05). Multivariate analysis confirmed these correlations and the interactions between variables (LVEF & EPSS). Graphs of estimated population-based TAPSE values adjusted by age and LV function are provided.**

**Conclusion: We determined values of TAPSE in Bangladeshi adult population with or without LV systolic dysfunction and assessed relationship of these values with age, sex, RVIDd, LVEF & EPSS. The TAPSE measurement was reproducible and associated directly with LV systolic function. These reference values could guide decision making in daily clinical practice.**

*Keywords: Left Ventricular Ejection Function, E Point Septal Separation, Tricuspid Annular Plane Systolic Excursion.*

*(Bangladesh Heart Journal 2023; 38(2): 92-101)*

## Introduction

Cardiovascular disease remains a leading cause of death. Right ventricular (RV) function is a strong predictor of outcome in many cardiovascular diseases, but its significance is often neglected. Little is known about the

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2. Department of Cardiology, Birdem General Hospital, Dhaka
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*DOI: https://doi.org/10.3329/bhj.v38i2.70280*

prognostic value of RV systolic function in the general population. Therefore, we aimed to determine the value of RV systolic function, evaluated by tricuspid annular plane systolic excursion (TAPSE), in patient with or without LV systolic dysfunction.

The complex geometry of the right ventricle (RV) makes systolic function evaluation difficult. The thick trabeculae in the endocardial surface and muscular elongated outflow tract—located in a different plane to that of the inflow tract—prevent us from adopting the theoretical volumetric models that can be applied in the left ventricle.[1, 2, 3, 4, 5] interventions. The RV functional situation can condition therapeutic management and clinical course in certain diseases. [6,7] Hence, in daily clinical practice, we need a means to reliably, reproducibly measure RV systolic function.[8, 9]

In M-mode echocardiography, tricuspid annular plane systolic excursion (TAPSE) measures the variation during the cardiac cycle, in the situation of the lateral portion of the annulus of the tricuspid valve, from the apical 4-chamber view. TAPSE is an echocardiographic parameter that estimates RV systolic function adequately and correlates well with reference techniques like cardiac magnetic resonance imaging.[10] Recommendations for echocardiographic evaluation of RV and TAPSE values in the adult population can be found in the literature.[11, 12]

The principle objective of the present study was to determine baseline TAPSE values in Bangladeshi adult patient with or without LV dysfunction and to assess the influence of age, sex , RVIDd & LV systolic function variables on those values.

**Material & Methods:**

This was an prospective observational study in patients undergoing comprehensive transthoracic echocardiography for any indication. From April 2022 to April 2023, we prospectively enrolled 100 adult (from 30 to age 80 years) of both sexes who had been referred to the cardiology service of LABAID Cardiac Hospital for routine health check up. We performed a complete transthoracic echocardiography study . M-mode and 2D echocardiograms were recorded on a Vivid $^{TM}$ E 95 with cSound $^{TM}$ ultrasound system (GE Medical System) with M5sc-D ( GE) multifrequency transducer. We followed a standard protocol, evaluated left ventricular function, The modified Simpson rule was used for calculating the LVEF . In addition to routine echocardiographic measurements, EPSS was measured by M-mode in the para-sternal long axis view (PLAX) of the heart. We additionally measured TAPSE in 2-dimensional M-mode echocardiograms from the apical 4-chamber view, positioning the cursor on the lateral tricuspid annulus near the free RV wall and aligning it as close as possible to the apex of the heart (Figure 1). To prevent systematic errors in obtaining or interpreting the echocardiograms, 2 different cardiologists performed the echocardiograms and the mean values were taken by at least 2 measurements for reducing interobserver and intraobserver variability's. We excluded patients with congenital & valvular heart disease.

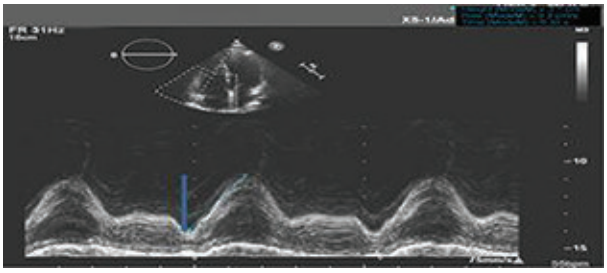


**Fig.-1 :** *Standard technique for measuring tricuspid annular plane systolic excursion using two-dimensional M mode echocardiography.*

Statistical Analysis : Numerical data obtained from the study were analyzed and significance of difference was estimated by using statistical method. The statistical data were analyzed using IBM SPSS 25.0. The continuous data were expressed as frequency, the mean±standard deviation, and the categorical data were expressed as percentages. Significance of difference between groups was evaluated by unpaired student t test. Graphical representation, Correlation test & Pearson correlation coefficient were used to measure the relationship between TAPSE & other variables. Stepwise simple & multiple linear regression analysis were used to estimate the relation between different variables and TAPSE and also to identify best predictor of TAPSE. Probability values ($P<0.05$) were considered statistically significant in the analyses.

**Results:**

Echocardiographic tracings of sufficient quality for analysis were obtained in all patients.

Fig 2 & 3 showed sex and age distribution of study patients. In total, 100 patients were enrolled in the study. We examined 53 male (53%) and 47 female (47%) Age range 30 – 103yrs, majority of the cases (>60%) are in between 41-to 70 yrs of age . Age - Mean ±SD (58.7±11.66 yrs), Male and Female ratio 1.1: 1 Majority of male patient are in between 51-70 yrs of age and majority of female patient are in between 61 to 70 yrs of age.

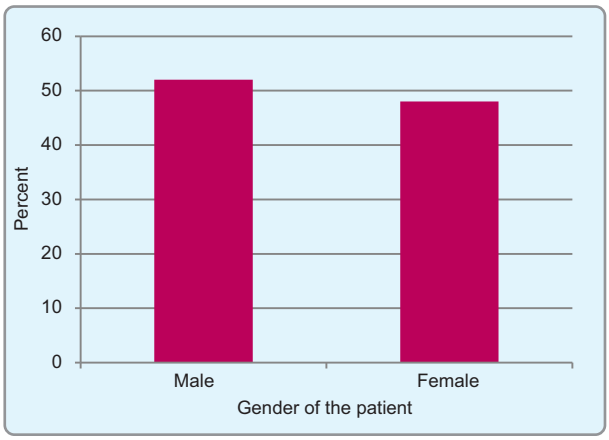



**Fig.-2:** *Sex distribution of the study patients.*

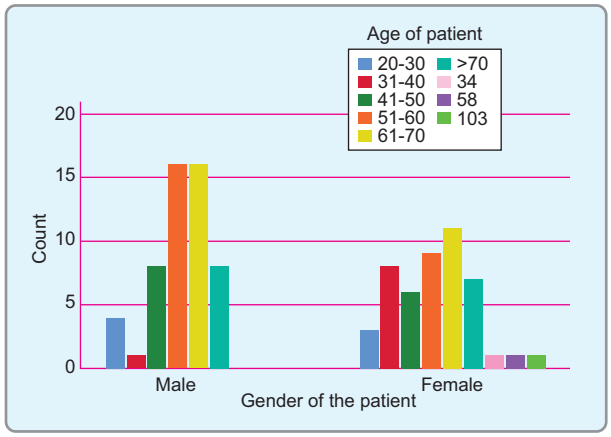



**Fig.-3:** *Age and sex distribution of the study patients*

Table I showed Distribution of Echocardiography parameters. The LVEF ranged from 20% to 68% (mean±SD 47.14±15.77), the EPSS ranged from 4 to 28 mm (mean ±SD 9.26±5.60), the LVIDd ranged from 30 to 72 mm ( mean ±SD 50.43±8.97), LVIDs ranged from 12mm to 62 mm (mean ± SD 34.77±12.32) ,. TAPSE ranged from 12 to 25 mm (mean ±SD =19.15± 3.878) , RV Dimension ranged from 17 to 34 mm (mean ±SD =24.28± 3.975).

Table II showed that TAPSE declined with increasing age.

Table III showed mean TAPSE value in the study population in relation to Gender. TAPSE value was 19.94±3.853 ( mean±SD ) in female & 18.45± 3.801 (mean±SD) in male. There was only a small gender difference but correlation is insignificant (r=.192 P=.056).

Fig 4 showed Distribution of TAPSE in respect of gender

Table IV showed correlation of TAPSE value to other variables .TAPSE declined with increasing age but the correlation with age was not significant (r=-.185 , P=.065). Correlation with RVIDd was negative but not significant ( r =.-.063, P=.533) . Very significant positive correlations of TAPSE was found with LVEF (r =.813, P=.000) & significant negative correlation was found with EPSS (r =-.639, P=.000).

Table V showed that an LVEF > 50% is evidence of TAPSE >20 mm, (P<.001). Of note, LVEF <40% correlates with decreased TAPSE value with an estimated TAPSE of <17 mm. (P<.001) suggestive of reduced RV systolic function.

Table VI showed Pearson Correlation between different variables & TAPSE. A statistically significant negative correlation of EPSS (r=-.639) and very significant positive correlation of LVEF (r=.813) were observed with TAPSE (p<0.001). But no significant correlation of TAPSE was found with age (r=-.185)), gender (r=.192) & RVIDd (r= -.063)) (p >0.05). In the analysis, LVEF presented the best positive correlations with TAPSE values (r=0.813 ; *P*<.001), whereas EPSS maintained a negative correlation (r=–0.639; *P*<.001).

**Table I**

*Distribution of Echocardiography parameters*

| Echocardiographic Parameters | N | Minimum | Maximum | Mean | Std Deviation |
|---|---|---|---|---|---|
| Left Ventricle Diastolic Dimension | 100 | 30 | 72 | 50.43 | 8.976 |
| Left Ventricle Systolic Dimension | 100 | 12 | 62 | 34.77 | 12.321 |
| Left Ventricular Ejection Fraction | 100 | 20 | 68 | 47.14 | 15.777 |
| E Point Septal Seperation | 100 | 4 | 28 | 9.26 | 5.601 |
| Tricuspid Annular Plane Systolic Excursion | 100 | 12 | 25 | 19.15 | 3.878 |
| Right Ventricle Dimension | 100 | 17 | 34 | 24.28 | 3.975 |

Data presented as Mean± SD

**Table-II**

*Age related Values of TAPSE*

| Age ( in yrs) | TAPSE in mm (mean±SD) |
|---|---|
| 20-30 | 23±1.000 |
| 31-40 | 22±3.333 |
| 41-50 | 18±3.759 |
| 51-60 | 18±3.845 |
| 61-70 | 18±3.965 |
| >70 | 18±3.135 |

Data presented as Mean± SD

**Table-III**

*Correlation of mean TAPSE value with gender*

| Gender | N | Mean TAPSE (mm) | SD | Correlation (r value ) | Sig (P value) |
|---|---|---|---|---|---|
| Male | 53 | 18.45 | 3.801 | .192 | .056 |
| Female | 47 | 19.94 | 3.853 | | |

P value reached from Paired sample t test,*$p$- value significant at <0.05.

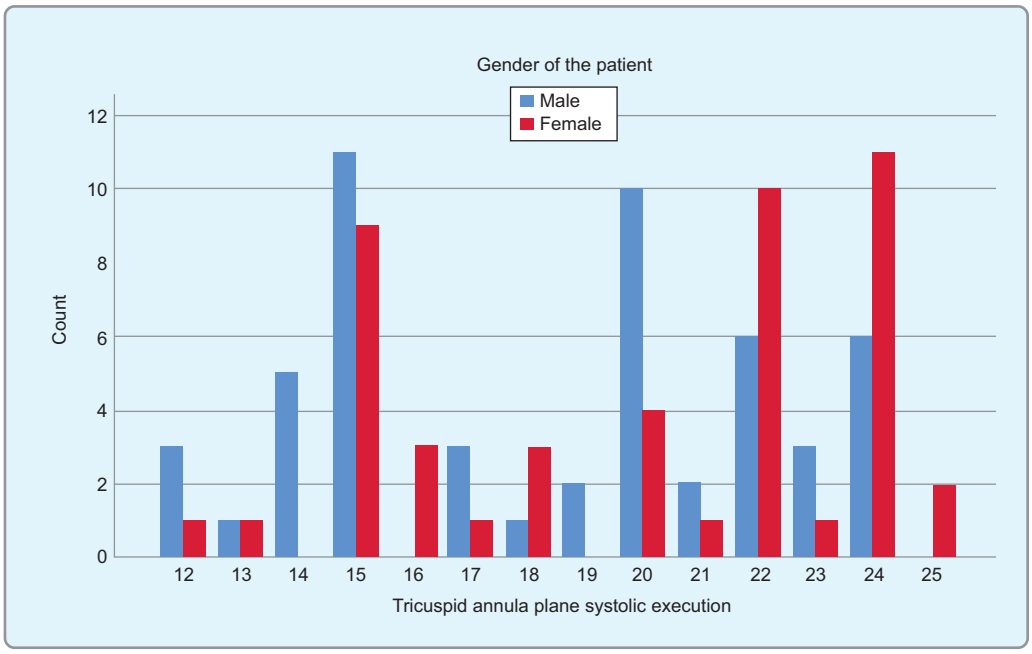



**Fig 4:** *Distribution of TAPSE in respect of gender*

**Table-IV**

*Correlation of mean TAPSE with other variables*

| | TAPSE | Mean 19.15mm | SD 3.878 | N 100 | Correlation ( r value) | Sig ( p value) |
|---|---|---|---|---|---|---|
| Pair -1 | Age | 58 yrs | 11.663 | 100 | -.185 | .065 |
| Pair -2 | RVIDd | 24.28mm | 3.975 | 100 | -.063 | .533 |
| Pair- 3 | LVEF | 47.14% | 15.777 | 100 | .813 | .000 |
| Pair -4 | EPSS | 9.26mm | 5.601 | 100 | -.639 | .000 |

P value reached from Paired sample t test , $p$- value significant at<0.05.

**Table-V**

*Prediction of TAPSE in respect of LVEF*

| LVEF (%) | TAPSE (mm) | Std Deviation | N | P value |
|---|---|---|---|---|
| 55 | 22 | 1.581 | 5 | .000[s] |
| 35 | 16 | 2.455 | 13 | .000[s] |

*P value reached from unpaired student t test, S = significant, P 0<.01

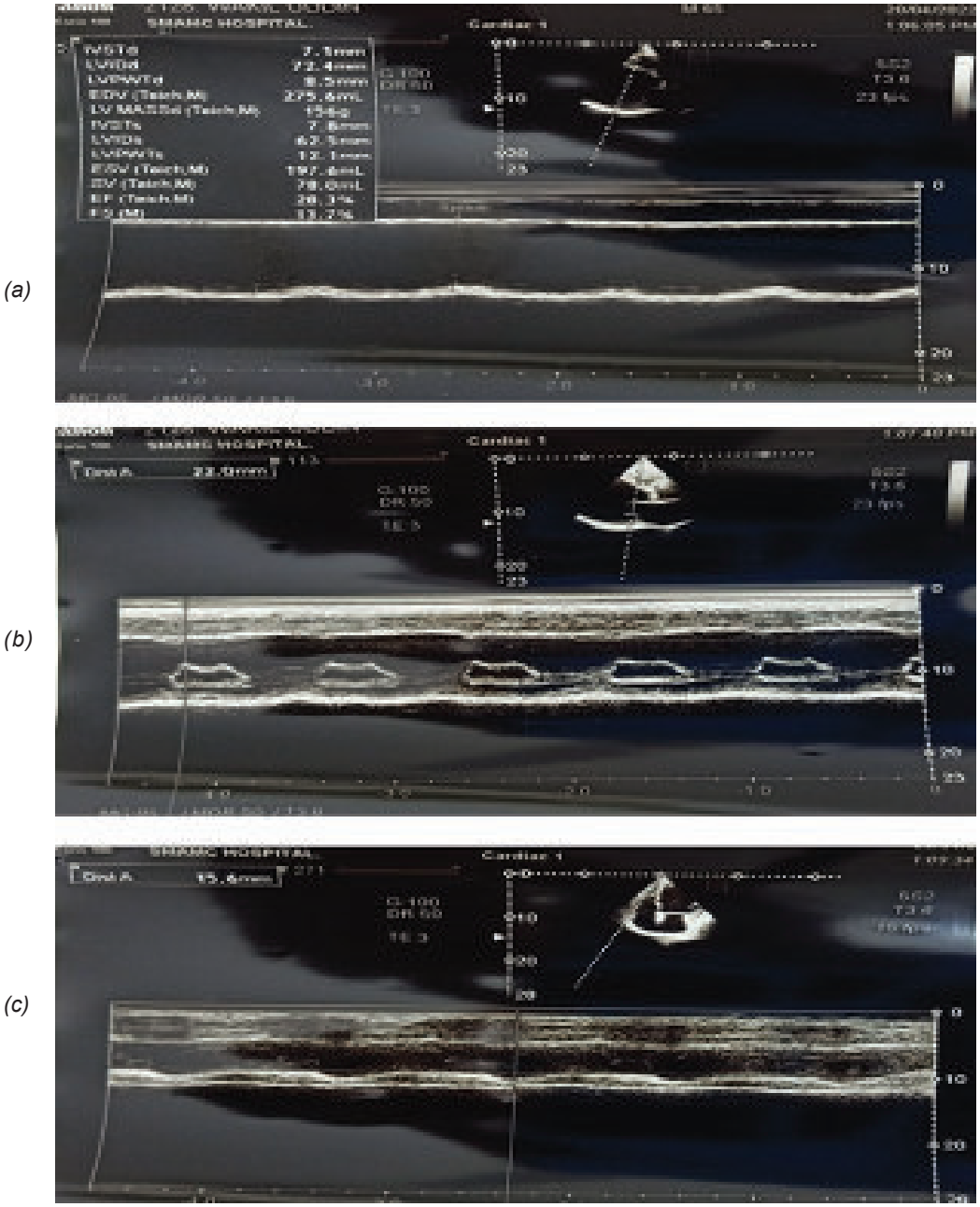



**Fig 5 :** *Measurement of LVEF In the image above (a) , EPSS in the image middle (b) & TAPSE in the image below (c). LVEF is ~28% , EPSS is ~22 mm & TAPSE is ~15 mm indicating both LV & RV systolic dysfunction.*

**Table VI**
*Pearson Correlation between different variables & TAPSE*

| Variable vs. TAPSE | Pearson Correlation Co-efficient ( r value) (N=100) | Sig (P value) |
|---|---|---|
| EPSS | -.639** | .000s |
| LVEF | . 813** | . 000s |
| Age | -.185 | .065 |
| Gender | .192 | .056 |
| RVIDd | -.063 | .533 |

P value reached from Correlation test. **. Correlation is significant at the 0.01 level (2-tailed). S =significant

Table VII showed Simple Linear Regression analysis. In linear regression analysis with all of the variables only LVEF & EPSS were significant predictor of TAPSE. Most important determinant of TAPSE was LVEF (R=.813, p<0.001) followed by EPSS (R=.639, p<0.001)

**Table-VII**
*Simple Linear Regression analysis.*

| Simple Linear Regression analysis | R value | R Square | P value |
|---|---|---|---|
| LVEF | .813 | .662 | .000s |
| EPSS | .639 | .408 | .000s |
| Gender | .192 | .037 | .056 |
| Age | .185 | .034 | .065 |
| RVIDd | .063 | .004 | .533 |

Dependent Variable: TAPSE, Predictor: LVEF, EPSS, Age, Gender, & RVIDd . P value derived from Pearson correlation, S= significant, **. Correlation is significant at the 0.01 level (2-tailed).

In Table VIII by combining different variables in stepwise multiple linear regression analysis an attempt for predicting TAPSE was done. When other variables were included with the variable LVEF into multiple linear regression analysis the resultant correlation coefficient was ((R=.818, P < .001). So it was observed that contribution of other variables is very insignificant & LVEF was the best independent predictor of TAPSE (R=.813, P<.001).

Table IX showed Pearson Correlation between TAPSE and Calculated LVEF. It was found that TAPSE has highly significant positive correlation with calculated LVEF (r=.813, p<0.001)

Fig 6. Scatter plots showed the relationships of TAPSE with LVEF ( Fig 6a) & EPSS ( Fig 6b) , indicating their sample distribution. Plots showed TAPSE is directly proportionate to LVEF & inversely proportionate to the EPSS

**Table VIII**
*Stepwise Multiple linear regression analysis:*

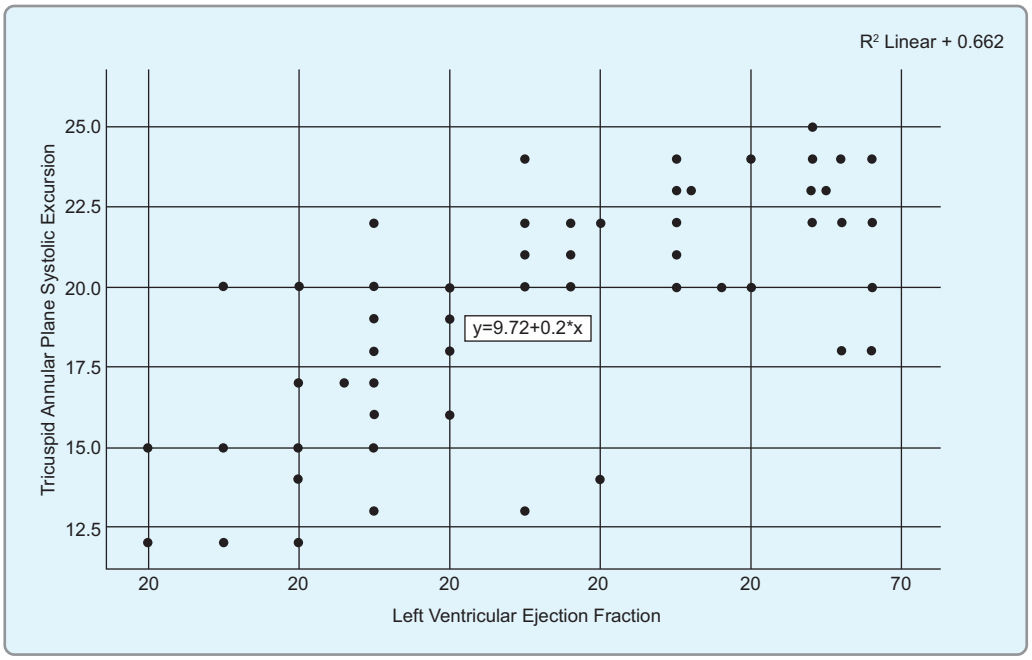
| Stepwise Multiple Linear regression analysis | R value | R square | P value |
|---|---|---|---|
| LVEF | .813 | .662 | .000s |
| LVEF+EPSS | .814 | .662 | .000 s |
| LVEF+EPSS+Age | .816 | .667 | .000 s |
| LVEF+EPSS+Age+ Gender | .817 | .667 | .000 s |
| LVEF+EPSS+Age+ Gender +RVIDd | .818 | .669 | .000 s |

P value derived from Pearson correlation, S= significant, **. Correlation is significant at the 0.01 level (2-tailed). A). Dependent Variable: TAPSE
B) Predictors: (Constant), LVEF, EPSS, Age, Gender & RVIDd

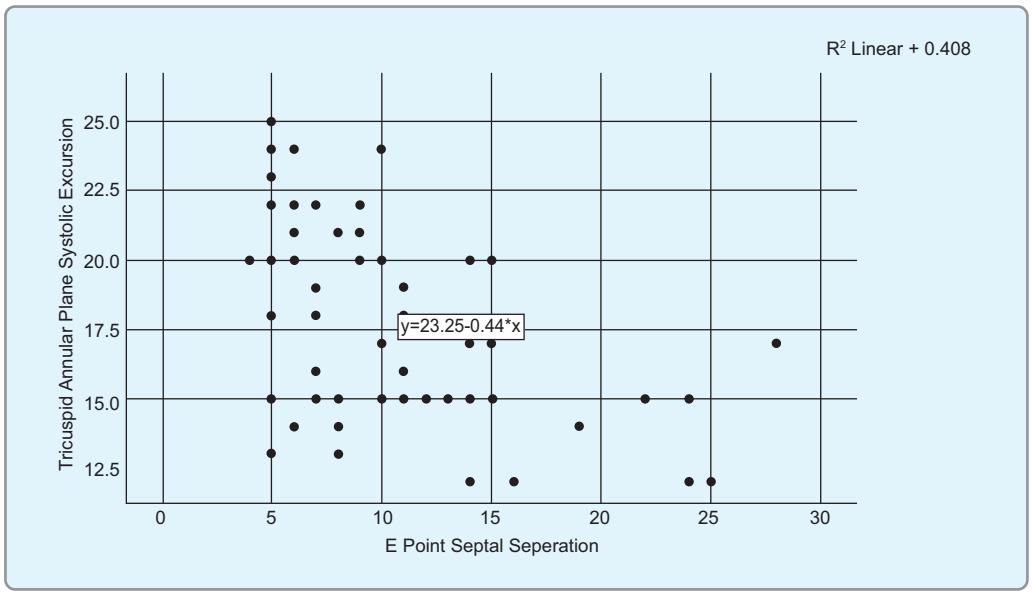
**Table IX**
*Pearson Correlation between TAPSE and Calculated LVEF*

| LVEF | Pearson Correlation Co –efficient ( r value) (N=100) | P value |
|---|---|---|
| TAPSE | . 813** | . 000s |

P value derived from Pearson correlation, S= significant, **. Correlation is significant at the 0.01 level (2- tailed).




*(a)*




*(b)*

**Fig.-6:** *(a) Scatter plot (BIVAR) = LVEF with TAPSE. (b) Scatter plot (BIVAR)=EPSS with TAPSE*

**Discussion:**

We present the values for TAPSE in a sample of adult with or without LV systolic dysfunction. TAPSE is a measure of RV systolic function. Assessment of the RV systolic function may be beneficial for risk stratification of individuals from the general population. This may be because of TAPSE's simplicity, ease of measurement, and good reproducibility.[13] It does not require state of the art image quality or high frame rate conditions for optimal measurement,[13]as is the case for other measures of RV systolic function, such as 2 dimensional speckle tracking of the RV free wall.[13] In addition, it can often be hard to acquire high quality images of the entire RV free wall, whereas imaging only the RV base and

tricuspid annular plane is much more feasible. Despite its simplicity, TAPSE correlates well with RV ejection fraction determined by radionucleotide angiography.[13,14]

Current guidelines define the normal range of RV systolic function determined by TAPSE in the general population as a mean±SD of 24±3.5 mm.[15] and abnormal RV systolic function is defined as TAPSE <17 m*m.[15]*

In our sample values of TAPSE were maximum 25 mm, minimum 12 mm , mean±*SD* 19.1 ± 3. 878. Mean TAPSE value was 19.94±3.853 in female & 18.45± 3.801 in male. There was only a small gender difference but insignificant (r=.192, P=.056). The reason for lower mean value in our study was the inclusion of patients with or without LV systolic dysfunction. In our study mean value of TAPSE was 22±1.581 in person with normal LVEF (P<.001) & 16 ±*2.455* in person with reduced LVEF*( P<.001).* LV systolic function is a significant determinant of RV systolic function through mechanical interventricular dependence.[16] In our study, decreasing LV systolic function, was significantly associated with decreasing RV systolic function, as determined by TAPSE. It was found that TAPSE has very significant positive correlation with calculated LVEF (r=.813, p<0.001)

In our study LVEF > 50% is evidence of TAPSE >20 mm, (P<.001). Of note, LVEF <40% correlates with decreased TAPSE value with an estimated TAPSE of <17 mm. (P<.001) suggestive of reduced RV systolic function. TAPSE value of d"17 mm was significantly associated with a reduced LV systolic function (LVEF<40%) which is predictive of CVD as shown in Table V. RV function, determined by TAPSE, remained a strong predictor of CVD. However, more research is needed to validate our findings.

In other study , the relationship between TAPSE and age was positive. On the other hand, relation between TAPSE and HR was linear and negative. Although not all studies have found HR has a clear influence of on tricuspid annular plane movement.[17] In our study we found TAPSE declined with increasing age but the correlation with age was not significant ( ( r=-.185, P=.065). And we did not correlate HR with TAPSE.

In this study , a statistically significant negative correlation of EPSS (r=-.639 ) and significant positive correlation of LVEF (r=.813) were observed with TAPSE (p<0.001). But no significant correlation of TAPSE was found with age ( r=-.185)). ), gender ( r=.192 ) & RVIDd (r= -.063)) (p >0.05). In the analysis, LVEF presented the best positive correlations with TAPSE values (r=0.813; *P*<.001). In linear regression analysis with all of the variables only LVEF & EPSS were significant predictor of TAPSE. Most important determinant of TAPSE was LVEF (R=.813, p<0.001) .

Measuring TAPSE as a parameter to evaluate RV systolic function was reproducible. In our study, we found good concordance for TAPSE[18], in the line with published recommendations [19]and in parallel with other studies conducted in different circumstances.[20] The same conclusion about reproducibly has been reached by other methods.[21.] Moreover, in contrast to other less readily available MRI- (Magnetic resonance imaging ) or more invasive diagnostic right heart catheterization tech niques , this method is accessible in any Echocardiography laboratory . Future large scale studies will probably needed to determine the clinical role of TAPSE measurement in adult.

**Study Limitations**

A limitation of the present study is the lack of information on RV systolic pressure. It would be interesting to assess whether the prognostic value of RV systolic function is independent of RV afterload. Unfortunately, information on RV systolic pressure was not available in this study. Another limitation is the number of patients. Our result could not be generalized because we included patient with or without LV systolic dysfunction which was associated with variability of mean value of TAPSE.

**Conclusion:**

We presented TAPSE reference values of Bangladeshi adult male and female with or without LV systolic dysfunction. TAPSE was directly proportional to LV systolic dysfunction & age. But relation to age was not found statistically significant in this study. TAPSE was found inversely proportionate to EPSS & RVIDd. Though relation to RVIDd was not statistically significant in accordance with our study.A statistically significant positive correlation of LVEF & significant negative correlation of EPSS were observed with TAPSE. This result could be used to help with decision making in daily clinical practice. RV systolic function as assessed by TAPSE, is associated with CVD in general population. In the general population assessment of RV systolic function as evaluated by TAPSE may provide novel prognostic information about the risk of CVD. In concordance with other pioneering studies, we presented reference values to guide diagnostic, prognostic and therapeutic decision making.

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*Original Article*

# Association Between Systemic Immune- Inflammation Index and Severity of Coronary Artery Disease in Acute Myocardial Infarction Patients

Tania Easmin[1], Md. Khalequzzaman[2], Md. Mohsin Ahmed[3], Md. Mehadi Hasan[4]



**Abstract:**

**Background: Acute myocardial infarction is one of the leading causes of death across the world. Determination of severity is important in patients with acute myocardial infraction for the therapeutic decision making. Systemic immune-inflammation index (SII) has been proposed as a new prognostic marker in patients with acute MI. Several international studies have found to compare the relation between SII and severity of coronary artery disease. In these studies, they demonstrated that the SII is higher in severe CAD. In our country, no such study has been done yet to predict the severity of coronary artery disease by estimating SII in acute MI patients. Moreover, SII is cheap, easily available, non-invasive and routinely done procedure.**

**Objectives: This study was conducted to find out the association of SII to severity of CAD in acute MI patients.**

**Methods: This observational cross sectional analytical study was carried out in the Department of Cardiology, Dhaka Medical College Hospital, SSMC and Mitford Hospital and NICVD, Dhaka from March 2021 to February 2022. Patients with acute MI (STEMI and NSTEMI) were approached for this study according to inclusion and exclusion criteria. Coronary angiogram was done during index hospitalization. The severity of coronary artery disease was assessed by Vessel score and Gensini score. According to Gensini score CAD severity detected as mild to moderate (d"50) , severe (>50). Patients were divided into two groups according to Gensini score: Group A, severe CAD ( Gensini score >50) and Group B, mild to moderate CAD( Gensini score d"50). SII calculated from admission CBC report.**

**Results: Among 70 patients in our study 33 (47.1%) were in the high Gensini group (Group A) and 37 (52.85%) were in low Gensini group (Group B). Mean systemic immune inflammation index was found significantly higher in group A than group B, p value 0.001. We found strong positive correlation between SII and Gensini score (r= 0.7, p= 0.001). With the increase of SII, Gensini score increases demonstrating more severe CAD. In multivariate logistic regression analysis, after adjustment of confounding, hypertension (p=0.01, OR=4.84), NLR (P=0.004, OR=1.81) and SII (P=0.011. OR=1.002) remain independent predictor of severe CAD. In ROC curve analysis, the AUC of SII for predicting severity of CAD is 0.8 with p value < 0.001, 95% CI (0.71-0.91) and SII cut off value 686 can predict severe CAD with 78% sensitivity and 76% specificity. So, from this study, it is evident that SII is directly associated with coronary artery disease severity.**

**Conclusion: Increased SII was associated with angiographically severe coronary artery disease in acute Myocardial Infarction patients and this association is independent of conventional cardiovascular risk factors.**

*Key words: SII: Systemic immune inflammation index; CAD: Coronary Artery Disease*

*(Bangladesh Heart Journal 2023; 38(2): 102-109)*

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*DOI: https://doi.org/10.3329/bhj.v38i2.70263*

**Introduction:**

Cardiovascular diseases (CVDs) are the leading cause of death globally and major contributor of disability. An estimated 17.9 million people died from CVDs in 2019, representing 32% of all global death, of these 85% due to heart attack and stroke. Three quarters of CVD death take place in low and middle-income countries. [1]

CAD is growing by epidemic proportion day by day in Bangladesh.[2] The exact prevalence of coronary artery disease in Bangladesh is not known. Only a limited number of small-scale epidemiological studies are available.[3] Recent data indicates CAD prevalence in Bangladesh is between 1.85% and 3.4% in rural and 19.6% in urban population.[4]

The dynamic nature of the CAD process results in various clinical presentations, which can be conveniently categorized as either acute coronary syndromes (ACS) or chronic coronary syndromes (CCS).

ACS are further classified into ST-elevation MI (STEMI), Non-ST elevation MI (NSTEMI) and Unstable angina (UA).[5] Acute myocardial infarction is the most severe manifestation of coronary artery disease.

Atherosclerosis plays a dominant role in the pathophysiological process of CAD and atherosclerosis are closely associated with inflammation.[6] Atherosclerosis is primarily an inflammatory disease and the role of inflammation in the process of initiation, progression and plaque de-stabilization in atherosclerosis has been well studied.[7] Evidence from various studies has demonstrated that increased levels of inflammatory markers are associated with increased rates of cardiac events in patients with CAD.[8]

The role of inflammatory markers in cardiovascular diseases has been studied extensively and a consistent relationship between various inflammatory markers and cardiovascular diseases has been established in the past. Among these C reactive protein (CRP), Highly sensitive CRP, Fibrinogen, Interleukin -6 (IL-6), Monocyte/ Macrophage colony stimulating factor (MCSF), Tumor necrosis factor alpha, Lipoprotein associated phospholipase A2, and Interlukin-1 isoform are noteworthy.

Different white blood cell (WBC) subtypes play crucial role in the pathogenesis of atherogenesis and atherothrombosis.[9] Neutrophils are the most abundant subtype of WBC which play major role in mediating inflammatory response. Neutrophils have been shown to mediate tissue damage and inflammation in advanced stage of atherosclerosis. It has been positively associated with necrotic core area, lesion size and plaque vulnerability. On the other hand, lymphocyte play an important role in regulating the inflammatory response and atherosclerotic process. A low lymphocyte count is associated with progression of atherosclerosis. Lymphopenia is associated with a poor prognosis in various disease like stable CAD, acute coronary syndromes and heart failure. Platelets are one of the major determinants of prothrombotic potential in arterial thrombosis and they also participate in the inflammatory process and atherogenesis. Active platelets interact with the endothelium, leukocyte and inactivated platelets. So, platelets have role in development of CAD.[10]

Biomarkers derived from the counts of these three cell types have been widely investigated in

recent years like neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and they

have been found to be associated with severity of coronary artery disease. Systemic Immune-

Inflammation Index (SII) is a novel and intriguing marker of inflammation and immune system.[11]

SII is determined as absolute platelet count × absolute neutrophil count/absolute lymphocyte count. SII gathers neutrophil, lymphocyte and platelet and reflects the balance between inflammatory and immune status. It has been suggested that since SII includes 3 cell types, it may provide valuable information regarding inflammation. It is a potential biomarker for cardiovascular diseases.[12]

Coronary angiography is the gold standard for the clinical judgement of CAD whereas the Gensini score is a quantitative indicator for the estimation of the severity of coronary artery stenosis on the basis of coronary angiography.

Several international studies have shown the relationship between SII and severity of CAD. They showed that higher the SII, higher the severity of CAD. So, purpose of our study is to demonstrate relation between SII and severity of CAD in acute MI patients.

Methods: This cross-sectional observational study was carried out in the Department of Cardiology of DMCH, Sir Salimullah Medical College and Mitford Hospital and National Institute of Cardiovascular Diseases, Dhaka from March,2021 to February 2022. Patients with acute myocardial infarction who undergone coronary angiogram during the study period were selected by purposive sampling. Patients who underwent prior PCI and/or CABG, patients with heart failure - NYHA class III, IV,

hematological diseases, malignancy, chronic kidney disease, chronic liver disease, ongoing infection, chronic inflammatory disease, autoimmune disease, pregnancy were excluded from the study. Total 70 cases were included in the study and were divided into two groups on the basis of severity of coronary artery disease according to Gensini score: Group A (Severe CAD, Gensini score > 50) and Group B (Mild-Moderate CAD, Gensini score d" 50). After taking informed written consent from each patient, meticulous history was taken and detailed clinical examination was performed and recorded in predesigned structured proforma. Levels of hemoglobin, white blood cells, neutrophils, lymphocytes, other differentials of white blood cells and platelets were determined by automated hematology analyzer. Serum creatinine, random blood sugar, fasting lipid profile and other screening tests for coronary angiogram were done. Coronary angiogram was done by conventional method in the same hospital setting. Severity assessment was done by Gensini score and vessel score.

SII was calculated by multiplying the number of platelets with NLR (Neutrophil-Lymphocyte Ratio) obtained from peripheral blood sample. Angiographic pattern and severity of coronary artery disease were assessed by interpretation of coronary angiogram by visual estimation by two cardiologists. Severity of coronary stenosis was graded according to the number of major epicardial vessel with significant stenosis (vessel score) and Gensini score.

In vessel score, significant coronary artery disease was defined as > 70% stenosis in any of

the three major epicardial coronary arteries or a left main coronary artery stenosis > 50%. Angiograms revealing coronary artery stenosis < 70% in major epicardial coronary arteries were termed non-obstructive CAD. Extent of coronary artery disease was defined as significant single, double or triple vessel coronary artery disease. Score ranged from 0 to 3 depending on the number of vessels involve. Left main coronary artery was scored as single vessel disease.

i) Score 0 = no vessel involvement, ii) Score 1 = single vessel involvement, iii) Score 2 = double vessel involvement, iv) Score 3 = triple vessel involvement.

The Gensini score was developed by Gensini and takes into consideration the geometrical severity of lesions by angiography, the cumulative effects of multiple obstructions, and the significance of jeopardized myocardium. A nonlinear score was assigned to each lesion based on the severity of stenosis as indicated by the reduction of lumen diameter. A multiplier was applied to each lesion score based upon its location in the coronary tree depending on the functional significance of the area supplied by that segment. The final Gensini score was the sum of the lesion scores. The score assessed 14 coronary artery segments, which were scored according to their anatomical importance (ranging from 0.5 to 5) multiplied by the score regarding the maximum degree of obstruction. The points of the 14 segments were summed up to yield a final score.

Total Gensini score was calculated as:

| % of stenosis | Score |
|---|---|
| 1-25% | 1 |
| 26-50% | 2 |
| 51-75% | 4 |
| 76-90% | 8 |
| 91-99% | 16 |
| 100% | 32 |
| Vessel (S) involved | Vessel multiplier score |
| Left Main | 5 |
| Proximal LAD / LCX | 2.5 |
| Mid LAD/Mid LCX | 1.5 |
| Distal LAD/ Distal LCX /First Diagonal/ First OM/RCA/PDA/PLV | 1 |
| Second Diagonal/Second OM | 0.5 |

Total Gensini score = Sum of (Score for % of stenosis X Score for Vessel(s) involved)

Interpretation of coronary angiogram will be made as the Gensini score. According to Gensini score, CAD was categorized as mild-moderate CAD (d"50), severe CAD (>50).

SPSS 23 was used for data analysis. Continuous variables were expressed as mean ± SD and categorical variables as frequency and percentage. The Kolmogorov-Smirnov test was used to verify the normality of distribution of continuous variables. Quantitative variables were analyzed by student's t test and Man Whitney U test. Categorical variables were analyzed by Chi-square test. To test association between SII and coronary artery disease severity Spearman's rank order correlation test were used. Simple logistic and multivariate logistic regression analysis were done to evaluate the independent predictor of severe CAD and results are shown as odds ratio and 95 % confidence intervals. P

value < 0.05 was considered significant and p value <0.001 was considered as highly significant. ROC curve analysis was done to obtain a cut-off value of SII to predict severe CAD with maximum sensitivity and specificity.

**Results:**

This cross-sectional observational study was conducted in the department of cardiology, DMCH, SSMCH, NICVD from March 2021 to February 2022. The main objective of this study was to find out the association between systemic immune-inflammatory index (SII) and coronary artery disease severity in acute MI patients. Among the total 70 patients' group-A had 33 and group- B had 37 patients. Most of the patients are above 50 years of age (Figure 1). Among the sample populations 90% were male and 10 % were female (Figure 2). The mean age differences between the group were statistically significant (p=0.03). Male: Female ratio was 10.6:1. Among the conventional CVD risk factors, hypertension and dyslipidemia were significantly high in group-A (p<0.05). No significant difference (p>0.05) between two groups was found in case of diabetes, smoking and family history of CAD (Table 1).



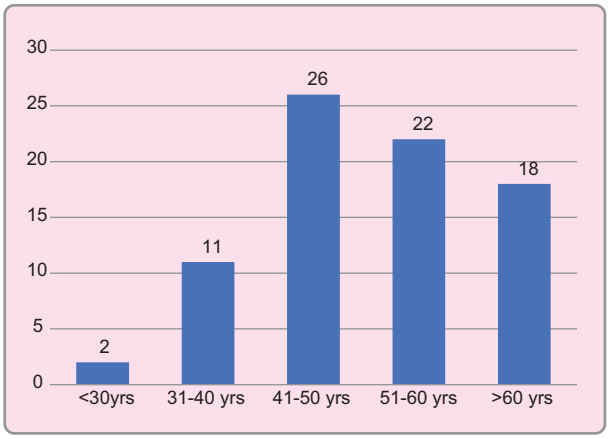


**Fig.-1:** *Distribution of age among sample populations (N=70)*

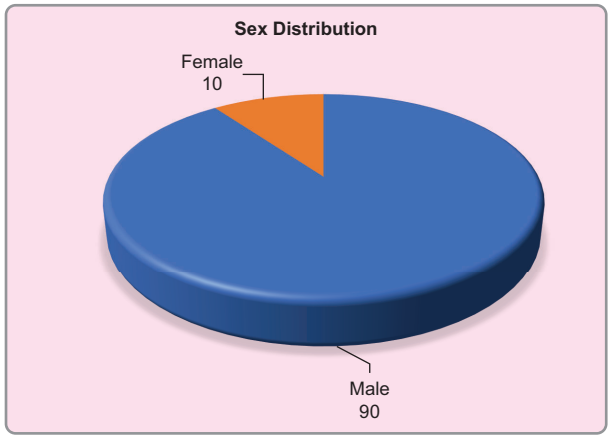


**Fig.-2:** *Distribution of sex among sample populations (N=70)*

**Table-I**

*Demographic and risk factors variables of study patients (N=70)*

| Variables | Group A (n=33) | Group B (n=37) | P value |
|---|---|---|---|
| Age, mean ± SD,yrs | 53.39±8.8 | 48.27±10.60 | $0.03^{S}$ |
| Sex | | | |
| Male | 30(91%) | 33(89%) | |
| Female | 3(9%) | 4(11%) | $0.81^{NS}$ |
| Smoker, n (%) | 17 (51.5%) | 16(43.2%) | $0.33^{NS}$ |
| Hypertension, n (%) | 27 (81.8%) | 19 (51.3%) | $0.007^{S}$ |
| Diabetes Mellitus, n (%) | 21 (63.6%) | 15 (40.5%) | $0.08^{NS}$ |
| Dyslipidaemia, n (%) | 28 (84.8%) | 19 (51.3%) | $0.003^{S}$ |
| Family history of CAD, n (%) | 3 (9%) | 7 (19%) | $0.31^{NS}$ |

Group A= Severe CAD, Gensini score > 50
Group B= Mild -Moderate CAD, Gensini score d" 50
s =significant
ns = not significant
p value reached from Students t -test and Chi square test.

The differences in mean hemoglobin, RBS and serum creatinine levels between two groups were insignificant (p>0.05). In lipid profile study, HDL was significantly low in group A

(p<0.01). LDL and serum TG were significantly higher in group-A (p value 0.001). Patients of group-A showed significantly higher mean WBC counts (p<0.01). Mean count of neutrophil and lymphocyte were statistically significant (p<0.001) across the group. The Mean NLR was 4.43± 2.27 in group-A & 2.01±1.56 in group-B and the difference was statistically significant (p=0.001). Mean LVEF also showed statistically significant difference between two groups (p<0.001) (Table 2 & Table 3).

Mean systemic immune-inflammation index was significantly higher in group A than group B and p value <0.05 (Table 4). Mean systemic immune -inflammatory index was significantly higher among patients with vessel score 2 and 3 than vessel score 0 and 1, p value 0.002 (Table 5).

There was a positive correlation between SII and coronary artery disease severity in terms

of Gensini score (r =0.7). With the increase of SII, Gensini score also increases. It was found statistically significant (p=0.001) by Spearman rank order correlation test. (Figure 3).

In ROC curve analysis, the AUC of SII for predicting severity of CAD is 0.8 with p value< 0.001, 95% CI (0.71-0.91). SII cut-off value 686 can predict severe CAD with 78% sensitivity and 76% specificity (Figure 4).

In multiple logistic regression analysis hypertension, NLR and SII were found independent predictors of severe CAD with ORs being 4.84, 1.81 and 1.002 respectively. (Table 6).



**Table-II**
*Comparison of haematological parameters between groups (N=70)*

| Parameters | Group A (n=33) mean±SD | Group B (n=37) mean±SD | P value |
|---|---|---|---|
| Hb (gm/dl) | 12.40 ± 1.68 | 12.79 ± 1.54 | $0.32^{NS}$ |
| Total WBC count | 10684.2±3244.7 | 8710.5±2266.5 | $0.004^{S}$ |
| Neutrophil count | 73.87± 8.59 | 58.00± 8.33 | $0.001^{S}$ |
| Lymphocyte count | 20.15±7.42 | 32.73±7.20 | $0.001^{S}$ |
| Platelet count, $\times10^3/mm^3$ | 254± 76 | 246± 87 | $0.232^{NS}$ |
| NLR | 4.43± 2.27 | 2.01±1.56 | $0.001^{S}$ |

Group A= Severe CAD, Gensini score > 50
Group B= Mild -Moderate CAD, Gensini score ≤50
s =significant; ns = not significant
p value reached from Students t -test / Man Whitney U test.

**Table-II**
*Comparison of laboratory parameters between groups (N=70)*

| Parameters | Group A (n=33) mean±SD | Group B (n=37) mean±SD | P value |
|---|---|---|---|
| Total cholesterol (mg/dl) | 231.54± 45.79 | 211.37±41.27 | $0.06^{NS}$ |
| LDL (mg/dl) | 120.18±27.57 | 107.64±25.05 | $0.05^{S}$ |
| HDL (mg/dl) | 34.69±5.9 | 37.75±5.4 | $0.02^{S}$ |
| TG (mg/dl) | 175.09±58.25 | 143.29±50.80 | $0.01^{S}$ |
| RBS (mg/dl) | 8.17±2.45 | 7.74±2.93 | $0.50^{NS}$ |
| Serum creatinine(mg/dl) | 1.29±0.6 | 0.9±0.5 | $0.24^{NS}$ |
| LVEF (%) | 47.45±4.95 | 52.27±5.95 | $0.001^{S}$ |
| Gensini score | 73.27±26.10 | 20.29±14.10 | $0.001^{S}$ |

Group A= Severe CAD, Gensini score > 50
Group B= Mild -Moderate CAD, Gensini score ≤50
s =significant; ns = not significant
p value reached from Students t -test / Man Whitney U test.

**Table-IV**

*Comparison of SII between the groups (N=70)*

| Parameters | Group A (n=33) mean±SD | Group B (n=37) mean±SD | P value |
|---|---|---|---|
| Systemic immune inflammation index (SII),× $10^3$ | 1064.11±365.57 | 706.55±399.73 | 0.001$^S$ |

Group A= Severe CAD, Gensini score > 50
Group B= Mild -Moderate CAD, Gensini score d" 50
s =significant; ns = not significant
p value reached from Man Whitney U test.

**Table-V**

*Distribution of SII among the sample populations (N=70)*

| Parameter | Vessel score "0" n=7 | Vessel score "1" n=23 | Vessel score "2" n=18 | Vessel score "3" n=22 | P value |
|---|---|---|---|---|---|
| Systemic immune inflammation index (SII), × $10^3$ | 590.67±75.89 | 790.91±510.67 | 863.83±339.93 | 1062.89±378.91 | 0.002$^S$ |

s =significant; ns = not significant
p value reached from Kruskal -Wallis test.

**Table-VI**

*Multivariate logistic regression analysis of determinant of severe coronary artery disease*

| Variables of interest | β | S. E | P value | OR | 95 % CI |
|---|---|---|---|---|---|
| Hypertension | 1.57 | 0.652 | 0.01$^s$ | 4.84 | 1.35 – 17.38 |
| Dyslipidaemia | 0.512 | 0.623 | 0.412 | 1.66 | 0.492 – 5.66 |
| LVEF | 0.085 | 0.078 | 0.277 | 0.919 | 0.789 – 1.09 |
| NLR | 0.595 | 0.211 | 0.004$^s$ | 1.813 | 1.19 – 2.74 |
| SII | 0.002 | 0.001 | 0.011$^S$ | 1.002 | 1.001-1.004 |

Dependent variable: Severe CAD (Gensini score > 50)
Independent variables: Hypertension, Diabetes mellitus, Dyslipidaemia, LVEF, NLR and SII.
s =significant.

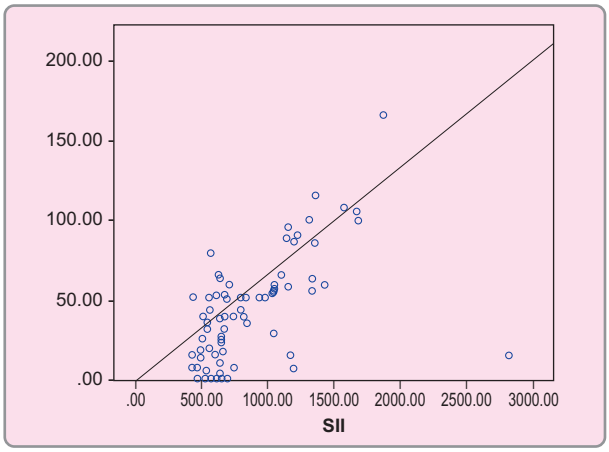


**Fig 3:** *Scatter diagram showing correlation between SII and Gensini score by Spearman's rank order correlation test.*

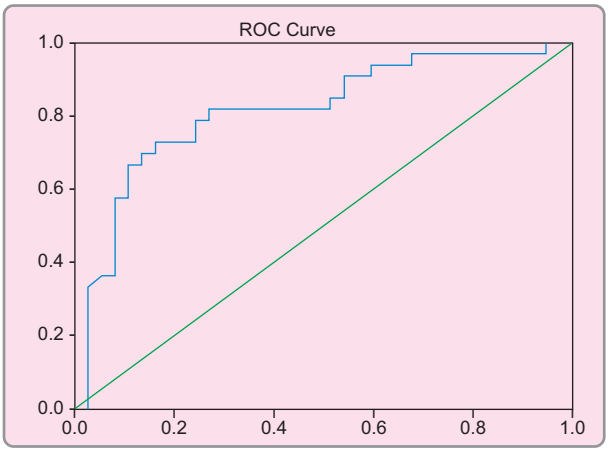


**Fig 4:** *The receiver-operating characteristics curve (ROC) analysis of SII for predicting severe CAD.*

**Discussion:**

The mean age of study patients was 50.16 ± 9.9 years ranging from 24 to 70 years. The mean age of group A patients was 53.39±8.8 years and that of group B was 48.27±10.6 years. The mean age of group A patients was significantly higher than group B. In a similar study conducted by Zhang et al,[13] mean age was significantly (p=0.001) higher in high Gensini score (>50) group.

The distribution of risk factors for coronary artery disease in the present study revealed that the most common risk factors, such as hypertension present in 81.8% (27) patients in group A and 51.3% (19) in group B, and the difference between two groups was statistically significant (p=0.007). Dyslipidemia was found in 84.8% (28) patients in group A and 51.3% (19) patients in group B and the difference between the groups was statistically significant (p value 0.03). Diabetes mellitus was found 63.6% (21) and 40.5% (15) patients in group A and B respectively and the difference was not statistically significant (p value=.08). Zhang et al, [13] also showed the similar findings. We didn't find any statistically significant difference of smoking and positive family history of premature CAD between the groups, which is consistent with previous study conducted by Kaya et al. [14]

In group A the mean WBC count was 10684.2±3244.7 (/ $mm^3$) and in group B mean WBC count was 8710.5±2266 (/$mm^3$) and this difference was statistically significant(p=.004). in a similar study conducted by Kaya et al [15]found mean WBC count 9.9 ± 3.1(K/μL) in higher Gensini score group and 8.3 ± 2.8 (K/μL) in lower Gensini score group and the difference was statistically significant. Mean neutrophil count was significantly higher and lymphocyte count was significantly lower in group A than group B. No significant difference in platelet count found between groups, which is similar with study done by kaya et al. [14] In our study,mean NLR significantly higher in group A than group B, which is consistent with study done by Zhang et al[13]

In case of Vessel score, mean SII was significantly higher in vessel score 2 and 3 group than vessel score 1 and 2 group, which p value is 0.002. In group A mean SII was 1064.11±365.57 and in group B mean SII was 706.55±399.73, the difference was statistically significant (p value 0.001) which is similar to study done by Liu et al. [16]

A positive correlation between SII and severity of CAD in terms of Gensini score was found in our study. Correlation co-efficient between SII and Gensini score was 0.7 (p=.001) which is statistically significant. With the increase of SII, Gensini score also increased, indicating more severe CAD.

In multivariate logistic regression analysis, after adjustment of confounding, NLR, hypertension and SII were found the independent predictor of severe coronary artery disease with OR 1.81, 4.84 and 1.002 & 95% confidence interval $^{1.19–2.74}$, $^{1.35-17.38}$ respectively. Zhang et al [13] & Candemir et al [10] also found NLR as an independent predictor of severe CAD.

By ROC curve analysis, our study found that SII > 686 can predict severe CAD in terms of Gensini score with 78% sensitivity, 76% specificity.

**Conclusion:**

From this study it may be said that increased systemic immune inflammation index is associated with angiographically severe coronary artery disease in acute myocardial infarction patients. So, this parameter might be useful for risk prediction of acute MI patients. Patients with acute MI, with SII level of more than 686, warrants more attention by the physicians and cardiologists in terms of more aggressive medical management and interventional treatment.

**Limitations**

Although the result of the study supports the hypothesis, there are some facts to be considered which might affect the results.

1. Relatively small sample size
2. The assessment of the severity of CAD was performed by coronary angiography, which has got its inherent limitations. Intravascular ultrasound may be more sensitive in the assessment of the severity of CAD.
3. The other synchronous inflammatory biomarkers of the patients were not evaluated in the study.
4. Cross-sectional study design was used in this study which was not ideal for proving cause or effect relationship between SII and severe CAD.

**Conflict of Interest** – None.

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*Original Article*

# Ultrasound Based Flow Measurements of the Left and Right Carotid System of Arteries in Bangladeshi Patients

Abdullah Al Mamun[1], Nazmul Hosain [2], Farzana Amin[3]



**Abstract:**

**Carotid arteries are the major supply to the head, neck and brain. The right common carotid artery usually originates from the brachiocephalic artery while the left common carotid artery arises as a direct branch of the arch of the aorta. Common carotid arteries bifurcate at the level of the carotid sinus into the internal carotid artery, which supplies the brain, and the external carotid artery. Approximately 15–20% of the cardiac output is distributed to the brain in healthy adults under resting conditions. Cardiovascular diseases are the leading cause of death globally, taking an estimated 17.9 million lives each year. US 2017 statistics shows that cerebrovascular disease or Stroke alone ranked fifth for males but fourth for females. Ultrasonography can measure the velocity of blood flow in the Carotid system of arteries. A total 139 patients, who underwent Carotid Duplex study between July 2021 and June 2022 were included in this cross-sectional study. The criteria for exclusion included age less than 13 years, presence of associated peripheral vascular diseases, hemodynamically unstable patients, incomplete data collection and patient's reluctance to join the study. Data analysis was performed using MS Office Excel. The Peak systolic velocity and the End diastolic velocity were measured at four levels, namely the Common carotid arteries and the Internal carotid arteries on the right and the left sides. No significant difference was observed in the Peak systolic velocity and the End diastolic velocity in either Common carotid or the internal carotid arteries between the right and left sides. Moreover, these findings were similar both in age groups above and below 50 years of age.**

*Key words: Carotid ultrasound, Internal carotid arteries,*

*(Bangladesh Heart Journal 2023; 38(2): 110-114)*



**Introduction:**

Carotid arteries are the major supply to the head and neck region and also to the brain. Although there may be anatomic variations, the right common carotid artery usually (RCCA) originates in the neck from the brachiocephalic artery while the left common carotid artery (LCCA) arises in the thorax as a direct branch of the arch of the aorta[1]. Furthermore, both right and left common carotid arteries bifurcate in the neck at the level of the carotid sinus into the internal carotid artery (ICA), which supplies the brain, and the external carotid artery (ECA), which supplies the exterior of the head, the neck and the face. External carotid artery classically has eight branches. These are Superior thyroid artery, Ascending pharyngeal artery, Lingual artery, Facial artery, Occipital artery, Posterior auricular artery, Superficial temporal artery and Maxillary artery (Fig 1A).

On the other hand, the course of the ICA is described as comprising of four sections. These sections include the cervical, petrous, cavernous, and cerebral parts of the ICA (Fig 1B). Inside the cranium, the ICAs anastomose

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*DOI: https://doi.org/10.3329/bhj.v38i2.70281*

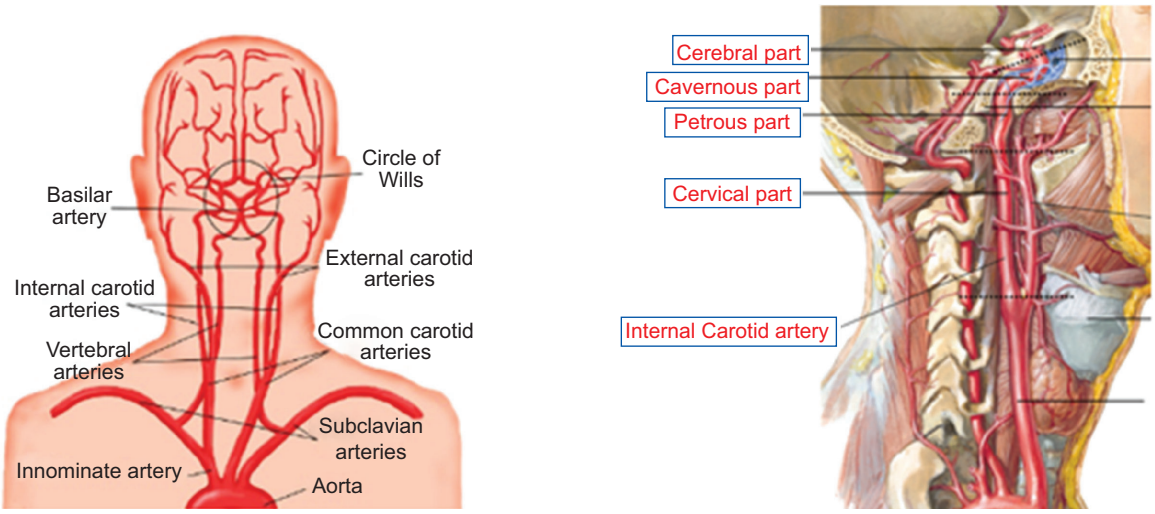


**Fig.-1:** *A. The Carotid system of arteries with arterial circle of Willis. 1B. Lateral view of Common carotid artery. Its branches and portions of Internal carotid artery.*

with the branches of the basilar artery and form the circle of Willis. The ICA divides at the circle of Willis to give rise to the middle cerebral artery (MCA) and anterior cerebral artery (ACA). The MCA supplies the motor and sensory cortices of the upper limb and face, as well as the Wernicke area of the temporal lobe and Broca's area of the frontal lobe. The ACA is mostly responsible for supplying the motor and sensory cortices of the lower limb. The ophthalmic artery is responsible for blood supply to the inner layers of the retina, as well as supplying other parts of the orbit, meninges, face, and upper nose[2]. The neurologists, neurosurgeons, and neuroradiologists often also use the Bouthillier classification to describe the ICA into different parts based on the angiographic appearance of the vessel. According to this classification, the ICA slits into seven parts named as C1 to C7, with each part providing branching into different vessels. These branches of the ICA are generally tiny and inconsistent, and often they might not be present. However, the ophthalmic artery is present pretty much all of the time[3].

A widely accepted dogma has been that approximately 15–20% of the cardiac output (CO) is distributed to the brain in healthy adults under resting conditions[4]. However, few studies have been conducted to determine whether the distribution of CO directed to the brain alters across the adult lifespan and is influenced by systemic and/or cerebral hemodynamic factors such as physical fitness level, cardiac function, and arterial stiffness[5]. This may play a crucial role in evolution of cerebrovascular diseases later in life.

Cardiovascular diseases (CVDs) are the leading cause of death globally, taking an estimated 17.9 million lives each year, and one third of these deaths occur prematurely in people under 70 years of age[6]. Cerebrovascular diseases are an important component of cardiovascular diseases in this lethal journey. US 2017 statistics shows that cerebrovascular disease or Stroke alone ranked fifth for males but fourth for females. Females had a higher relative burden of mortality from stroke, which accounted for 6.2% of all deaths to females but 4.3% of all deaths to males[7]. Carotid ultrasonography (CUS) is a proven noninvasive diagnostic tool to detect asymptomatic carotid artery stenosis (ACAS). A strong association between atherosclerotic coronary and carotid artery stenosis has been established since atherosclerosis is a progressive and systemic inflammatory disease that is also a forerunner of multiple adverse cardiovascular events[8]. However, studies show that the relationship between the occurrence of CV events and age is nonlinear, characterized with a sudden increase in event rate after age 50 years[9]. The flow pattern of Carotid arteries in Bangladeshi population hasn't been studied well till date. Here we made a small study analyzing the data available on Duplex scan of a small study population of 139 individuals.

**Methods:**

This cross-sectional study was conducted from May 2021 to July 2022. A total 139 patients, who underwent Carotid Duplex study in a vascular center at Dhaka were included in the study. All the patients were examined by the same vascular surgery consultant. Informed consent was

obtained from the patients. Carotid arterial system was assessed using a Philips Affiniti 70G system (Fig 2) equipped with a L12-5 real time linear B. Mode transducer. The severity of stenosis was measured according to consensus panel criteria by considering the following parameters- Peak systolic velocity (PSV) End diastolic velocity and the ratio of the PSV of internal and common carotid artery. Intimal plaque was described according to the Classification by Gray-Weale, as follows: Type I predominantly echolucent plaque with a thin echogenic cap; type II substantially echolucent lesion with small areas of echogenicity; type III, predominantly echogenic lesion with small areas of ceholucency; and type IV, uniformly echogenic lesion. A standard data sheet was utilized for each individual patient. Then the data was transferred to a master data sheet. Initially 152 patients were considered for inclusion in the study. However, for various reasons, 13 patients were excluded. The criteria for exclusion included age less than 13 years, presence of associated peripheral vascular diseases, hemodynamically unstable patients, incomplete data collection and patient's reluctance to join the study. Data analysis was performed using MS Office Excel. Velocity of flow at the both common carotid arteries and internal carotid arteries of both sides was measured. Comparison was made between Right and Left common carotid arteries and Right and Left Internal carotid arteries. Student's T Test was applied to compare the data.

**Results:**

The age range of the 139 persons under study ranged from 13 to 88 years. The average age was 54.8± 13.4 years. 101 (72.7%) of these patients were male and 38 (27.3%) were females. The Table 1 demonstrates the Velocity of blood flow at the Common carotid artery Level. As the Table demonstrates, the Peak Systolic Velocity at the Right Common Carotid artery was 74.6±16.1 and whereas that at the Left common carotid was 73.9±17.5. The difference was not significant with p value of 0.79. End Diastolic Velocity at the Right Common Carotid artery was 19.5±5.9 and whereas that at the Left common carotid was 19.5±7.1. There was no significant difference here as well.

**Table-I**

*Comparison of Flow/ Velocity at Common Carotid Artery Level*

| Criteria | CCA Right | CCA Left | P Value |
|---|---|---|---|
| Peak Systolic Velocity | 74.6±16.1 | 73.9±17.5 | 0.79 |
| End Diastolic Velocity | 19.5±5.9 | 19.5±7.1 | 0.97 |

The Table 2 demonstrates the Velocity of blood flow at the Internal carotid artery Level. the Peak Systolic Velocity at the Right Common Carotid artery was 73.3±20.9 and whereas that at the Left common carotid was 71.9±21.5. The difference was not significant with p value of 0.70. End Diastolic Velocity at the Right Common Carotid artery was 24.6±10.1 and whereas that at the Left common carotid was 22.0±8.87. There was no significant difference here as well with p value of 0.47.

**Table-II**

*Comparison of Flow/ Velocity at Internal Carotid Artery Level*

| Criteria | ICA Right | ICA Left | P Value |
|---|---|---|---|
| Peak Systolic Velocity | 73.3±20.9 | 71.9±21.5 | 0.70 |
| End Diastolic Velocity | 24.6±10.1 | 22.0±8.87 | 0.47 |

The age has an effect on carotid flow. It is often found that carotid flow may significantly reduce from sixth decade onwards and internal carotid artery is most commonly involved in cerebral circulation insufficiency. In this study, the flow was separately compared between the right and left internal carotid arteries. Table 3 demonstrates the Velocity of blood flow at the Internal carotid artery Level among 49 persons aged between 13 and 50 years of age. The Peak Systolic Velocity at the Right internal Carotid artery was 68.6±23.0 and that at the Left internal carotid was 70.1±22.8. The difference was not significant with a p value of 0.51. End Diastolic Velocity at the Right internal carotid artery was 22.7±9.0 and that at the Left internal carotid was 24.6±11.1. There was no significant difference here as well with p value of 0.70.

**Table-III**

*Comparison of Flow/ Velocity at Internal Carotid Artery Level among persons 13 to 50 years old, n=49*

| Criteria | ICA Right | ICA Left | P Value |
|---|---|---|---|
| Peak Systolic Velocity | 68.6±23.0 | 70.1±22.8 | 0.51 |
| End Diastolic Velocity | 22.7±9.0 | 24.6±11.1 | 0.70 |

The Table 4 demonstrates the Velocity of blood flow at the Internal carotid artery Level of 90 individuals aged above 50. The Peak Systolic Velocity at the Right internal Carotid artery was 75.9±30.0 and that at the Left internal carotid was 72.8±38.0. The difference was not significant with a p value of 0.35. End Diastolic Velocity at the Right internal carotid artery was 25.6±45.4 and that at the Left internal carotid was 20.7±19.2. There was no significant difference here as well with a p value of 0.47.

**Table-IV**

*Comparison of Flow/ Velocity at Internal Carotid Artery Level among persons more than 50 years old, n=90*

| Criteria | ICA Right | ICA Left | P Value |
|---|---|---|---|
| Peak Systolic Velocity | 75.9±30.0 | 72.8±38.0 | 0.35 |
| End Diastolic Velocity | 25.6±45.4 | 20.7±19.2 | 0.47 |


**Fig.-2:** *A The Philips Affiniti 70G system Duplex machine & 2B. a sample carotid duplex report.*

**Discussion:**

Carotid artery flow on the right and left side in Bangladeshi individuals was compared in this study. The Peak Systolic Velocity at the Right and Left common carotid arteries were 74.6±16.1 and 73.9±17.5 respectively. The difference was not significant with p value of 0.79. End Diastolic Velocity at the Right Common Carotid artery was 19.5±5.9 and whereas that at the Left common carotid was 19.5±7.1. There was no significant difference here as well. In their study Al-Sabbagh AA et al. (2022) found significant differences between the right and left common carotid and internal carotid arteries in patients with diabetes and hypertension which were more prominent in the young age group[10]. Loizou CP et al. (2015) observed in their study that values for common carotid Intima Media Thickness and lumen diameter were significantly higher in the left common carotid artery versus the right common carotid artery in both age groups. Differences between the 2 carotid sides may be attributed to anatomic variations in the common carotid artery origins which lead to differences in stress between the 2 sides[11].

Interestingly in our study, there wasn't any significant difference in terms of peak systolic velocity or end diastolic velocity of blood flow between the persons belonging to the age groups above and below 50 years of age. The peak systolic velocity of blood flow was not significantly different (p value 0.35) between the right and left at the Common carotid arteries in the age group above 50. The difference End diastolic velocity of flow between right and left side at the common carotid arteries was also not significant in persons above 50 (p value 0.45). Similarly, the Peak systolic velocity of blood flow was not significantly different (p value 0.35) between the right and left at the internal carotid arteries in the persons aged below 50. Similarly, the End diastolic Velocity of flow at the common carotid arteries level was also not significant between the sides (p value 0.41). Findings were similar for Internal carotid arteries as well. There has been disagreement in various studies measuring CAIMT in left and right common carotid arteries[12]. Bots et al in their 1997 study found no significant difference (p value 0.65) between the right and the left common carotid artery at the common carotid artery level examining 1500 patients[13]. However, in another large study involving 1655 patients in 2007 by Vicenzini et al, found significant difference between the sides (p value 0.001)[14].

Limitations of the study include the involvement of a single operator and a single center. There was no randomization of the patients. Some of the patients were left-handed. The issue of being left-handed or right-handed was not taken in consideration while analyzing the data. The study population was also small to assess the status of a country of 170 million people. Similar larger and well-organized studies are recommended to be conducted in future to reach appropriate conclusions.

**Conclusion:**

No significant difference was observed in the Peak systolic velocity and the End diastolic velocity between the Right and Left Common Carotid arteries in the Bangladeshi patients. Similarly, no significant difference was observed in the Peak systolic velocity and the End diastolic velocity between the Right and Left internal carotid arteries in these patients. These findings were similar both in age groups above and below 50 years of age.

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Vol. 38, No.2, - July 2023 Heart J.

*Original Article*

# Disease Characteristics of Chronic Venous Disease in Referral Hospital in Bangladesh

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**Abstract:**

**Introduction: Chronic venous disease (CVD) is widespread, underdiagnosed, and can progress to chronic venous insufficiency and venous ulcer, which can require extensive treatment. This condition negatively impacts patient quality of life and place substantial burdens on healthcare resources. In Bangladesh this problem is increasing with very poor awareness.**

**Materials and Methods: The prospective observational study was carried out in department of vascular surgery of National Institute of Cardiovascular disease. We randomly choose 180 patients with chonic venous disease (CVD) and evaluate their characteristics and prevalence of several types. Data collection started from May 2021 for next 6 months.**

**Results: The patients of this survey were aged between 24 to 70 years and the Mean±SD age was 43.6±12.2. 78.3% of total study population were male, 33.3% were businessman and 10% were housewife. 66.6% patients were having low socio-economic condition. C2 varicose veins were highly prevalent among the study population (35%) & lowest prevalence of C4b lipodermatosclerosis or atrophie blanche (11.7%) we have seen in the study. (31- 40) & (51-60) these two age group were more prone to have CVD, 28.33% (n51) & 26.67% (n48) (p <0.001*) respectively. Male were predominantly more prevalent to having CVD, 78.33% (n141), (p <0.001).**

**Conclusion: Patients having CVD, invariably presented with the complains of heaviness of leg and unexplained leg swelling and Varicose vein were highly prevalent irrespective of sex. Advanced stages are more common in male patients. In every age group were having different stages of CVD. More awareness can help patients to get proper management and relief from chronic venous disease.**

*Keywords: CVD, leg swelling, varicose veins, oedema, skin discolouration*

*(Bangladesh Heart Journal 2023; 38(2): 115-119)*

**Introduction:**

Patients with chronic venous disease (CVD) seek treatment for a variety of symptoms and signs that may substantially impact their quality of life (QoL). Symptoms include leg pain, discomfort, and heaviness, whereas the clinical signs of CVD are varicose veins (VVs), oedema, skin discolouration, lipodermatosclerosis, and, in severe cases, venous ulceration. Based on the presence of specific clinical signs, which may or may

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*DOI: https://doi.org/10.3329/bhj.v38i2.70285*

not be symptomatic but are associated with increasing clinical severity, CVD can be classified from C0 (no signs) to C6 (venous ulceration)[1]. This form of venous dysfunction may be the result of recanalisation of thrombosed venous segments, pathological dilation of the vein or due to congenital absence of competent valves [2]. CVD is a very common problem with varicose veins affecting more than 25 million adults in the United States and more than 6 million with more advanced venous disease[3]. Estimates from the west show that prevalence of varicose veins varies widely from 2–56% in men and from 1–60% in women and venous ulceration affect approximately 0.3% of the adult population[4]. In Bangladesh, there is no published data regarding the prevalence of CVD. However, unpublished data from the National Institute of Cardiovascular Diseases (NICVD) suggest that about 50% of all patients undergoing Duplex study for vascular diseases are venous patients and more than 80% of venous consultations are for C4-C6 disease[5]. Prevalence estimates for varicose veins are higher, <1% to 73% in females and 2% to 56% in males[6]. A lower prevalence has been observed in men but some recent surveys have suggested that the occurrence in men may be comparable to that in women [7]. This study was designed to see prevalence of chronic venous disease in NICVD and also to see the relationship to various symptoms of chronic venous disease with age, sex and body mass index of the patient.

**Materials and Methods:**

The prospective observational study was carried out in department of vascular surgery of National Institute of Cardiovascular disease.180 patients were randomly chosen with chronic venous disease (CVD) and evaluate their characteristics and prevalence of several types. Data collection started from May 2021 for next 6 months in patients who was admitted with CVD like symptoms. Who were aged 18 years and above and willing for treatment and given informed written consent were included this study and patients below 18 years of age were excluded in this study. Data were collected with a pre-tested structured questionnaire containing history, clinical, laboratory investigations, pre-operative, post operative complications and post operative follow up findings. Data were collected, compiled and tabulated according to key variables. The analysis of different variables was done according to standard statistical analysis by using SPSS-19.

**Results:**

The patients of this survey were aged between 24 to 70 years and the Mean±SD age was 43.6±12.2. 78.3% patient were male and male: female ratio was 3.6:1. around 80% patient were employed that includes service (23.3%), business (33.3%), farming(10%) and garments working(13.3%). 66.7% patients were from low socio-economic background [Table I]. All types of CVD patients were seen in our study [Table II], among them C2 varicose vein was more prevalent (35%). Advanced stage C5 healed venous ulcer also seen highly prevalent ( 21.7%).

**Table-I**

*Demographic characteristics of the study patients (n=180)*

| Variables | Number of patients | Percentage (%) |
|---|---|---|
| Age group (years) | | |
| 20-30 | 27 | 15.0 |
| 31-40 | 51 | 28.3 |
| 41-50 | 42 | 23.3 |
| 51-60 | 48 | 26.7 |
| 61-70 | 12 | 6.7 |
| Mean±SDRange | 43.6±12.2 | |
| (min-max) | 24-70 | |
| Sex | | |
| Male | 141 | 78.3 |
| Female | 39 | 21.7 |
| Male : Female ratio | 3.6:1 | |
| Occupation | | |
| Service | 42 | 23.3 |
| Business | 60 | 33.3 |
| Garments worker | 24 | 13.3 |
| Retired | 12 | 6.7 |
| Farmer | 18 | 10.0 |
| Housewife | 24 | 13.3 |
| Socioeconomic status | | |
| Low | 120 | 66.7 |
| Middle | 48 | 26.7 |
| High | 12 | 6.7 |

**Table-II**
*Distribution of the study patients by clinical classification (n=180)*

| Clinical classification | Number of patients | Percentage |
|---|---|---|
| C2 varicose veins | 63 | 35.0 |
| C3 edema | 24 | 13.3 |
| C4b lipodermatosclerosis or atrophie blanche | 21 | 11.7 |
| C5 healed venous ulcer | 39 | 21.7 |
| C6 active venous ulcer | 33 | 18.3 |
| Total | 180 | 100.0 |

31-40 years age group were most prevalent having CVD with 51 patients, then 41-50 years age group with 42 patients and 51-60 years age group with 48 patients showing diversified distribution of the disease in the several age groups [Table III]. Male were more prevalent having CVD [Table IV] with 78.3% presence. 27.7% male showed C5 healed venous ulcer (p<0.001*) whereas C2 varicose veins were most prevalent among female (69.2%) (p<0.001*). C5 healed venous ulcer and C6 healed venous ulcer were mostly prevalent among service holder and businessman [Table V]. Association of CVD with socio-economic status results were in Table VI.



**Table-III**
*Association of clinical classification of CVD with age group (n=180)*

| Age group (years) | | Clinical classification | | | | | p-value |
|---|---|---|---|---|---|---|---|
| | | C2 varicose veins | C3 edema | C4b lipodermato sclerosis or atrophie blanche | C5 healed venous ulcer | C6 active venous ulcer | |
| 20-30 | 27 | 24(88.9%) | 3(11.1%) | 0(0.0%) | 0(0.0%) | 0(0.0%) | <0.001* |
| 31-40 | 51 | 21(41.2%) | 0(0.0%) | 6(11.8%) | 9(17.6%) | 15(29.4%) | |
| 41-50 | 42 | 12(28.6%) | 9(21.4%) | 3(7.1%) | 3(7.1%) | 15(35.7%) | |
| 51-60 | 48 | 6(12.5%) | 12(25.0%) | 0(0.0%) | 27(56.3%) | 3(6.3%) | |
| 61-70 | 12 | 0(0.0%) | 0(0.0%) | 12(100.0%) | 0(0.0%) | 0(0.0%) | |
| Total | 180 | 63(35.0%) | 24(13.3%) | 21(11.7%) | 39(21.7%) | 33(18.3%) | |

p-value obtained by Chi-square test, *significant

**Table-IV**
*Association of clinical classification of CVD with sex (n=180)*

| Sex | | Clinical classification | | | | | p-value |
|---|---|---|---|---|---|---|---|
| | | C2 varicose veins | C3 edema | C4b lipodermato sclerosis or atrophie blanche | C5 healed venous ulcer | C6 active venous ulcer | |
| Male | 141 | 36(25.5%) | 12(8.5%) | 21(14.9%) | 39(27.7%) | 33(23.4%) | 0.001* |
| Female | 39 | 27(69.2%) | 12(30.8%) | 0(0.0%) | 0(0.0%) | 0(0.0%) | |
| Total | 180 | 63(35.0%) | 24(13.3%) | 21(11.7%) | 39(21.7%) | 33(18.3%) | |

p-value obtained by Chi-square test, *significant

**Table-V**

*Association of clinical classification of CVD with occupation (n=180)*

| Occupation | | Clinical classification | | | | | p-value |
|---|---|---|---|---|---|---|---|
| | | C2 varicose veins | C3 edema | C4b lipodermato sclerosis or atrophie blanche | C5 healed venous ulcer | C6 active venous ulcer | |
| Service | 42 | 18(42.9%) | 3(7.1%) | 9(21.4%) | 0(0.0%) | 12(28.6%) | <0.001* |
| Business | 60 | 18(30.0%) | 9(15.0%) | 0(0.0%) | 12(20.0%) | 21(35.0%) | |
| Garments worker | 24 | 12(50.0%) | 3(12.5%) | 0(0.0%) | 9(37.5%) | 0(0.0%) | |
| Retired | 12 | 0(0.0%) | 0(0.0%) | 12(100.0%) | 0(0.0%) | 0(0.0%) | |
| Farmer | 18 | 0(0.0%) | 0(0.0%) | 0(0.0%) | 18(100.0%) | 0(0.0%) | |
| Housewife | 24 | 15(62.5%) | 9(37.5%) | 0(0.0%) | 0(0.0%) | 0(0.0%) | |
| Total | 180 | 63(35.0%) | 24(13.3%) | 21(11.7%) | 39(21.7%) | 33(18.3%) | |

p-value obtained by Chi-square test, *significant

**Table-VI**

*Association of clinical classification of CVD with socioeconomic status (n=180)*

| Socioeconomic status | | Clinical classification | | | | | p-value |
|---|---|---|---|---|---|---|---|
| | | C2 varicose veins | C3 edema | C4b lipodermato sclerosis or atrophie blanche | C5 healed venous ulcer | C6 active venous ulcer | |
| Low | 120 | 45(37.5%) | 15(12.5%) | 9(7.5%) | 27(22.5%) | 24(20.0%) | <0.001* |
| Middle | 48 | 18(37.5%) | 9(18.8%) | 0(0.0%) | 12(25.0%) | 9(18.8%) | |
| High | 12 | 0(0.0%) | 0(0.0%) | 12(100.0%) | 0(0.0%) | 0(0.0%) | |
| Total | 180 | 63(35.0%) | 24(13.3%) | 21(11.7%) | 39(21.7%) | 33(18.3%) | |

p-value obtained by Chi-square test, *significant

**Discussion:**

In our body, venous system is an important and one of the largest organs of the body, and venous disease is a burden for the society and a cause of much disability [8]. The prevalence of CVD increases with age and it is more common in women than men [9]. However, estimates of CVD prevalence vary widely from study to study (15–80%) due to differences in study design and target population [10–15], A study conducted in 3000 primary care patients in Pakistan, which reported a CVD prevalence of 34.8% [16]. This study also reported a higher prevalence of CVD in men (36.4%) than in women (33.0%) and of C3 (36.7%) than symptomatic C0 (C0S) (14.6%), C1 (13.8%) and C2 (15.8%). Compared with other studies, the sample population of this study was younger (mean age 39 years) and consisted mostly of males (52.6%)[16]. Our study showed consistent result with the Pakistani one, showing high prevalence in male than female. Vein Consult was an international study that recruited 91,545 patients from 20 countries in Europe, Latin America, Middle East and South East Asia, while the study conducted by Vuylsteke and colleagues included 6009 patients from Belgium and Luxembourg[17] had a similar mean age (50.6 and 53.4 years, respectively) with which our result remain consistency with similar age group.

**Conclusion:**

Chronic venous disease is not uncommon in Bangladesh. Patients often faces heaviness of leg and unexplained leg swelling and engorged vein but rarely seek support from healthcare professionals at the first place. In our study we found there is no distinct age group was there with high prevalence rather CVD can be happened every group. Moreover, male are having more

CVD than female> advance stages comes with increasing age and also without proper follow up by the physicians. A well-designed awareness activity can be implemented nationally in order to increase awareness so that patients get to know the disease characteristics and seek support from health care professional.

**Conflict of Interest:** There is no conflict of interest in this study.

**Acknowledgement:**
Department of vascular surgery for their tremendous support in collecting data and counseling the patients.

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Vol. 38, No.2, - July 2023 Heart J.

*Original Article*

# Association of Platelet Count and Mean Platelet Volume in Acute ST- Elevated Myocardial Infarction

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**Abstract:**

**Background: Early prediction and quick diagnosis with simple, quick and easily available tool is essential part of early management of acute coronary syndrome e.g. ST segment elevated myocardial infraction. As platelet has a significant role in thrombus formation and larger sized platelets are more active in thrombotic pathogenicity, as such platelet indices can be the early predictor for acute coronary syndrome.**

**Objective: Aim of this study was to assess the association of platelet count and mean platelet volume (MPV) in acute ST-elevated myocardial infarction.**

**Methodology: This observational study was conducted at the department of Cardiology of National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh from November 2019 to October 2020. Total 166 subjects were enrolled in this study. Among them 82 subjects (Group I) had acute ST-elevated myocardial infarction on resting ECG were admitted at CCU of NICVD and without any prior history of anti-platelet drugs intake, another 84 subjects (Group II) were enrolled in this study as control group with normal 12 lead resting ECG with normal Troponin-I.**

**Results: No significant age difference observed between two groups (p =0.063). Significantly higher smoking and family history of coronary artery disease observed with ST elevated MI subjects (p:0.002 and <0.001 respectively). Associated risk factors like hypertension, diabetes and dyslipidaemia were significantly high (<0.001) in ST-elevated MI patients. No significant difference observed in platelet count between ST elevated MI groups compared with the control (258 X $10^9$/L vs. 267 X$10^9$/L). Mean platelet volume (MPV) was found to be higher in group I patients as compared to control (12.20±0.86 vs. 9.26±0.77) and it was significant (p <0.001).**

**Conclusion: In acute ST-elevated myocardial infraction, higher mean platelet volume (MPV) and lower platelet count may be a useful marker.**

*Key Wards: ST segment elevated myocardial infarction (STEMI), Platelet Count, Mean Platelet Volume (MPV)*

*(Bangladesh Heart Journal 2023; 38(2): 120-126)*

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*DOI: https://doi.org/10.3329/bhj.v38i2.70277*

## Introduction

Significant advancements have been made in using biomarkers and electrocardiogram to diagnose STEMI, these methods measure myocardial necrosis, as opposed to the cause and therapeutic target; coronary thrombosis. Since myocardial necrosis follows thrombosis, these diagnostic criteria for acute MI may fail to identify patients before the induction of irreversible myocardial necrosis. Additionally, the current diagnostic methods do not target the differentiation of thrombotic and non-thrombotic causes of MI such as demand ischemia and stress cardiomyopathy, which has varying therapeutic and prognostic implications.[1] While the fourth universal definition of acute MI identifies angiographic confirmation of coronary thrombus as a criterion for the diagnosis of acute MI and differentiating myocardial necrosis caused by thrombotic versus non-thrombotic etiologies.[2]

Acute coronary syndrome (ACS) refers to a group of conditions due to decreased blood flow in the coronary arteries such that part of the heart muscle is unable to function properly as a consequence of platelet rich coronary thrombus formation.[3] Platelets have a major role in the pathogenesis of acute coronary syndrome (ACS) .[4] Activated platelets are larger in size, which can be measured by mean platelet volume (MPV).[5] Larger platelets are more adhesive and tend to aggregate more as they contain more dense granules. They are metabolically and enzymatically more active than small platelets and produce more thromboxane A2.[6, 7] Increased platelet volume will increase the tendency for coronary thrombus formation in ACS patients.[8] The activated platelet is the major biological risk factor in the pathogenesis of ACS, so inhibition of this process could play an important role in prevention of ACS .[9]

The diagnostic criteria of ACS are clinical presentation, biochemical markers of acute ischemic injury and electrocardiographic findings.[10, 11] The present cardiac markers are not sufficiently sensitive at an early stage of ACS. That's why an early and reliable marker is needed for early diagnosis of ACS when patients will attend in cardiac emergency. Platelet parameters especially MPV may be an important marker in early detection of ACS when other markers are not available.

Platelets have a primary function of stopping hemorrhage from vascular endothelium or tissue following an injury.[5] In a pathological spin-off to their apportioned physiological function of plugging endothelial defects, platelet activation in response to plaque disruption, results in occlusive thrombosis, is the paradigm for acute MI. The process of plaque progression and disruption is triggered by inflammatory and immune changes that convert the surface endothelium into a pro-atherothrombotic surface via cell adhesion molecules, primarily P-selectin and E-selectin.[12] Upon damage to the plaque, platelet activation is enhanced through the secretion of storage granules and adhesive ligands, which further promote platelet aggregation.[9] In the event of atherosclerotic plaque disruption, elevated rates of platelet aggregation potentiate the release of larger, more reactive platelets from the bone marrow.[13]The enhanced reactivity of these newly released platelets is attributed to elevated concentrations of active substances within microgranules (e.g., thromboxane A2 and B2, platelet factor 4, P-selectin, platelet derived growth factor), as well as increased expression of adhesive receptors (glycoprotein IIb/IIIa).[14, 15] Prior studies have demonstrated a significantly higher mean platelet volume (MPV) in patients presenting with ACS.[14, 16]

The MPV is a measure of platelet size and activity and the role of platelet activation is fundamental in the development of an acute MI.[5] Thus, we hypothesize that platelet count and MPV could be used as surrogate for platelet consumption and activation and therefore aid in the diagnosis of an acute STEMI, specifically acute thrombotic STEMI. Increase platelet volume will increase the tendency of coronary thrombus formation in acute STEMI. So, platelet count and MPV can be used as an early marker in acute STEMI. There are few studies in abroad regarding this issue but in our country no significant study was done previously. So, this study was done to explore the results in Bangladeshi population at a tertiary care hospital.

## Methods

This cross-sectional observational study was carried out from November 2019 to October 2020 in the Department of Cardiology at National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh. The study protocol was approved by the Ethical Review Committee of NICVD. Informed consent was taken from each patient or near relatives and utmost confidentiality was maintained. Data was collected in an approved data collection form.

On the basis of inclusion and exclusion criteria by purposive sampling method 166 subjects were recruited as study population. In group I 82 patient with acute ST-elevated myocardial infarction admitted in CCU who did not take anti-platelet drugs were included. On the other

hand, in group II 84 patients with chest pain who underwent physical examination with normal ECG and normal cardiac biomarker and no prior history of anti-platelet therapy were included. Apart from that, patients with hematological diseases, severe co morbidity (CKD, CVD, COPD etc.), valvular heart disease, peripheral vascular disease, cardiomyopathies, previous history of CABG/ PCI and age below 18 years were excluded.

From all study subject's, meticulous history was taken and detailed clinical examination was done and recorded in predesigned structured questionnaire. Demographic data including age, sex and occupation were recorded. Conventional risk factors of CAD profile was noted. Hemodynamic data; pulse and BP was recorded. 12 lead resting ECG was done at a paper speed of 25 mm/s and 10 mm standardization at admission. Blood was collected aseptically for CBC with platelet count and MPV with EDTA tube and determined by automated Hematology analyzer (Beckman Coulter, Model-DxH 500) before getting anti-platelet and anti-thrombotic. Other laboratory investigations e.g., RBS, serum creatinine, serum electrolytes, and serum troponin were carried out. Loading dose of Aspirin 300 mg, Clopidogrel 300 mg and Atorvastatin 40 mg were given after collection of blood who were diagnosed as acute STEMI.

Data were analyzed by using SPSS version 20 (Statistical package for social science). Quantitative data was expressed as mean and standard deviation and comparison was done by "student t" test. Qualitative data was expressed as frequency and percentage and comparison was carried by Chi-square (÷2) Test. A two-tailed p<0.05 was considered statistically significant.

**Results**

In between the study groups, no significant gender difference was observed. Slight male predominance than female observed between two groups. Male, female ratio was 1.13. No significant difference observed in occupation between two groups. (Table I)

Incidence of all risk factors were significantly high in group I subjects (Table II). In table III presentation of symptoms of the subjects were analyzed, and as expected all symptoms were significantly high in group I. There was no significant difference observed in heart rate between the groups but both systolic and diastolic blood pressure was significantly high in group I subjects (Table IV).

In ST-elevated MI group mean platelet count was 258 $X10^9$/L and in control group mean platelet count was 267 $X10^9$/L. There was no significant difference observed in mean platelet count between the groups. In ST-elevated MI group mean platelet volume was 12.71 fl. and in control group mean platelet volume was 9.26 fl. In ST-elevated MI group mean platelet volume was significantly higher (<0.001) than control group. (Table V)

**Table-I**
*Patient Demographic Characteristics. n:166*

| Demographics | | Group I Case; n: 82 | Group II Control; n: 84 | p value |
|---|---|---|---|---|
| Age (mean ±SD) | | 48±6 | 47±7 | 0.063$^{ns}$ |
| Gender (n, %) | | | | |
| | Female | 37 (22.3) | 41 (24.7) | 0.634$^{ns}$ |
| | Male | 45 (33.1) | 43 (25.9) | |
| Occupation (n, %) | | | | |
| | Housewife | 22 (13.3) | 32 (19.3) | 0.060$^{ns}$ |
| | Farmer | 15 (9.0) | 5 (3.0) | |
| Service | 19 (11.4) | 26 (15.1) | | |
| | Business | 18 (10.8) | 15 (9.0) | |
| | Day labor | 8 (4.8) | 6 (3.6) | |

**Table-II**
*Distribution of risk factors in study subjects. n: 166*

| Characteristics | Group I (n=51) Frequency (%) | Group II (n=71) Frequency (%) | P value |
|---|---|---|---|
| Smoking | 50 (30.1) | 31 (18.7) | 0.002$^{s}$ |
| Diabetes | 50 (30.1) | 28 (16.9) | 0.001$^{S}$ |
| Hypertension | 49 (29.5) | 26 (15.7) | 0.001$^{S}$ |
| Dyslipidaemia | 22 (13.3) | 5 (3.0) | 0.001$^{S}$ |
| Family H/O IHD | 24 (14.5) | 06 (3.6) | 0.001$^{s}$ |

**Table-III**

*Clinical presentations of study subjects. n:166*

| Clinical Presentations | Group I Case; n: 82 | Group II Control; n: 84 | P-value |
|---|---|---|---|
| Chest discomfort | 68 (41.0) | 52 (31.3) | 0.002$^{S}$ |
| Chest pain | 76 (45.8) | 68 (41.0) | 0.026$^{S}$ |
| Shortness of breath | 59 (35.5) | 35 (21.1) | <0.001$^{S}$ |

**Table-IV**

*Heart rate and blood pressure of study subjects. n:166*

| On examination findings(Mean ± SD) | Group I Case; n: 82 | Group II Control; n: 84 | P-value |
|---|---|---|---|
| Heart rate in beat/min. | 79±8 | 77±7 | 0.236$^{ns}$ |
| Systolic blood pressure in mm of Hg | 129±15 | 119±12 | <0.001$^{S}$ |
| Diastolic blood pressure in mm of Hg | 82±15 | 74±9 | <0.001$^{S}$ |

**Table-V**

*Platelet count and mean platelet volume of study subjects. n:166*

| Test; (Mean ± SD) | Group I Case; n: 82 | Group II Control; n: 84 | P-value |
|---|---|---|---|
| Total platelet count in X $10^9$/L | 258±44 | 267±55 | 0.239$^{ns}$ |
| Mean platelet volume in fl | 12.20±0.86 | 9.26±0.77 | <0.001$^{S}$ |

**Discussion:**

This study aimed to compare total platelet count and mean platelets volume in ST-elevated MI cases (Group I) with control cases of normal ECG and normal Troponin-I biomarker (Group II) in our setting.

Acute coronary syndrome is the disease of middle and old age but the disease process usually starts in young age. In our study, overall mean age 46 years and there were no significant differences observed between cases and controls in respect of age. The mean age of the patients with ST elevated MI group was 48±6 years as compared to 55±10.73 years, 66±16 years, 56.59±13.6 years, 63.8 years and 63.4±13.0 years and 55.4±13.1 years in studies done by Pervin S et al., Ulusoy R E et al. Assiri A S et al, the ENACT study, Euro Heart Survey ACS and SPACE registry respectively is relatively lower than other study groups.[17, 18, 11, 19, 20, 21]

Except mild male predominance, no significant gender difference observed in our study (p - 634) like other studies of Pervin S et al., Ulusoy R E et al. Assiri A S et al, the ENACT study, Euro Heart Survey ACS and SPACE registry. [17, 18, 11, 19, 20, 21] In Birader S B et al., Ahmed H et al., Hassan N A E et al. study, their sample size was also had male predominance.[22, 23] Though occupation is not an established risk factor for MI but it can provide information about lifestyle. In this study, no significant difference (p: 0.060) observed between two groups among different occupation groups.

We found overall 48.8% of study subjects were smoker and all were male and in group I (cases) had significantly higher (30.1%, p: 0.002) smoking history than control which indicates that smoking in an important risk factor in occurrence of MI. No smoking history in females as in our country traditionally female smoking is negligible. Ahmed H. et al. had found 30% smoker in cases, Assiri A S et al. had found 35% smokers in cases group, 29.7% smokers in cases in Manchanda, J. et al. meta-analysis, 46% smokers found with MI in Europian population observed in the ENACT study is more or less similar with our study.[23, 11, 25, 19]

In our study, significantly high (p <0.001) positive family history of CAD is more (14.5%) in ST-elevated MI groups than control. So, positive family history of CAD is also an important risk factor for coronary artery diseases. Similar result observed in Assiri A S et al. study where 37.7% study subjects of ACS groups than control.[11] In

Manchanda, J. et al. meta-analysis Positive family history was also high in acute coronary syndrome groups observed.[25]

Diabetes, hypertension and dyslipidemia are well established risk factors for coronary artery disease. Pre-existing co-morbidity, we found, significantly high incidence of hypertension, diabetes and dyslipidemia (29.5%, 30.1% and 13.3% respectively) in ST elevated MI group than control group (15.7%, 16.9% and 3.0% respectively). But ethnic variation observed in meta-analysis the ENACT study of European population with MI had Hypertension was 41%, Diabetes 19% and 20% were treated for dyslipidemia. Similar result observed like European population observed in Saudi population differs from our study.[19, 21] But different result observed in an Indian meta-analysis, where in ST-elevated MI groups had 17.7% hypertension, 19.4% diabetes probably due to lack of randomization in our study.[25]

Regarding presenting symptoms, our suspected patients of both groups had chest discomfort, chest pain and shortness of breath. But in group I, that is subjects with MI had significantly high (p: 0.002, 0.026 and <0.001 respectively) incidence of chest discomfort, chest pain and shortness of breath than control group indicates these symptoms are more in MI patients and urgent ECG and Troponin I are essential investigations to exclude MI.

In our study, no significant difference (p - 0.226) observed in heart rate between two groups. But we found significantly high (p <0.001) systolic and diastolic blood pressure in MI groups than control groups, that is relative high blood pressure is significant indicator in occurrence if MI where early ECG and Troponin I biomarker is indicated for confirmation of MI. Al Habib K F et al., Gheissari A et al. also found significant high Systolic blood pressure in MI but Gheissari A et al. found no difference in diastolic blood pressure between two groups.[21, 26]

The study reveals that the mean (±SD) value of total platelet count was lower in cases than controls without any significant statistical difference (p - 0.239). Total platelet count was 258±44 X $10^9$/L in ST-elevated MI group and 267±55 X $10^9$/L in control groups. Another Bangladeshi study by Pervin S et al. also reports similar findings like ours.[17] Saudi study of Assiri AS et al. and Turkish study of Ulusoy, R.E. et al. also found similar observation like our study.[11, 18] On the other hand, Cameron H A et al. and Hassan, N.A.E. et al. observed significantly lower platelet count on admission in ST elevated MI subjects than normal control group.[27, 24]

In our study, we found that ST-elevated MI was associated with higher mean platelet volume (MPV) which was significantly higher (p <0.001) in group I than group II. In our study, MPV was 12.20±0.86 fl and 9.26±0.77 fl respectively. MPV was significantly higher in patients with ST-elevated MI cases compared to control group. These results are consistent with the results of Pervin S et al., Biradar, S.B. et al., Ahmed H et.al., Hassan, N.A.E. et al., Mathur A et al. meta-analysis of Manchanda, J. et al., meta-analysis of Chu S. G. et. al. Huczek, Z. et al., Ulusoy, R.E. et al. and Assiri AS et al. They conclude that platelets parameters mainly MPV was raised in ACS compared to controls. So, mean platelet volume is a significant useful predictor of MI.[17, 22, 23, 24, 25, 14, 8, 18, 11]

In our study, we found no significant difference (p - 0.239) in mean platelet count between two groups. In such the prediction of MI is not possible from platelets count. In similar studies of Assiri AS et al., Ulusoy R E et al., Pervin S et al. also found no significant difference in platelets count.[11, 18, 17] All these findings lead to the hypothesis that higher mean platelets volumes (MPV) can be significant useful markers in patients with ST-elevated MI patients for early detection.

**Conclusion:**

In conclusion, larger platelet may contribute to the pre-thrombotic state in acute ischemic syndromes. In this study, mean platelet volume was higher and platelet count was lower in patients with acute coronary syndrome who had ST-elevation than those in control group. Larger platelets are haemostatically more active and hence carry risk for developing coronary thrombosis leading to acute coronary syndrome. Patients with increased mean platelet volume and lower platelet count could be easily identified during routine haematological analysis. It could play an important role in early detection of acute coronary syndrome.

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Vol. 38, No.2, - July 2023 Heart J.

*Original Article*

# Comparison of COVID-19 Infection Among Vaccinated and Unvaccinated Patients in Bangladesh During Second Wave: Single Centre Study

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**Abstract:**

**Background: Vaccination may positively influence the clinical outcome of corona virus disease-19 (COVID-19) patients. But there is a lack of data regarding efficacy of vaccine against COVID-19 infection. This study aimed to compare the baseline characteristics, clinical profiles, and outcomes of COVID-19 infection in vaccinated and non-vaccinated patients in Bangladesh in the second wave.**

**Methods: This single centre prospective observational cohort study was carried out at National Heart Foundation Hospital & Research Institute from 27th February 2021 to 25th September, 2021 during the second wave. All COVID-positive patients & cardiac patients who became COVID-19 positive during the period of admission were included in this study for comparison.**

**Results: A total of 858 patients were included. Most patients in the second were unvaccinated (n= 691, 80.5%), while of the 167 individuals who were vaccinated, 125 (14.6%) patients were partially vaccinated while 42 (4.9%) were fully vaccinated. The mean age of the unvaccinated patients was 52.63±16.4 years, partially vaccinated patients was 39.74±14.88 years, and fully vaccinated patients was 50.55 ± 12.48 years (p=0.001). Male were predominant in all groups. In the unvaccinated (98.4% vs 1.6%; p=0.001) and fully vaccinated (81% vs 19%; p=0.001) groups non healthcare personnel (non-HCP) were most commonly affected. Most of the patients (48.7%) in unvaccinated group had e"4 co-morbidities, while in partially- (51.2%) and fully vaccinated (54.7%) groups most of the patients had <4 co-morbidities (p=0.001). In unvaccinated group asymptomatic & severe disease (11.4% vs 7.2% vs 2.4%; p=0.001) were more prevalent than partially- and fully vaccinated group (table 3). Mortality rate was significantly higher in unvaccinated group than partially vaccinated group (6.2% vs 0.8%; p=0.001). There was no death in fully vaccinated group.**

**Conclusion: Unvaccinated individuals were more prone to COVID-19 infection. Most of the patients in unvaccinated group had e"4 co-morbidities. In unvaccinated group asymptomatic & severe disease were more prevalent than partially- and fully vaccinated group. Mortality rate was high in unvaccinated group.**

*Key wards: COVID-19, vaccine status, clinical features, in-hospital outcome.*

*(Bangladesh Heart Journal 2023; 38(2): 127-134)*

**Introduction:**

The novel severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) originated from Wuhan, China, in 2019 and struck the world like a tsunami. The healthcare system of the developing countries was paralyzed by

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*DOI: https://doi.org/10.3329/bhj.v38i2.70283*

this deadly virus. A country like Bangladesh, with limited resources and scarce healthcare facilities experienced major challenges while combating this transmission [1]. There was an acute shortage of hospital beds, oxygen supply, medicines, and ventilators across the country for COVID-19 patients [2].Before availability of vaccine, the only way to prevent the spread of the virus was to wear masks in public places, wash hands diligently, cover mouth when coughing, maintain social distance, identify positive cases by large-scale testing and to isolate the infected[3,4]. With time, several vaccines (Covishield, Pfizer–BioNTech, AstraZeneca, Covaxin)were invented to provide acquired immunity against the coronavirus [5]. Maintaining the necessary measures and proper dose of vaccines, several nations have succeeded in controlling the disease [5]. Bangladesh was one of the few countries that started vaccine rollouts timely [6]. As of April 19, 2021, 5.73 million people have received at least one dose of the Oxford-AstraZeneca vaccine and 1.51 million people are fully vaccinated with two doses (0.8% population fully vaccinated) [7]. However, a large fraction of people, mostly residing in villages and slums were hesitant toward vaccination, primarily due to lack of knowledge [8]. Anti-vaccine proponents, belief of being at a low risk of infection, concerns about adverse events, toxicity, and the overall efficacy of vaccines strongly discouraged many from the procedure of vaccination [9]. Some were also apprehensive about the long-term effects of the vaccines[10].

In randomized placebo-controlled Phase III trials, the BNT162b2 mRNA COVID-19 vaccine (Pfizer- BioNTech) [11], the mRNA-1273 vaccine (Moderna) [12], the ChAdOx1 nCoV-19 vaccine (AZD1222; Oxford-AstraZeneca) [13], the absorbed COVID-19 (inactivated) vaccine (CoronaVac) [14], and Ad26.COV2.S (Janssen) [15] vaccines showed 95%, 94.1%, 70.4%, 50.7% and 67% efficacy against symptomatic disease due to SARS-CoV-2. An interim analysis of four randomized control trials (RCTs) of Covishield vs control has reported an overall efficacy of 70·4% among 11,636 participants.[13]. In India, recent RCT of Covaxin vs placebo on 25,798 individuals reported vaccine efficacy of 93.4% against severe COVID 19 and 63% against asymptomatic COVID 19, with an overall vaccine efficacy of 77.8%.[16]. Studies in the real-world setting around the world have shown that the approved vaccines are highly protective against SARS- CoV-2 [17].

However, there is a lack of data regarding efficacy of vaccine against COVID-19 infection in Bangladeshi population. This study aimed to compare the baseline characteristics, clinical profiles, and clinical outcomes of fully vaccinated individuals with SARS CoV 2 infection with those of unvaccinated and partially vaccinated individuals in the second wave.

**Material and Methods:**

This single centre prospective observational cohort study was carried out at National Heart Foundation Hospital & Research Institute from 27th February, 2021 to 25th September, 2021 in the second wave. COVID-positive patients & all admitted cardiac patients who become COVID-19 positive during this period were included in this study for comparison. Based on the duration of having the symptoms from the date of vaccination, patients were classified into three groups: unvaccinated, partially vaccinated and fully vaccinated [18]. Unvaccinated patients were defined as those who had not received any vaccine or became symptomatic in <2 weeks of receiving the first dose. Partially vaccinated patients were defined as who got symptomatic two or more weeks after the first dose but not received the second dose or received the second dose <2 weeks before getting symptomatic. Participants who became symptomatic two or more weeks after the receipt of the second dose of the vaccine were defined as fully vaccinated [18].The degrees of severity of COVID-19 were classified as mild, moderate, severe, and critical ill [19,20].

Continuous variables are described using the mean and standard deviation (SD), and compared using unpaired Student's'‘t' test. Discrete variables are expressed as number of cases and percentage. Comparison between variables was performed using the two-sided chi-square tests for discrete variables, or Fisher's exact tests (expected frequency <5). A two-sided p value <0.05 was considered statistically significant. All analyses were performed using SPSS statistical software version 16.0 (SPSS Inc., Chicago, IL, USA).

**Results:**

Most patients in the second wave were unvaccinated (n= 691, 80.5%), while of the 167 individuals who were vaccinated, 125 (14.6%) patients were partially vaccinated while 42 (4.9%) were fully vaccinated (Figure 1).

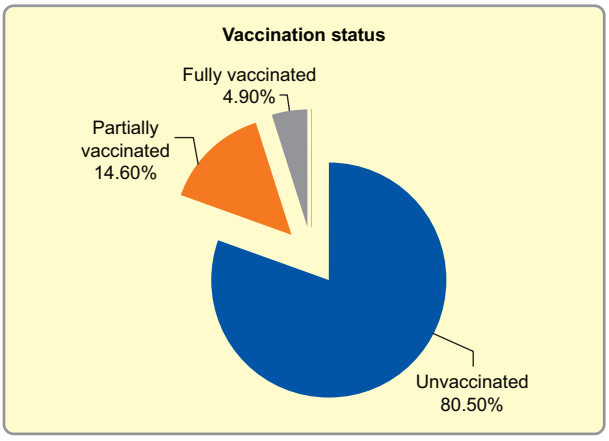


**Fig.-1:** *Vaccine status of study cohort (n=858).*

The mean age of the unvaccinated patients was 52.63±16.4 years, partially vaccinated patients was 39.74±14.88 years, and fully vaccinated patients was 50.55 ± 12.48 years (p=0.001). Among unvaccinated cases, the number of patients <20 years, between 21 and 40 years, 41 and 60 years, and >80 years were 3.8%, 16.6%, 47.8%, 29.6%, and 2.2%, respectively. Among partially vaccinated cases, the number of patients <20 years, between 21 and 40 years, 41 and 60 years, and >80 years were 0.0%, 58.4%, 28.0%, 13.6%, and 0.0%, respectively. The number of patients <20 years, between 21 and 40 years, 41 and 60 years, and >80 years among fully vaccinated cases were 0.0%, 21.5%, 59.5%, 19.0%, and 0.0%, respectively.

Male were predominant in all groups. In the unvaccinated (98.4% vs 1.6%; p=0.001) and fully vaccinated (81% vs 19%; p=0.001) groups, non healthcare personnel (non-HCP) were more infected. Cardiovascular disease (80.5%), hypertension (69.3%), chronic kidney disease (45.3%) and diabetes mellitus (DM) (43.1%) were more prevalent in unvaccinated group; while Hypertension (32.8%), obesity (31.2%), cardiovascular disease (29.6%) and DM (24%) were more prevalent in partially vaccinated group & cardiovascular disease (71.4%), HTN (66.7%), smoking (40.5%) and DM (35.7%) in fully vaccinated group (p=0.001). Comparison of demographic profile of study cohort is outlined in table 1. Most of the patients (48.7%) in unvaccinated group had e"4 co-morbidities, while in partially- (51.2%) and fully vaccinated (54.7%) groups most of the patients had <4 co-morbidities (p=0.001).

Abbreviation: COVID-19: coronavirus disease 2019; HCP: healthcare personnel; non-HCP: non-healthcare personnel; SD: standard deviation; HTN: hypertension;

**Table-I**
*Demographic profile of study cohort*

| Variables | Vaccination status (n=858) | | | P value |
|---|---|---|---|---|
| | Unvaccinated (n=691) | Partially vaccinated (n=125) | Fully vaccinated (n=42) | |
| Age (Mean age ±SD) | 52.63 ±16.4 | 39.74 ± | 50.55 ± | 0.001# |
| years | 14.88years | 12.48years | | |
| <20 years | 26(3.8%) | 0(0.0%) | 0(0.0%) | |
| 21-40 years | 115(16.6%) | 73(58.4%) | 9(21.5%) | 0.001 |
| 41-60 years | 330(47.8%) | 35(28.0%) | 25(59.5%) | |
| 61-80 years | 205(29.6%) | 17(13.6%) | 8(19.0%) | |
| >80 years | 15(2.2%) | 0(0.0%) | 0(0.0%) | |
| Gender | | | | |
| Male | 462(66.9%) | 64(51.2%) | 31(73.8%) | 0.002* |
| Female | 229(33.1%) | 61(48.8%) | 11(26.2%) | |
| HCP | 11(1.6%) | 83(66.4%) | 08(19.0%) | 0.001* |
| Non-HCP | 680(98.4%) | 42(33.6%) | 34(81.0%) | |
| Risk factors & co-morbidities HTN | 479(69.3%) | 41(32.8%) | 28(66.7%) | 0.001* |
| DM | 298(43.1%) | 30(24.0%) | 15(35.7%) | 0.001* |
| Smoking | 257(37.2%) | 19(15.2%) | 17(40.5%) | 0.001* |
| Dyslipidemia | 150(21.7%) | 16(12.8%) | 10(23.8%) | 0.06* |
| Cardiovascular disease | 556(80.5%) | 37(29.6%) | 30(71. 4%) | 0.001* |
| COPD/BA | 53(7.3%) | 46(5.4%) | 46(5.4%) | 0.114* |
| Obesity | 176(25.5%) | 39(31.2%) | 15(35.7%) | 0.19* |
| CKD | 313(45.3%) | 28(22.4%) | 11(26.2%) | 0.001* |
| Number of co-morbidities | | | | |
| 0 | 47(6.8%) | 39(31.2%) | 3(7.2%) | |
| <4 | 307(44.5%) | 64(51.2%) | 23(54.7%) | 0.0001* |
| ≥4 | 337(48.7%) | 22(17.6%) | 16(38.1%) | |

DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; BA: Bronchial asthma; CKD: chronic kidney disease. *Chi square test was done to find out the significance; #Student's 't' test was done to find out the significance.

Asymptomatic patients were more predominant in unvaccinated group than in partially- and fully vaccinated group (30.1% vs 12.8% vs 16.7%; p= 0.001). In unvaccinated group, fever, shortness of breath, cough and fatigue were the predominant symptoms. In partially vaccinated group fever, cough, fatigue and headache were the predominant symptoms & fever, cough, fatigue, shortness of breath in fully vaccinated group. Comparison of baseline clinical profile of study cohort is depicted in table 2.

In unvaccinated group asymptomatic & severe disease (11.4% vs 7.2% vs 2.4%; p=0.001) were more prevalent than partially- and fully vaccinated group (table 3). Mortality rate was significantly higher in unvaccinated group than partially vaccinated group (6.2% vs 0.8%; p=0.001). There was no death in fully vaccinated group. Comparison of in-hospital outcome of study cohort COVID-19 patients is shown in table 3.



**Table-II**

*Baseline clinical profile of study cohort*

| Variables | Vaccination status (n=858) | | | P value* |
|---|---|---|---|---|
| | Unvaccinated vaccinated (n=691) | Partially (n=125) | Fully vaccinated (n=42) | |
| **Clinical presentation** | | | | |
| Symptomatic | 483(69.9%) | 109(87.2%) | 35(83.3%) | 0.001 |
| Asymptomatic | 208(30.1%) | 16(12.8%) | 7(16.7%) | |
| Presenting symptoms | | | | |
| Fever | 316(45.7%) | 83(66.4%) | 26(61.9%) | 0.001 |
| Fatigue | 155(22.4%) | 59(47.2%) | 17(40.5%) | 0.001 |
| Cough | 221(32.0%) | 69(55.2%) | 23(54.8%) | 0.001 |
| Body ache | 71(10.3%) | 40(32.0%) | 10(23.8%) | 0.001 |
| Headache | 35(5.1%) | 49(39.2%) | 9(21.4%) | 0.001 |
| Anosmia | 15(2.2%) | 42(33.6%) | 5(11.9%) | 0.001 |
| Sore throat | 9(1.3%) | 33(26.4%) | 3(7.1%) | 0.001 |
| Shortness of breath | 314(45.4%) | 40(32.0%) | 15(35.7%) | 0.013 |
| Diarrhea | 6(0.9%) | 22(17.6%) | 2(4.8%) | 0.001 |
| Generalized itching | 15(2.2%) | 7(5.6%) | 1(2.4%) | 0.09 |

Abbreviation: COVID-19: coronavirus disease 2019. *Chi square test was done to find out the significance.

**Table-III**

*In-Hospital outcome of study cohort*

| Variables | Vaccination status (n=858) | | | P value* |
|---|---|---|---|---|
| | Unvaccinated (n=691) | Partially vaccinated (n=125) | Fully vaccinated (n=42) | |
| Disease severity | | | | |
| Asymptomatic | 208(30.1%) | 16(12.8%) | 7(16.7%) | 0.001 |
| Mild | 400(57.9%) | 98(78.4%) | 34(81.0%) | 0.001 |
| Moderate | 1(0.1%) | 2(1.6%) | 0(0.0%) | 0.0370.041 |
| Severe | 79(11.4%) | 9(7.2%) | 1(2.4%) | |
| Critical ill | 3(0.4%) | 0(0.0%) | 0(0.0%) | 0.695 |
| Mortality | 43 (6.2%) | 1(0.8%) | 0(0.0%) | |

Abbreviation: COVID-19: coronavirus disease 2019. *Chi square test was done to find out the significance.

**Discussion**

Important findings of this study are: 1) Most of the infected persons were unvaccinated (80.5% vs 19.5%; p=0.001); 2) Unvaccinated patients were older than fully vaccinated and partially vaccinated patients (52.63± 16.4 yrs vs 50.55 ± 12.48 years vs 39.74 ± 14.88 years; p=0.001); 3) Vaccinated people were less affected by COVID-19; 4) Most of the patients (48.7%) in unvaccinated group had e"4 co-morbidities, while in partially- (51.2%) and fully vaccinated (54.7%) groups most of the patients had <4 co-morbidities (p=0.001); 5) Asymptomatic patients were more predominant in unvaccinated group than in partially- and fully vaccinated group (30.1% vs 12.8% vs 16.7%; p= 0.001); 6) In unvaccinated group asymptomatic & severe disease (11.4% vs 7.2% vs 2.4%; p=0.001) were more prevalent than partially- and fully vaccinated group; and, 7) Mortality rate was high in unvaccinated group (6.2% vs 0.8% vs 0.0%; p=0.001).

In our study, 4.9% (42) patients were fully vaccinated which is also defined as vaccine breakthrough infection. It could be due to emergence of newer mutant strains capable of escaping the host immune response [21], ineffectiveness of the vaccine secondary to various factors including a break in the cold chain, etc, faulty techniques of vaccination, and host factors leading to ineffective antibody production [22,23].

Unvaccinated patients were older than fully vaccinated and partially vaccinated patients (52.63± 16.4 yrs vs 50.55 ± 12.48 years vs 39.74 ± 14.88 years; p=0.001). This may be due to targeting of vaccination program from frontline fighters and people aged >40 years in the first phase in Bangladesh (combination of young and older age). Later people >18 years were included in vaccination program so younger age was predominant in partially vaccinated group. Elderly patients were more prone to COVID-19 infection and they afraid of vaccination. In contrast to our study, the fully vaccinated individuals were older than the partially vaccinated and the unvaccinated patients (66 vs 59 vs 55 years, p-value <0.001) [24].

Fatima et al. [24] from Pakistan recruited 434 COVID-19 patients. Of them, 37.7% (n = 164), 6.6% (n = 29) and 55.5% (n = 241) were fully vaccinated, partially vaccinated, and unvaccinated, respectively. Majority (35.7%) of the patients had received Sinopharm vaccination and the median time interval from the last dose of vaccination to symptom onset was 74 (42-114) days. The severe (33.2% vs 34.5% vs 30.5%) and critical disease (44.8% vs 48.3% vs 34.8%) was significantly higher in the unvaccinated and partially vaccinated group as compared to the vaccinated group (p-value 0.04). Comparatively higher number of unvaccinated and partially vaccinated patients required invasive ventilation than the fully vaccinated cohort (7.9% vs 3.4% vs 1.8%, p-value 0.025). Unvaccinated patients had significantly higher rate of sepsis (19.5% vs 6.7% p-value <0.001), septic shock (7.5% vs 0.6% p-value 0.002) and multi-organ dysfunction (9.1% vs 1.2% p-value 0.002) as compared to fully vaccinated patients. Overall, mortality rate was also significantly higher in unvaccinated patients (16.2%, n = 39) as compared to 6.1% (n = 10) in fully vaccinated patients (p-value 0.006). Age, gender, and presence of e"2 co-morbid conditions, vaccination status was an independent predictor of mortality and unvaccinated patients had statistically significant mortality risk with p-value <0.001 (OR 5.04, CI 2.04-10.55).

Balachandran et al.[25] analyzed 1446 COVID-19 patients. Most patients were non-vaccinated (n = 1100, 76.1%), while of the 346 individuals who were vaccinated, 189 were partially vaccinated while 157 were fully vaccinated. Comparing between the vaccinated and the unvaccinated COVID-19 patients, ICU admissions (3.5% vs 7.1%), gastrointestinal symptoms (9.5% vs 6.9%), non-invasive ventilation use (10% vs 4.3%), death (5.8% vs 1.4%), mechanical ventilation (5.9% vs 5.2%),oxygen use (9% vs 7.5%), antibiotics (19% vs 12.4%), use of steroids (12.8% vs 9.2%), antivirals (16% vs11.5%) and length of stay in hospital 11.33 ± 9.9 days for the unvaccinated and 8.06 ± 4.18 days in the vaccinated group were all favourable for the vaccinated cohort with ICU admissions, need for non-invasive ventilation and death reaching statistical significance. Mechanical Ventilation (5.9 %vs 5.2%), non-invasive ventilation (8% vs 4.3%) and moderate-severe symptoms (9% vs 7.5%) were all more favourable for the vaccinated as compared to the unvaccinated patients. Deaths occurred in 0.63% of the fully vaccinated, 2.1% of the partially vaccinated, and in 5.8% of the unvaccinated patients. Thangaraj et al. [26] enrolled 539 COVID-19 patients (241 partially vaccinated patients, 113 fully vaccinated patients, and 185 unvaccinated individuals) in the study. The median age of the individuals who were unvaccinated, partially vaccinated and fully vaccinated were 47 years (IQR; 33–57), 53 years (IQR;46–60) and 54 years (IQR: 42–64), respectively. The proportion of patients with moderate/ severe illness was significantly lower in the fully vaccinated group (7/104. 6.7%) than in the unvaccinated (34/176, 19.3%) group ($p$ = 0.003). No deaths were reported in the fully vaccinated group, whereas 3 partially vaccinated group (1.3%) and seven unvaccinated (4%) COVID-19 patients died. The proportion of COVID-19 deaths was significantly lower in the partially vaccinated

(1.3%, *p* value (1-tail) = 0.046) and fully vaccinated (0%, *p* value (1-tail) = 0.018) than the unvaccinated (4.0%).

Sagiraju et al.[18] from India, compared the differences in clinical, biochemical parameters and the hospitalization outcomes of 53 (35) fully vaccinated individuals with those of 1464 (83.8%) unvaccinated and 231 (13.2%) partially vaccinated individuals. Vaccination status of their patients was similar to our study. They showed that completing the course of vaccination protected individuals from developing severe COVID 19 as evidenced by lower proportions of those with hypoxia, abnormal levels of inflammatory markers, requiring ventilatory support, and death compared to unvaccinated and partially vaccinated individuals. In our study, in unvaccinated group asymptomatic & severe disease (11.4% vs 7.2% vs 2.4%; p=0.001) were more prevalent than partially- and fully vaccinated group.

Completing the vaccination schedule for COVID 19 significantly decreased the inflammatory response caused by the SARS CoV 2 virus, thereby reducing the risk of developing serious complications during illness [18]. Even receiving a single shot of the COVID 19 vaccine seemed to reduce the inflammatory response after 14 days of receiving the vaccine, making the individual less prone to severe COVID 19[18]. More individuals in the unvaccinated and partially vaccinated groups had a hyper inflammatory response as evidenced by high d Dimer, IL 6 and CRP levels as compared to fully vaccinated individuals [18]. This may indicate that vaccination reduces the risk of developing hypoxia and cytokine storm, but once the patient develops hypoxia and ARDS, the odds of developing critical illness and death are similar to those of unvaccinated individuals [18,27,28].

In our study, mortality rate was 6.2% in unvaccinated group, 0.8% in partially vaccinated group and no death in fully vaccinated group (p=0.001). Almost similar death rate was observed in study by Thangaraj at al.[26] (4.0% vs 1.3% vs 0.0%; p=0.001), and by Balachandran et al.[25] (5.8% vs 2.1% vs 0.63%).But in other studies mortality rate was higher than our studies: (22.8% vs 19.48% vs 5.66%) [18], and (16.2% vs 13.8% vs 6.1%; p=0.006) [24]. Muthukrishnan et al. [29] in their hospital-based cross-sectional study reported a higher mortality rate of 31.45% vs 12.5% among unvaccinated as compared to those fully vaccinated. Moreover 70% lower risks of mortality were reported in the fully vaccinated cohort.

There have several limitations to our study. Firstly, study conducted in non-COVID-dedicated hospital. Secondly, the genomic variants were not considered. Thirdly, COVID variants were not determined and fourthly. Fourthly, the brand name of vaccine was not included. Fifthly, COVID-19 antibodies tests were not done to see the effectiveness of the vaccine.

**Conclusion:**

Unvaccinated individuals were more prone to COVID-19 infection. Most of the patients in unvaccinated group had e"4 co-morbidities, while in partially-and fully vaccinated groups most of the patients had <4 co-morbidities. In unvaccinated group asymptomatic & severe disease were more prevalent than partially- and fully vaccinated group. Mortality rate was high in unvaccinated group. The vaccine offers strong protection against the most serious outcomes of COVID-19, increasing vaccination rates is key to limiting severe COVID-19 cases and saving lives.

**Acknowledgement:**

We would like to thank Mrs Rehana Akter and Mr. Rasel Hasan, National Heart Foundation Hospital & Research Institute, for their sincere hard work in collecting and tabulating the data.

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Vol. 38, No.2, - July 2023 Heart J.

*Original Article*

# Established and Emerging Biomarker in Chronic Heart Failure

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**Abstract:**

**Background : More than one million hospital admissions each year are due to heart failure as the major diagnosis. One in six patients over 65 who visit a primary care facility complaining of dyspnea with exertion has undiagnosed HF. By far, the most thoroughly investigated, extensively used, and acknowledged biomarkers for heart failure are natriuretic peptides. B type natriuretic peptide (BNP) and its biologically inactive fragment N-terminal pro B-type natriuretic peptide (NT-ProBNP), which are both primarily released by the ventricles in response to stretching, have been suggested to be useful for determining the prognosis or disease severity of chronic heart failure in earlier studies[1]. Uric acid levels rise in CHF primarily due to increased production and occasionally due to decreased excretion or both. Elevated uric acid levels are a sign of developing heart failure and cardiac dysfunction. Numerous studies have demonstrated a connection between morbidity and death in CHF and elevated serum uric acid levels[2].**

**Objective: To find out the relationship between on admission serum uric acid level with established prognostic factors and Biomarkers such as different classes of NYHA, LVEF, NT-PROBNP, and their prognostic significance.**

**Methods: From April 2018 to March 2019, this study was carried out at the National Heart Foundation Hospital and Research Institute's Department of Cardiology. After considering the inclusion and exclusion criteria, 148 patients with chronic heart failure who had admission serum uric acid measurement and telephone follow-up within 30 days were included. The study patients were divided into two groups based on Serum uric acid level Group I (SUA in men<7mg/dl) (SUA in women <6mg/dl), Group II (SUA in men e"7mg/dl), (SUA in women e"6mg/dl) Baseline characteristics, Left ventricular ejection fraction (LVEF) were then compared between the two groups.**

**Results: On 148 patients, the level of serum uric acid was assessed, and follow-up was done, patients with chronic heart failure were shown to have significantly higher levels of hyperuricemia, and there was a strong association between the severity of the rise in serum uric acid (SUA) and the severity of the heart failure. Elevated blood uric acid levels and ejection fraction have an antagonistic relationship. The severity of heart failure can be predicted by hyperuricemia, as evidenced by the association between patients with elevated blood UA levels and a worse New York Heart Association (NYHA) functional class. Higher uric acid levels in patients were linked to negative outcomes and a poor prognosis..**

**Conclusion: As with NT Pro BNP or other well-established prognostic indicators, lower uric acid levels upon admission can be utilized to predict the prognosis of CHF patients.**

*Keywords: Serum Uric Acid, Chronic Heart Failure, Echocardiogram, Left Ventricular Ejection Fraction, NYHA Classification. Biomarkers.*

*(Bangladesh Heart Journal 2023; 38(2): 135-142)*

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*DOI: https://doi.org/10.3329/bhj.v38i2.70276*

**Introduction:**

The leading cause of death worldwide during the past ten years has been cardiovascular disease (CVD). 28 percent of the 50.4 million fatalities worldwide in 1990 were caused by CVD. In 2001, 29 percent of all fatalities were attributable to CVD. By 2030, there will be 7.8 billion people on the planet, and cardiovascular disease will be the root cause of 32% of all deaths. A significant concern for the health sector is the increasing burden of cardiovascular diseases (CVDs) in developing nations, particularly in low- and middle-income nations. World Health Organization estimated that in 2012, CVDs caused 17.5 million deaths worldwide, accounting for 31% of all deaths, with 80% of these deaths occurring in LMICs (WHO, 2015). Additionally, CVDs were also responsible for 85% of all global disabilities[3]. More than one million hospital admissions each year are due to heart failure as the major diagnosis. One in six patients over 65 who visit to a primary care facility complaining of dyspnea with exertion have undiagnosed HF (mainly HFpEF). At age 55, the lifetime chance of having heart failure is 28% for women and 33% for men. For Americans over 40, the risk of having HF over their lifetime is 20%[4].

We lack information on the precise frequency and incidence of heart failure in Bangladesh. Heart failure affected about one-seventh of all hospitalized patients. The average age was 54.1 years (15.3). Ischemic heart disease (IHD) was the majority's main cause (35.79 percent), but it frequently coexisted with a history of hypertension (46.8 percent ). In 29.14 percent of cases, high blood pressure was thought to be the main risk factor for heart failure. Diabetes Mellitus (DM) was shown to be more common in Dilated Cardiomyopathy (DCM) and co-existed with IHD in 41.4 percent of cases[5].

Congestive heart failure is a complex syndrome that can develop as a result of any anatomical or functional cardiac condition that hinders the heart's capacity to pump blood throughout the body adequately. Congestive heart failure is a complex syndrome that can develop as a result of any anatomical or functional cardiac condition that hinders the heart's capacity to pump blood throughout the body adequately. The syndrome of heart failure is characterized by symptoms such as breathlessness with features of circulatory congestion such as jugular venous distension, rales, peripheral edema, and ascites[6].

Insulin resistance and obesity are important risk factors for the onset of heart failure. It has been demonstrated that obesity alone is a risk factor for incident heart failure[7]. In addition to monitoring ventricular rate control in patients with atrial fibrillation, ECG monitoring is useful in the evaluation of individuals who exhibit symptoms that could indicate an arrhythmia or bradycardia, such as palpitations or syncope. Heart failure may be made worse by ventricular arrhythmias, episodes of ischaemia and bradycardia, and conduction defects[8].

Elevated NPs help establish an initial working diagnosis, identifying those who need additional cardiac testing; Patients do not need an echocardiogram if their readings are below the cutoff for significant heart dysfunction. It is unlikely that patients with normal plasma NP concentrations have heart failure[9]. The most extensively researched heart failure biomarkers are natriuretic peptides. The ventricles respond to stress by producing B type natriuretic peptide (BNP) and its physiologically inactive component NT-ProBNP[10].

For patients with suspected HF, an effective and commonly accessible diagnostic to make the diagnosis is echocardiography[11]. Since the late 19th century, researchers have recognized that gout, hypertension, and obesity are all related to serum uric acid (SUA)[12]. Chronic heart failure is frequently accompanied by hyperuricemia (CHF). As the condition gets worse, serum uric acid rises. In a cross-sectional study, hyperuricemia was present in 51% of patients with chronic heart failure who were hospitalized[13]. Patients with end-stage CHF and cachectic patients had greater SUA levels, and SUA is inversely correlated with functional NYHA class II.

SUA (Serum Uric Acid) was the most powerful predictor of survival for patients with severe CHF (NYHA class III or IV): in patients with high levels of SUA (> 9.5 mg/dl). Patients with higher uric acid levels were linked to long-term negative outcomes, and other studies have linked elevated serum uric acid levels in patients with congestive heart failure to higher rates of morbidity and mortality[14]. Heart failure brought on by hyperuricemia is caused by a number of processes. Higher XO substrate (ATP breakdown to adenosine and hypoxanthine) and up-regulated and increased XO activity may be the causes of the increased SUA formation. SUA can have adverse effects on the cardiovascular system and can influence the immunological response when it is released from necrotic tissue. Hyperuricemia in heart failure is a sign of activated XO[15].

Anemia, renal impairment, cardiac rhythm abnormalities, a long corrected QT interval, complete LBBB, and advanced age are prognostic factors for CHF. Left ventricular ejection fraction of 40% is also a poor prognostic factor[16]. High serum uric acid was present in HF patients. Elevation of serum uric acid in HF is multifactorial. Diuretic treatment, elevated production, and diminished renal function may explain this[17].

Serum SUA in this population may provide predicting data about the patient. This simple, low-cost marker can identify CHF high-risk individuals.

**Objective:**

To find out the relationship between on admission serum uric acid level with different classes of NYHA, LVEF, NT-PROBNP, and its prognostic significance

**Methodology:**

This was a prospective cohort study. The study was carried out in the Department of Cardiology, National Heart Foundation Hospital & Research Institute, Mirpur2 , Dhaka Bangladesh. After presentation and acceptance of the protocol and getting ethical clearance, the study was carried out from April, 2018 to March, 2019 (1 year). Considering inclusion and exclusion criteria, a total number of 148 patients of both sexes were included in the study.

**Inclusion Criteria:**

Patients of both sex between 20-80 years who were admitted with chronic heart failure to the Department of Cardiology in NHFH & RI, with heart failure (both with preserved as well as reduced ejection fraction).

**Exclusion Criteria:**

1. Patients who were not willing to enroll in the study.
2. Patients who were unable to be reached via phone for follow-up.
3. Patients with previously diagnosed hyperuricemia who are using anti hyperuricemic medication.
4. Patients with severe comorbid conditions, such as severe chronic obstructive pulmonary disease, severe renal impairment, pneumonia, pulmonary embolism, adult respiratory distress syndrome, and any cancer.
5. Renal Impairment (Serum creatinine e" 1.5 mg/dl)
6. Recent Acute Coronary Syndrome (< 1 month)

**Data Collection and Analysis:**

Data was gathered through in-depth patient assessment, extensive history taking, clinical examination, and conducting relevant investigations. Demographic information, age, gender, occupation, and BMI (kg/m2) were recorded. Each patient's height and weight were recorded in meters and kilograms for the purpose of calculating BMI. Hypertension, diabetes, and dyslipidemia was noted. NYHA Class of heart failure was noted. Routine Investigations like FBS, serum creatinine, fasting lipid profile, Pro BNP, Hemoglobin level was measured. Serum Uric acid assay was be carried out by using Siemens Dimension RXL Max analyzer and enzymatic colorimetric method. Left ventricular ejection fraction (LVEF), LVIDd, and LA size were assessed by 2D trans thoracic echocardiography. After 30 days, patients were followed up with either hospital records or trans-telephonic follow-up, whichever was appropriate. All the above data was collected by face to face interview using questionnaire. All available data were processed, and statistical analyses were then performed to determine their significance. The collected data were expressed as appropriate in the form of frequency, percentage, mean, and standard deviation. For continuous variables, Student's t-test was used to compare groups. By using the Chi-square test, categorical data was assessed. Logistic regression was done in order to adjust for established prognostic factors for chronic heart failure (Tachycardia, anemia, LVEF, serum uric acid, Anti- pro BNP, advancing age >70). Version 16 of the computer-based SPSS (Statistical Program for Social Science) program was used to conduct the entire analysis. P-value of <0.05 was considered significant.

**Result:**

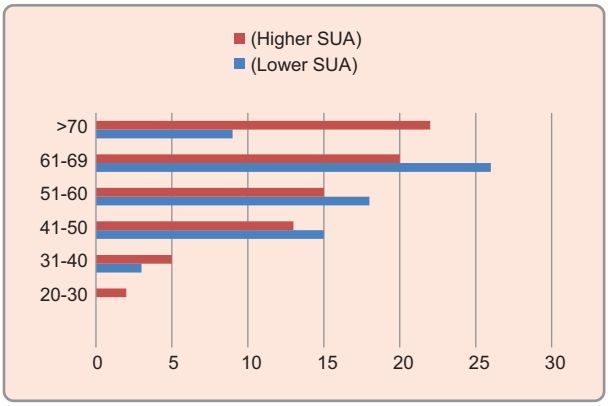


**Fig.-1:** *Showing Age Distribution among Group I & II*

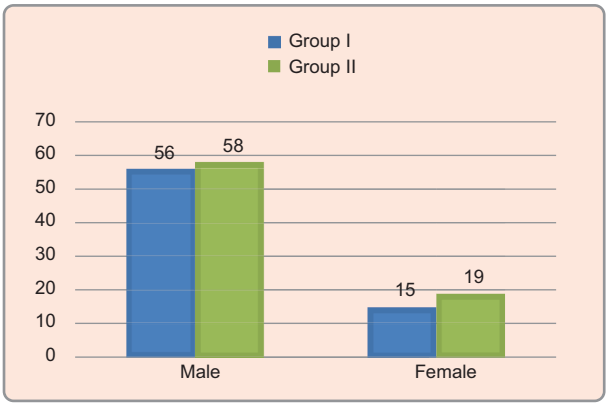


**Fig.-2:** *Bar Graph Showing Male And Female distribution among Group I & II*

**Table-I**

*Association of BMI of the study patients between two groups*

| | | | |
|---|---|---|---|
| BMI (kg/m$^2$) | | | 0.099$^{ns}$ |
| Normal (18.5-22.9) | 9(12.7%) | 4(5.2%) | |
| Overweight (23.0-24.99) | 8(11.3%) | 12(15.6%) | |
| Obese (³25.0) | 54(76.1%) | 61(79.2%) | |
| Total | 71(100%) | 77(100%) | |
| Mean±SD | 26.58±3.60 | 28.03±4.48 | |

ns = not significant

**Table-II**

*Association drug history of the study patients between two groups (n=148)*

| Drug history | Group I (Lower SUA) (n=71) No. (%) | Group II (Higher SUA) (n=77) No. (%) | p value |
|---|---|---|---|
| Beta blockers | 30(42.3) | 34(44.2) | 0.815$^{ns}$ |
| ACE inhibitors | 34(47.9) | 43(55.8) | 0.333$^{ns}$ |
| ARB | 34(47.9) | 30(39.0) | 0.273$^{ns}$ |
| Loop diuretics | 70(98.6) | 74(96.1) | 0.351$^{ns}$ |
| Spironolactone | 64(90.1) | 62(80.5) | 0.100$^{ns}$ |
| Nitrates | 35(49.3) | 45(58.7) | 0.264$^{ns}$ |
| Anti-platelet Clopidogrel | 53(74.6) | 52(67.5) | 0.341$^{ns}$ |
| Aspirin | 71(100.0) | 74(96.1) | 0.093$^{ns}$ |
| Statin | 32(45.1) | 28(36.4) | 0.281$^{ns}$ |
| Digoxin | 1(1.4) | 4(5.2) | 0.203$^{ns}$ |

Figures in the parentheses indicate corresponding percentage;
Chi-squared Test ($\chi^2$) was done to analyze the data.
ns = not significant

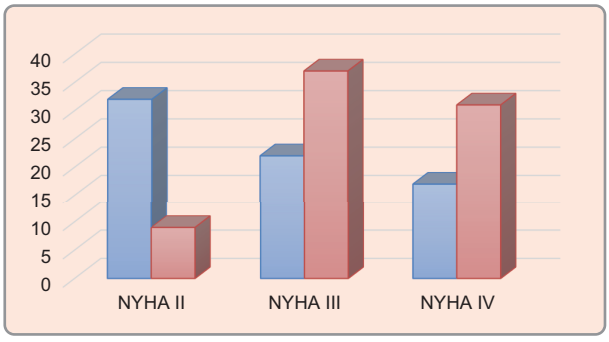


**Fig.-3:** *Bar Graph showing Uric acid levels higher with higher NYHA Class*

**Table-III**

*Comparison of biochemical variables between two groups (n=148)*

| Biochemical variables | Group I (Lower SUA) (n=71) Mean±SD | Group II (Higher SUA) (n=77) Mean±SD | p value |
|---|---|---|---|
| Serum uric acid | 5.57±1.01 | 9.46±1.99 | |
| Hb | 12.18±1.35 | 10.80±1.17 | 0.001$^{s}$ |
| RBS | 9.01±3.87 | 8.92±1.87 | 0.851$^{ns}$ |
| NT PRO BNP | 2889.11±1392.9 | 3594.59±1241.43 | 0.001$^{s}$ |
| HBA1C | 7.73±10.50 | 7.54±1.26 | 0.409$^{ns}$ |
| Troponin I | 0.04±0.03 | 0.04±0.04 | 0.528$^{ns}$ |
| Serum creatinine | 1.23±0.15 | 1.23±0.20 | 0.953$^{ns}$ |
| SGPT | 69.26±89.04 | 62.55±100.98 | 0.699$^{ns}$ |
| Na | 138.85±3.15 | 137.10±4.52 | 0.008$^{s}$ |
| K | 3.89±0.43 | 4.05±0.54 | 0.089$^{ns}$ |
| Cl | 97.46±7.23 | 99.85±8.92 | 0.077$^{ns}$ |

Data were expressed mean±SD
Unpaired student t-test was done to analyze the data.
s=significant, ns = not significant

**Table-IV**

*Association of echocardiograph findings between two groups (n=148)*

| Echocardiographic findings | Group I (Lower SUA) (n=71) | Group II (Higher SUA) (n=77) | p value |
|---|---|---|---|
| LA size | 35.15±4.36 | 37.23±5.15 | 0.009$^{s}$ |
| LVED | 53.48±8.99 | 56.92±6.25 | 0.008$^{s}$ |
| LVEF | 41.96±7.39 | 37.16±6.17 | <0.001$^{s}$ |

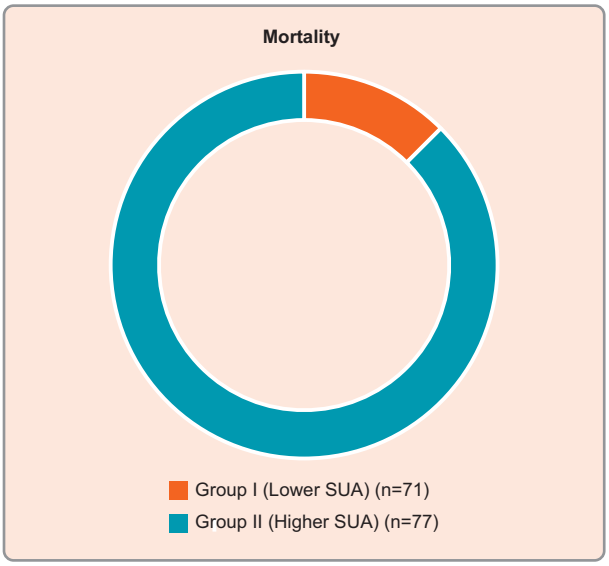


**Fig 4:** *Association of mortality between two groups (n=148)*

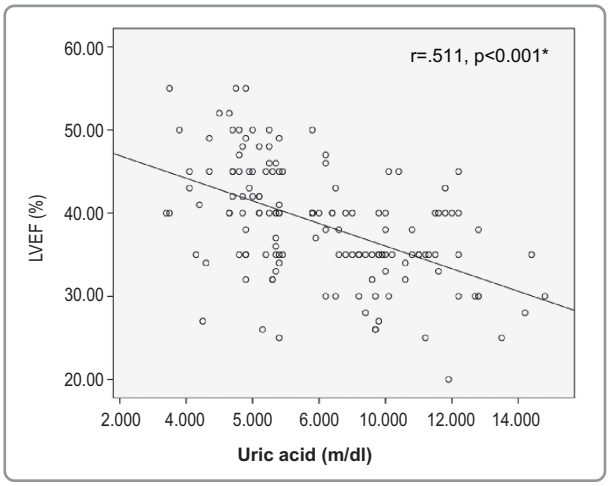


**Fig.-5:** *Scatter diagram showed correlation between LVEF and on admission Uric acid level of the study population (n=148). It showed statistically significant negative correlation with medium strength (r= -0.511, p= <0.001).*

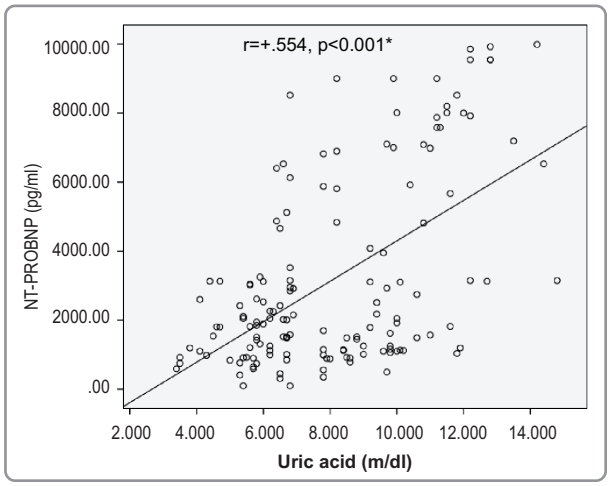


**Fig.-6:** *Scatter diagram showed correlation between NT-PROBNP and Uric acid level of the study population (n=148). It showed statistically significant positive correlation with medium strength (r= -0.554, p= <0.001).*

**Table-V**
*Regression analysis (n=148)*

| Variables | p-value | OR | 95% CI | |
|---|---|---|---|---|
| | | | Lower | Upper |
| Anemia d"11gm/dl | .637 | .789 | .294 | 2.114 |
| LVEF (d" 40%) | .012 [s] | 3.806 | 1.227 | 4.858 |
| NT PRO BNP | .024 [s] | 2.100 | 1.000 | 4.000 |
| Serum uric acid | .033 [s] | 2.004 | 2.475 | 3.767 |

Table V shows Regression analysis done to clarify the independent association of various prognostic factors

**Discussion:**

Previous research has demonstrated that serum uric acid in HF patients may also serve as a predictive risk factor. Increased ventricular filling pressures cause an adaptive increase in BNP, whereas increased xanthine oxidase activity causes a maladaptive increase in uric acid levels in HF. According to this study, which is consistent with Roberts' research investigations, hyperuricemia is present in the majority (73 %) of heart failure patients and is more common in men than in women [18].

Serum uric acid levels are markedly higher in acute decompensation than in chronic heart failure, indicating that acute heart failure syndromes are more likely to have hyperuricemia than chronic states, and that the majority of patients with acute decompensation-related hyperuricemia have severe clinical impairment. Acute heart failure patients with elevated uric acid levels had worsening left ventricular remodeling due to increased oxidative stress and xanthine oxidase activity [19].

There was no substantial difference in the drug use between Group I and Group II in this experiment. A statistically significant difference between the hyperuricemic group that received diuretics and the control group that did not was found in a study [20]. Classifying HF patients according to LVEF is essential because to disparities in aetiology, demographics, co-morbidities, and treatment response. Patients in Group I had an LVEF of 41.967.39, whereas those in Group II had an LVEF of 37.166.17. Patients with a greater SUA had a mean LVEF of 38.20 according to research by Ehmouda [21]. Consistent with Suresh [22], there was a

statistically significant (p 0.05) gap between the two groups in our investigation. Because individuals with HF have varied underlying etiologies, demographics, co-morbidities, and therapeutic responses, it is crucial to differentiate them based on LVEF [22]. In this study, LVEF in Group I patients was 41.96±7.39 in group II 37.16±6.17. Ehmouda [21] showed mean LVEF 38±20 in patients with higher SUA. In this study difference between two groups was statistically significant ($p < 0.05$) which was similar to Suresh [22].

Xanthine oxidase, an enzyme crucial in the conversion of purines to uric acid, has been linked to the production of superoxide free radicals. It has been demonstrated that coronary endothelial cells have ncreased xanthine oxidase activity during ischemia and increases even more after reperfusion [23]. Allopurinol decreases the size of infarcts and hastens the recovery of myocardium that has been stunned, presumably through reducing the generation of dangerous free radicals. Recent research reveals that xanthine oxidase activation and congestive heart failure are related [24].

Allopurinol may have enhanced LV function was by improving endothelial function, which therefore increased myocardial perfusion. Alternatively, allopurinol may improve myocardial oxygen consumption and other energy efficiency, which would then have the secondary impact of strengthening endothelial function, to directly affect LV function [25,26].

Even if improving LV function does contribute to improved endothelial function, the underlying process may still be related to oxidative stress reduction because oxidative stress is an interesting regulator of unfavorable LV remodeling. According to findings from a study in Germany, patients with CHF who had a high blood uric acid level were more likely to pass away if heart transplant is not done [2,6]. Given that hyperuricemia may be brought on by increased renal excretion of UA due to renal impairment or diuretics, it is unknown if serum uric acid is a standalone prognostic biomarker in relation to renal dysfunction in patients with CHF [18].

In this study, patients with high uric levels had an increased risk of severe heart failure, frequent hospital readmissions, longer hospital stays, and death within 30 days of follow-up compared to patients with normal uric acid levels. The use of uric acid as a prognostic marker may be very advantageous in patients with prior heart failure who have high blood uric acid levels and poor left ventricular ejection fraction. For individuals with persistent heart failure, individualized therapy is necessary for the best outcome. For this reason, it's crucial to accurately predict each patient's prognosis.

After Performing the multivariable logistic regression analysis in present study, it showed adjusted prognostic factors by multivariate logistic regression analysis for chronic heart failure. It was found serum uric acid is independently associated with outcome OR 2.004, p value 0.033. Analysis also showed LVEF (d" 40%) and NT PRO BNP as expected, remained strong predictor of outcome.

The critical importance of uric acid level as a prognostic marker may be demonstrated by the substantial association between the level of blood uric acid and reduced left ventricular ejection fraction in patients with established heart failure. In chronic heart failure, individualized treatment is needed to achieve optimal outcome. This requires a reliable assessment of individual prognosis.

Further prospective studies are required to show that routine measurement or lowering of blood uric acid levels will improve outcomes in patients with chronic heart failure, regardless of whether these levels are prepared for routine clinical use as a prognostic indicator.

**Conclusion:**

It was discovered that the severity of heart failure was correlated with the prevalence of hyperuricemia. The inverse relationship between elevated blood uric acid levels and ejection fraction suggests that growing hyperuricemia in chronic heart failure is a sign of deteriorating cardiac function. Patients with greater uric acid levels had a worse prognosis, as evidenced by their higher NYHA class at presentation, longer hospital stays, and higher 30-day mortality rate.

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*Case Report*

# A Case of Chronic Thromboembolic Pulmonary Hypertension in Association with Deep Vein Thrombosis and Pulmonary Embolism: A Case Report of a Young Female in Bangladesh

Saurav Das*[1], Uday Shankar Roy[2], Umme Maimuna[3], Swarna Paul[4], Anisul Awal[5], Asish Dey[6]

**Abstract:**

**Chronic thromboembolic pulmonary hypertension (CTEPH) is classified as Group 4 Pulmonary Hypertension (PH) in current categorization by WHO. The initial suspicion with clinical presentation, then screening with imaging and confirmation with Right heart catheterization (RHC) are the steps of diagnostic algorithm for CTEPH. We report the case of a 35 years old female presented with progressive swelling of left lower limb for 2 months and shortness of breath for 1 and half months. Examination revealed respiratory rate 28 breaths/min, pitting edema of left leg, left parasternal heave and palpable P2. Doppler study of both lower limbs and Computed tomography pulmonary angiography (CTPA ) confirmed the diagnosis of deep vein thrombosis of left leg (DVT) and pulmonary embolism (PE), respectively. The echocardiography suggested presence of pulmonary hypertension. We approached the patient with conservative management and discharged her home, once she improved, with advice of life-long anticoagulation.**

*(Bangladesh Heart Journal 2023; 38(2): 143-147)*

**Background:**

World Symposium on Pulmonary Hypertension (WSPH) categorized CTEPH as group 4 PH. [1-6] The epidemiology of CTEPH is variable across the ethnicities; the commonest presentation at an average age of 63 years, without any gender-specific predisposition .[2,3,7] The disease entity was underrepresented due to lack of availability of gold-standard investigations in the past.(1,8 )With the growing consciousness among the physicians and availability of diagnostic tools, cases of CTEPH have been frequently reported in the recent years.[1] The reported incidence rate is 0.9 cases per million.[3]The long-standing CTEPH progresses to right heart failure with high mortality rate.[2,3]

An analysis of the data from international registry of CTEPH patients evidenced a history of acute pulmonary embolism (PE) and a history of vein thrombosis in 74.8% and 56.1% of them, respectively.[6]

We present the case of a 35-year-old female with DVT with chronic pulmonary embolism whose physical findings and echocardiogram suggestive of pulmonary hypertension.

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*DOI: https://doi.org/10.3329/bhj.v38i2.70266*

**Case presentation:**

A 35- year old hypertensive female got admitted with progressive swelling of left leg for 2 months and shortness of breath for 1.5 months.The swelling was gradual in onset.Her shortness of breath can be described as initially NYHA class II, later deteriorating to NYHA class IV associated with orthopnoea, paroxysmal nocturnal dyspnoea and productive cough.On physical examination, blood pressure 100/70mmhg, Respiratory rate 28 breaths/min , pulse rate 92 beaths/min, swollen left leg with pitting, tender edema. Precordial examination revealed palpable p2 and left parasternal heave.

Echocardiography showed dilated right atrium, right ventricle, moderate tricuspid regurgitation, systolic pulmonary arterial pressure(sPAP) 60mm Hg.



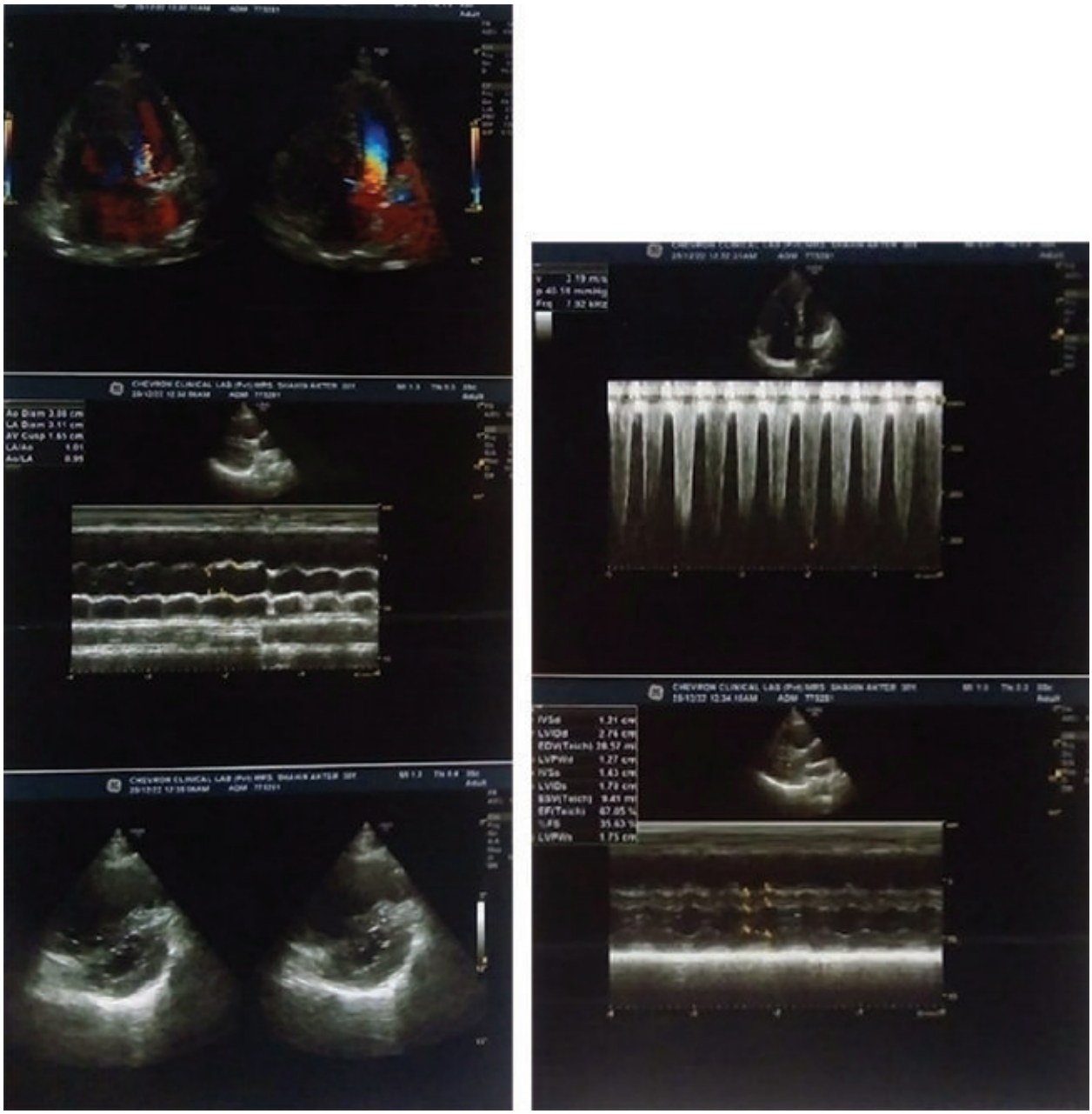

**Fig.-1:** *Two-dimensional and m-mode Echocardiography suggestive of pulmonary hypertension*

Color doppler ultrasonography of both lower limbs revealed presence of deep vein thrombosis involving the left femoral-poplitial segment with no sign of recanalization.

CTPA showed bandlike defect in right pulmonary artery (PA) .Short segment filling defect within anterior segment branch of right upper lobar pulmonary artery, with webs in lower lobar PA extending into posterior segment artery with reduced calibre and poor contrast opacification and layered filling defects at PA bifurcation.

Chest radiograph showed cardiomegaly with bilateral pleural effusion more prominent on the right side.

D-dimer was raised with a value of 2.76mg/l(reference range <.50mg/l).

Due to unavailability of RHC and digital subtraction angiography (DSA) in our centre, we couldn't perform these tests. We treated the patient conservatively. The patient was discharged accordingly with the advice of lifelong anticoagulation.



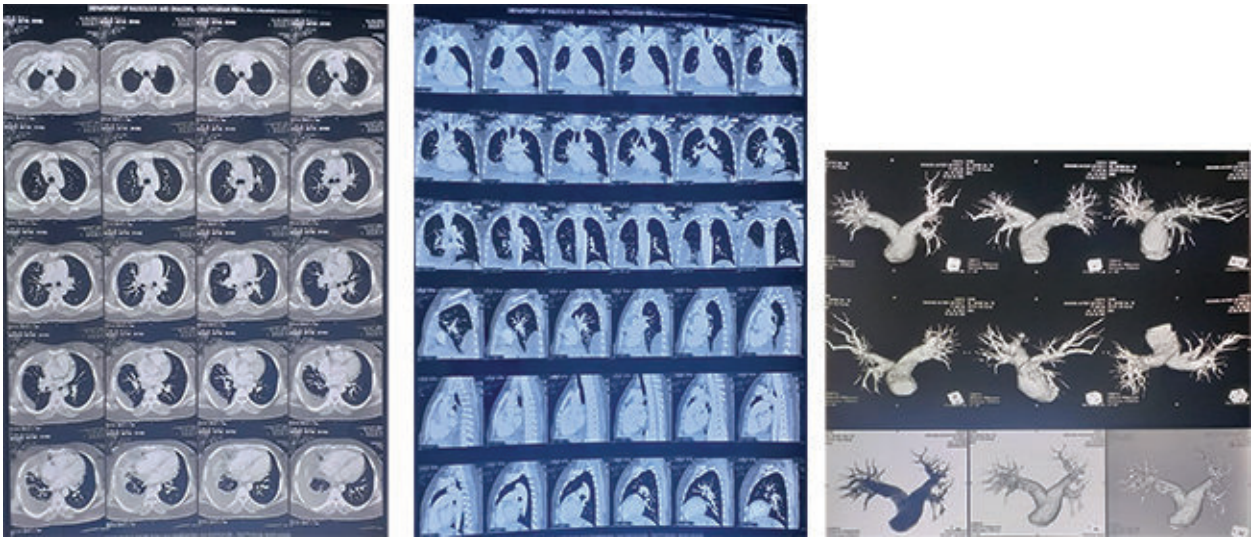

**Fig.-2:** *CTPA shows filling defects in right pulmonary artery and left pulmonary artery, favouring pulmonary embolism*

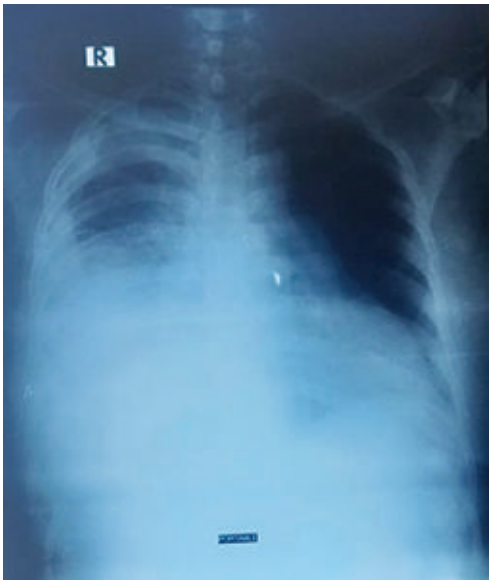


**Fig.-3:** *Chest x ray showing cardiomegaly with bilateral pleural effusion.*

**Discussion:**

CTEPH is a distinct entity of pulmonary hypertension that involves subsegmental, segmental, and main branches of the pulmonary arteries. [2,3] Presence of fibrotic thromboembolic materials cause an increase in pulmonary vascular resistance (PVR). [3] Pulmonary vasculature undergoes remodeling.[3,9]The condition consistent with the pre-capillary PH (mean pulmonary arterial pressure >20 mmHg, pulmonary artery wedge presure d"15 mmHg,pulmonary vascular resistance >2 Woods Unit).[1,3] Insufficient clot resolution are key pathophysiological feature of this disease.[1]

Preceding events of DVT and PE have been frequently reported with CTEPH; but not essential for diagnosis in all cases.[1-6,9] A large prospective study showed that cumulative incidence of CTEPH in patients with PE diagnosed for the first time was 11.2% at 3 months, 12.7% at 1 year, 13.4% at 2 years, and 14.5% at 3 years. [8] The other predisposing conditions include permanent intravascular devices (pacemaker, long-term central lines, ventriculoatrial shunts), inflammatory bowel diseases, essential thrombocythaemia, polycythaemia vera,splenectomy,antiphospholipid syndrome, high-dose thyroid hormone replacement, and malignancy.[1]

Initial screening for the presence of intermediate/high probability of PH with echocardiography is mandatory.Systolic pulmonary artery pressure ( sPAP )>60 mmHg is a predictor of CTEPH.[1]

A ventilation/perfusion (V/Q) lung scan (preferably single-photon emission computed tomography [SPECT]) has sensitivity of 90–100% and a specificity of 94–100% in detection of CTEPH. [2] V/Q scan is indicated in patients with persistent or new-onset dyspnoea or exercise limitation following PE, also in suspected or newly diagnosed cases of PH to rule out or detect signs of CTEPH.[1]

CTPA has 100% sensitivity, 93.7% specificity in diagnosis of CTEPH and supports the technical evaluation for surgery eligibility. [1-3]The typical signs observed in pulmonary angiography are ring stenosis, reticular lesions, tortuous lesions, and complete vascular obstructions, filling defects, webs or bands in the PAs, PA retraction/dilatation, mosaic perfusion, and enlarged bronchial arteries. [1,3]

Digital subtraction angiography (DSA) is mainly used to confirm CTEPH with characterising vessel morphology and assess treatment options .[1,2]

Right heart catheterization is the gold-standard confirmatory test to establish CTEPH.[1-6]

CTEPH is a potentially treatable disease.[1,3] The current guidelines suggest multidisciplinary care and multimodal approach of combinations of pulmonary endarterectomy (PEA), Balloon pulmonary angioplasty (BPA), and medical therapies to target the mixed anatomical lesions.[1] Treatment of choice is pulmonary endarterectomy with accessible PA lesions.[3] BPA is preserved for the cases which are technically inoperable.It is also indicated in residual PH after PEA and distal obstructions amenable to BPA.

Vitamin K antagonists(VKAs) remain preferred choice till the date, particularly in patients with antiphospholipid syndrome.[1] Non-vitamin K antagonist oral anticoagulants(NOACs) have been investigated in several studies, but stronger evidences are required.[1] Treprostinil (subcutaneous injection) and Riociguat have been approved for inoperable CTEPH and the residual PH after PEA.

Long-term follow up should be emphasized. [1]

**Conclusion:**

CTEPH is a rare form of pulmonary hypertension which needs appropriate recognition for management purpose. We identified a younger case in comparison with the average age of presentation in CTEPH. In spite of limitations of availability of diagnostic tools in our centre, we attempted to manage the case with the existing facilities.

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*Case Report*

# Pulmonary Embolism Successfully Treated with Tenecteplase: A Case Report

Masuma Jannat Shafi,* Sahela Nasrin, M Maksumul Haq, Md Rezaul Karim, K Ferdoush Siraj, R Tasfea Naab

**Abstract:**

**Acute pulmonary embolism is a life threatening situation when presenting with hypotension is called high-risk (massive) pulmonary embolism (PE) which is associated with mortality, especially if there is hemodynamic instability, right ventricular dysfunction with thrombus. Thrombolytic therapy can be lifesaving and leads faster improvement in hemodynamics in patients with acute pulmonary embolism and cardiogenic shock which accelerates the resolution of thrombus, reduction of RV dilatation, mortality and recurrent PE. Only three fibrinolytic agents namely Recombinant tissue-type plasminogen activator (rtPA), Streptokinase and Urokinase have been approved in the treatment of PE. We report the case of a 64 years old Bangladeshi female with a history of immobilization due to unilateral cut injury of foot, who presented with shortness of breath and intermittent chest pain for a duration of 7 days during OPD visit. ECG showed sinus tachycardia (HR-120bpm, regular) and poor progression of R wave. Echocardiography revealed dilated RV,PA with RV dysfunction, presence of McConnell's sign , RV apical & PA thrombus, flattened IVS, PHT, and minimal pericardial effusion, normal LV systolic function which was reported as suspected pulmonary embolism. Urgent hospitalization and CT pulmonary angiogram (CTPA) was done for confirmatory diagnosis which revealed large pulmonary thrombus in both right and left pulmonary artery. Thrombolysis with Tenecteplase (100ml) over 2 hours was started immediately along with intravenous normal saline and norepinephrine for hypotension, although, it was not recommended by the European Society of Cardiology (ESC) guideline, resulting a successful resolution of the PA thrombus and clinical improvement. She was discharged with oral anticoagulant Rivaroxaban.**

*Key Words: High-risk pulmonary embolism, Pulmonary artery thrombus, tenecteplase.*

*(Bangladesh Heart Journal 2023; 38(2): 148-154)*

**Introduction:**

Acute pulmonary embolism (PE) is one of the most common, life-threatening cardiovascular events. In the past few years, the proportion of hospitalized PE patients has been gradually increasing.[1] The most dreaded acute complication of PE is death & the estimated incidence of PE ranges from 39-115 per 100 000 population.[2] Venous thromboembolism (VTE), clinically presenting as deep venous thrombosis or pulmonary embolism, is globally the third most frequent acute cardiovascular syndrome behind myocardial infarction and stroke. In 2019 guideline of the European Society of Cardiology (2019 ESC) presents risk stratification of patients with acute PE as high, intermediate and low risk.[2] High- risk (Massive) pulmonary embolism (PE) is frequently complicated with hypotension and shock (hemodynamic compromise) leading to 90 days mortality rates of 58.3 % compared to 15.1% in intermediate-risk (sub-massive) PE.[3] Up to 4% of patients who survive will develop chronic

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*DOI: https://doi.org/10.3329/bhj.v38i2.70278*

thromboembolic pulmonary hypertension (CTEPH).[4] Hemodynamic instability indicates a high risk of early (in-hospital, or 30 day) mortality and encompasses three forms of clinical presentation, cardiac arrest, obstructive shock and persistent hypotension.[2] Conventional treatment of PE mainly refers to anticoagulation therapy including parenteral anticoagulation, such as low-molecular weight heparin (LMWH) or unfractionated heparin (UFH), and direct oral anticoagulation (DOACs). Those patients in particular benefit from more intensive therapy with thrombolytic agent in comparison to anticoagulant therapy alone, resulting in reduced mortality to less than 30% and improve right ventricular wall motion at 24h from baseline.[5,6,7,8] Thrombolytic therapy leads to faster improvement in hemodynamics in patients with high-risk PE accompanied by a reduction in RV dilatation and RV dysfunction in echocardiography, a significant reduction in the combine outcome of mortality and recurrent PE, improving other parameters, such as pulmonary blood flow, lung perfusion.[2,7] While its application in intermediate-risk PE was controversial.[9] Streptokinase, urokinase and recombinant tissue-type plasminogen activator (rtPA, Alteplase) are thrombolytic agents approved for the treatment of PE, with Alteplase being explicitly identified as the agent indicated for acute massive PE. The international PEITHO (pulmonary embolism thrombolysis) trial [10] found fibrinolytic therapy was associated with a 2.0% rate of hemorrhagic stroke and a 6.3% rate of major extra cranial hemorrhage for patients with intermediate-risk PE. Tenecteplase, a genetically modified variant of alteplase, can be administered as a bolus in an emergency and weight-based dosing may be preferable in elderly patients.[10] It is less likely to cause allergic reaction compare to streptokinase, an antigenic thrombolytic agent.[11,12]

This case report aims to demonstrate the importance of prompt imaging , early management and the efficacy of thrombolysis by TNK in complicated high risk (massive) PE. About 10% or more of cases of symptomatic PE are thought to be rapidly fatal and another 5% of patients are left with some residual symptoms and 2% developed thromboembolic pulmonary hypertension due to unresolved PE .[13]

Case report:

A 64 years old hypertensive, diabetic Bangladeshi female visited as outdoor patient with complaints of progressive nature of shortness of breath associated with intermittent retrosternal chest pain for the duration of 7 days. One month prior to this event she reported that she had a cut injury on her left leg which was treated with suturing and was immobilized for a month. She was advised for echocardiography with relevant blood investigations. Her vital signs upon arrival to echo lab where a palpable SBP was 90 mmHg, HR of 120bpm, regular and Oxygen saturation of 90% at room air. ECG showed sinus tachycardia and poor progression of R wave (Figure-1). Emergency echocardiography was done, which showed dilated RV,PA with RV dysfunction, presence of McConnell's sign (RV free wall hypokinetic with sparing apex) and RV apical and PA thrombus, flattened IVS, PHT, minimal pericardial effusion with normal LV function which was suspected pulmonary embolism (Figure-2). Urgent hospitalization and CTPA was done for confirmation of diagnosis and treatment.

On arrival to the CCU, patients was anxious, unable to speak a full sentence, cyanosed and needed 15 l of oxygen for maintaining oxygen saturation of 95%. Cardiac exam demonstrated tachycardia, raised JVP, fixed wide of the second heart sound, a right ventricular heave. Pulmonary findings consisted of bilateral crackles at the bases. RR-28 breaths /min. Her extremities were cool with non-recordable pulse and BP, healed wound in the left foot with no pain or swelling, rest of the general and systemic examination was unremarkable. Intravenous normal saline and Inotrope (noradrenalin) started to maintain BP and CTPA revealed multiple filling defects in both distal RPA/LPA, lobar and segmental branches predominantly lower vessels suggesting thrombus ( Figure-3) . Immediate thrombolysis was started with intravenous tenecteplase (100ml) over 2 hours as patient was elderly, hemodynamically unstable and needed urgent thrombolysis though it is not recommended in ESC guideline. The patient developed asystole 15 minutes after initiation of thrombolysis and reverted to sinus rhythm following 5 minutes of cardiopulmonary resuscitation (CPR). Tenecteplase was continued & $2^{1/2}$ hours after thrombolysis there was subsequent clinical improvement with HR of 112bpm and BP found 100/60 mmHg with inotropic support, spo2 was 95% with high flow 02, RR was 32breath/min. Bed side echo revealed global hypokinesia with LVEF-45%, normal RV and resolution of PA thrombus 7 hours after thrombolysis. The next day the patient developed VT asystole and got DC shock with CPR multiple times, put on mechanical ventilator and reverted to sinus rhythm. D-dimer assay was positive, troponin I was raised, complete blood count (CBC) revealed nutrophilic leukocytosis the day after intubation. She also developed atrial fibrillation (Figure-4) with first ventricular rate and frequent non-sustained VT, got amiodaron during the course of her treatment. Gradually over day's the patient's condition was improved

and inotropic support was decreased, Fio2 kept low. She was extubated on 6th day. Repeat CT pulmonary angiogram showed significant improvement of disease process compared with previous CTPA scan. Review echo revealed no thrombus or pulmonary hypertension, normal RV and normal LV function. Duplex USG of lower limb showed diffuse atherosclerotic changes in both lower limb arteries, mild flow reduction in right and left proximal ATA, PTA and severe flow reduction in left distal ATA and ADP. No venous thrombus or varicosity. Her treatment was followed by subcutaneous low molecular heparin (LMWH) for 5 days. Rivaroxaban given initially 15 mg twice daily for 21 days, then 20 mg once daily for 6 months. ECG during discharge showed sinus tachycardia, poor progression of R wave and SVE (Figure-5). She was asymptomatic at follow-up.



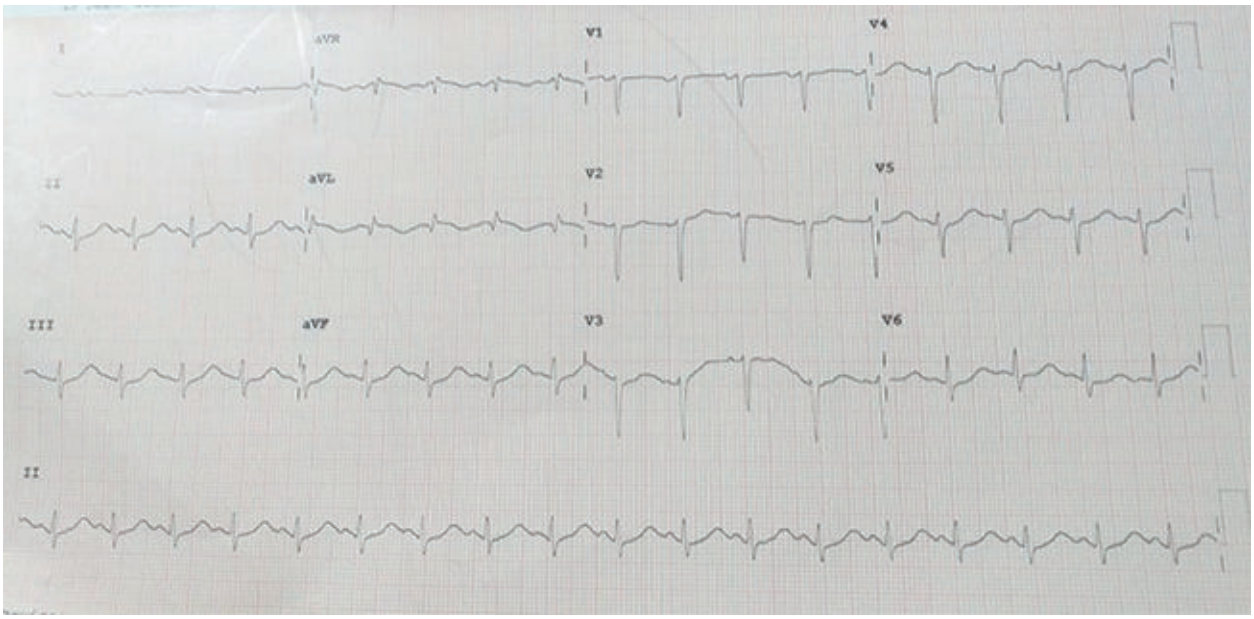


**Fig.-1:** *Showing sinus tachycardia, poor progression of R wave.*

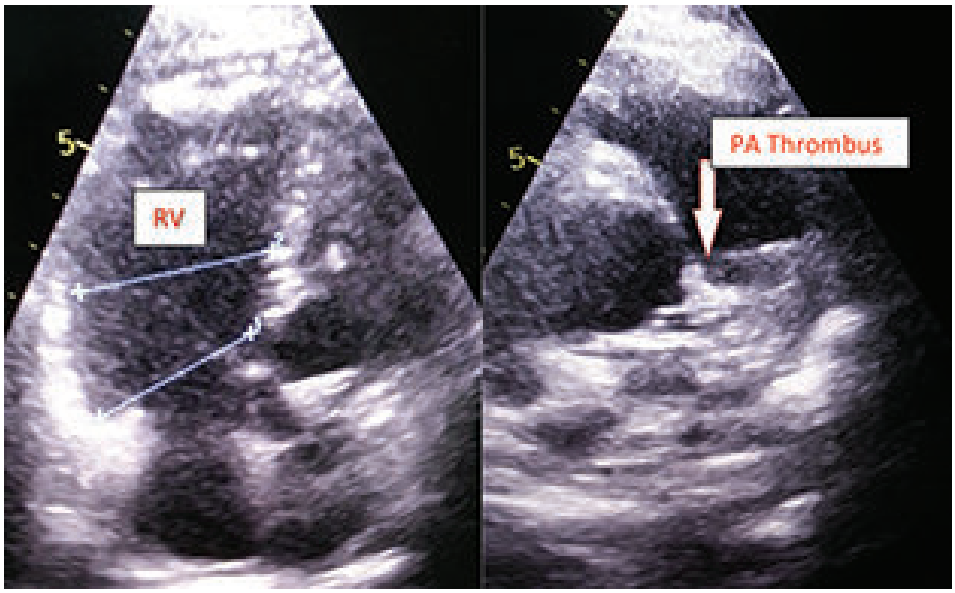


**Fig.-2:** *Trans thoracic echocardiogram RV focused and short axis view of PA showing dilated RV and thrombus.*

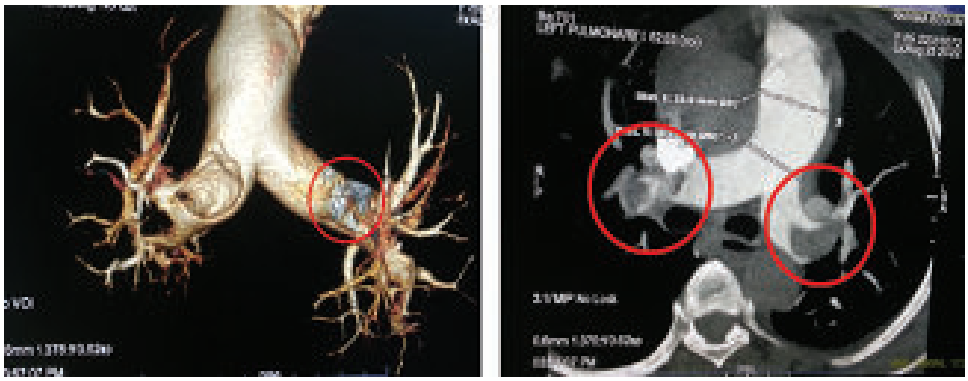

**Fig.-3:** *CT pulmonary angiogram showing multiple filling defects in both distal Right & Left pulmonary artery, lobar and segmental branches suggesting thrombus.*

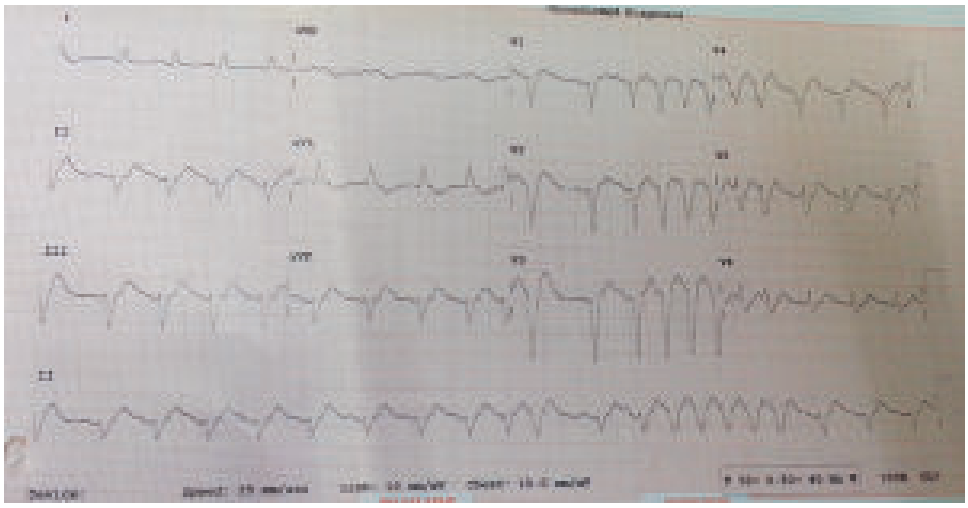

**Fig.-4:** *ECG after thrombolysis, showing Atrial fibrillation , HR 140 beats/min.*

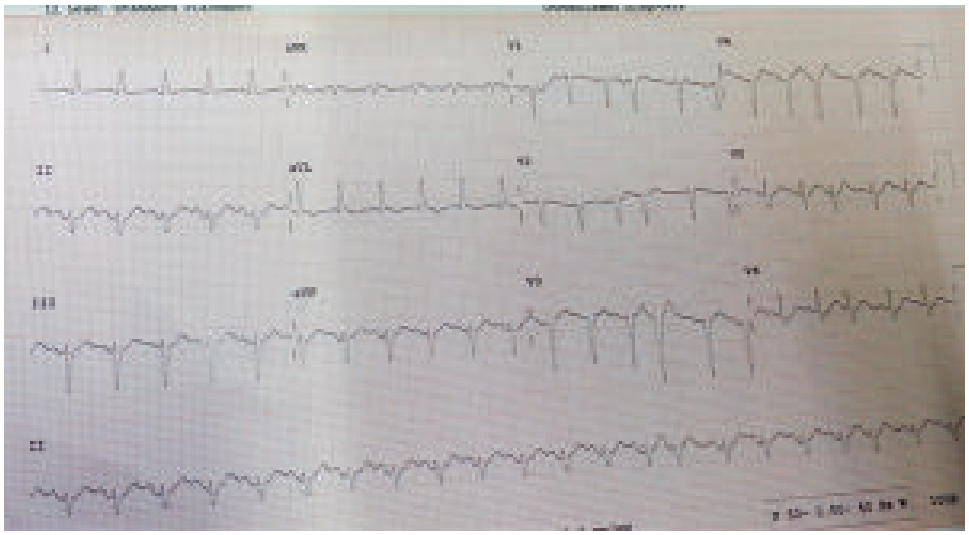

**Fig.-5:** *ECG during discharge sinus tacycardia, poor progression of R wave and SVE.*

**Discussion:**

This case of acute PE was presented with shock and followed by cardiorespiratory arrest is classified as high-risk pulmonary embolism as per European society of cardiology [2] and massive PE according to American heart association (AHA).[13] The ESC defines acute high-risk PE with persistent hypotension (systolic BP <90 mmHg, or systolic BP drop e"40 mmHg, lasting longer than 15 minutes and not caused by new onset arrhythmia, hypovolemia or sepsis or LV dysfunction).

Emergency multi-detector CTPA should be performed in hemodynamically unstable patients who are hypotensive or in shock because it allows adequate visualization of the pulmonary arteries down to the sub segmental level and it has 97% sensitivity for detecting emboli in the main pulmonary artery.[2, 8] If unavailable without delay, echocardiography should be performed to confirm the presence of right ventricular dysfunction.[8]

Echocardiographic features of RV dysfunction such as RV dilatation (without hypertrophy), paradoxical septal systolic motion and pulmonary hypertension are independent predictive factors of adverse outcome in acute PE.[14] It can also detect right heart & pulmonary artery thrombus which is a marker of worse prognosis with a prevalence of 4% to18% in the setting of an acute PE [15] and those more hemodynamically compromised.[7, 8]

Elevated D-dimer which have a high negative predictive value, can be used for immediate risk stratification [2, 13, 16] which increased in the short-term risk of death from PE. A normal D-dimer level renders acute PE or DVT unlikely.[2] Elevation of cardiac troponin I or T indicated increased mortality and risk of complication.[16]

Risk stratification of patients with acute PE is mandatory for determining the appropriate therapeutic management. Initial risk stratification is based on clinical symptoms and signs of hemodynamic instability, which indicate a high risk of early death.[2] Remaining group of patients with PE without hemodynamic instability, further risk stratification requires to assess the prognostic criteria, namely clinical imaging and laboratory indicators of PE severity. This is related to the presence of RV dysfunction, presence of comorbidity and any other aggravating conditions that may adversely affect early prognosis. Of the clinical scores integrating PE severity and comorbidity, the pulmonary embolism severity index (PESI) score is the one most extensively validated to date.[2] our patient had a pulmonary embolism severity index (PESI) score of 134, putting her in class-V with 30 day very high mortality risk of (10.0-24.5%) [2] and warranting primary reperfusion.[2] Pulmonary embolism severity index (PESI) scores used to estimate 30 day mortality and also be used as a tool to determine who can be safely managed as an outpatient and who should be considered for admission.[17]

Thrombolytic treatment accelerates the dissolution of thrombus in acute PE and is potentially lifesaving. In critically ill patients where patient transport for CT is unsafe or unfeasible, thrombolysis should be considered in case of unequivocal signs of RV overload on bedside echocardiography has been associated with increased mortality in PE and multidetector CT should be performed later when the patient's condition has been stabilized and the patients can be moved safely.[8]

There are three thrombolytic regimens approved for the treatment of PE by the food and drug administration (FDA): streptokinase, urokinase and alteplase, with alteplase being explicitly identified as the agent indicated with a reduction in mortality among hemodynamically unstable patients with PE and This leads to a prompt reduction in pulmonary artery pressure and resistance, with a concomitant improvement of RV function and preventing of PE recurrence.[13] A meta-analysis and systemic review done by Zhu Zhang et al.,[21] showed a total of six studies , with four randomized controlled trials (RCTs) and two cohort studies were included out of the 160 studies reviewed. For patients with high-risk PE, tenecteplase increased 30 day survival rate (16% vs. 6%, P=0.005) and did not increase the incidence of bleeding (6% vs. 5%; P=0.73). For patients with intermediate-risk PE, suggested that tenecteplase reduce RV insufficiency at 24 hour early in the onset and the incidence of hemodynamic failure without affecting mortality in a short /long term [<30 days RR=0.83, 95% CI(0.47,1.46); e"30 days RR=1.04, 95% CI (0.88, 1.22)]. However tenecteplase was associated with high bleeding risk [<30 days RR=1.79, 95% CI (1.61, 2.00);e"30 days RR=1.28, 95% CI (0.62, 2.64)]. Tenecteplase may represent a promising candidate for patients with high-risk PE. But tenecteplase is not recommended for patients with intermediate-risk PE because of high bleeding risk. LMWH +tenecteplase at 3-month follow-up showed a better prognosis, quality of life, and functional capacity.[18] In whom thrombolysis has failed or is absolutely contraindicated surgical embolectomy can be a lifesaving treatment option. Catheter based embolectomy is reserved for cases in which thrombolysis and surgical embolectomy is not possible.[19]

As patients with acute pulmonary embolism are the risk for recurrent thromboembolism they should be given long term anticoagulation. The recommendation for PE secondary to a reversible risk factor is therapy with vit K antagonist for 3 months, titrated to a target INR of 2.0 to 3.0.[2, 8] Novel oral anticoagulation (NOACs) I.e. Debigatran, rivaroxaban, apixaban are as effective and safe as warfarin for the treatment of venous thromboembolism.[2, 8, 13] The Anti-Clot Treatment Scale (ACTS): rivaroxaban treatment was reported to result in improved treatment satisfaction compared with enoxaparin/VKA, particularly by reducing the patient-reported anticoagulation burden.[20]

Follow-up of patients is important due to implications of long term anticoagulation and the probability of chronic thromboembolic pulmonary hypertension after or acute PE, the incidence of which up to 3.8% two years after the acute events.[4]

**Conclusion:**

Acute high-risk pulmonary embolism can present with hemodynamic instability and RV dysfunction in predisposed patients. Pulmonary artery thrombus, although common, therefore, prompt diagnosis by confirmation with appropriate imaging techniques and rapid decision to thrombolysis such cases can be life- saving. Tenecteplase may represent a promising candidate for patients with high-risk PE. More large scale studies focused on tenecteplase are needed for PE patients.

**Conflict of interest:** None

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*Case Report*

# Cardiac Resynchronization Therapy in Anomalous Coronary Sinus: A Case Report

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**Abstract:**

**A 37-year-old man, a known case of Dilated Cardiomyopathy (DCM) with Post PPM (Permanent Pacemaker) status for last 3 years underwent upgrading of PPM to Cardiac Resynchronization Therapy Pacemaker (CRT-P) in a specialized cardiac center. During the implantation procedure, there was anomalous branching of coronary sinus with absence of lateral branch & presence of a highly tortuous posterior branch causing difficulty in lead placement. Finally left ventricular (LV) lead was placed in the tortuous branch using Judkin's right catheter. Lead position was stable with excellent threshold. The patient has been followed up with improvement of symptoms.**

*Key words: CRT-P, PPM, Coronary Sinus, DCM*

*(Bangladesh Heart Journal 2023; 38(2): 155-157)*



**Introduction:**

Cardiac resynchronization therapy (CRT), via atrial-synchronous biventricular pacing, is an effective treatment for moderate to severe heart failure (HF) patients having ventricular dyssynchrony. Following CRT implantation, patients have been observed to have significant improvement of symptom, exercise capacity, along with quality of life.[1] CRT is shown to improve ventricular systolic function, decrease functional mitral regurgitation, and induce favorable remodeling with reduction of cardiac chamber dimensions by modification of ventricular electromechanical delay.[2, 3 & 4] Meta-analyses of clinical experiences and larger subsequent trials of CRT confirmed an approximately 30% decrease in hospitalizations and a mortality rate benefit of 24% to 36%.[5] To maximize the benefit of CRT, careful patient selection is mandatory along with proper positioning of the implanted leads. The LV lead in coronary sinus should be placed in a location so that it can stimulate the entire left ventricle. The posterolateral region of left ventricle shows the maximum contractile delay. Thus studies have shown the posterolateral region as the ideal position for stimulation. Problems may be encountered during LV lead placement in a small number of patients e.g., absence of suitable vein, venous tortuosity, unfavorable angle of the vein or a small vein/ atretic vein.[6] We report a case of anomalous coronary sinus with absence of lateral vein. Thus left ventricular lead implantation was done in highly tortuous posterior branch.

**Case presentation:**

A 37-year-old male presented with DCM with implantation of PPM 3 years back. Permanent pacemaker was implanted due to complete heart block. He was on maximally tolerated medical treatment for heart failure with partial improvement of symptoms. ECG showed pacing ECG with a wide QRS complex (184 milliseconds) associated with left bundle branch block and extreme left axis deviation. His echocardiography revealed

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*Doi: https://doi.org/10.3329/bhj.v38i2.70279*

moderate left ventricular dysfunction with ejection fraction of 35%. His coronary angiogram (CAG) revealed normal coronary arteries. Based on his ECG findings, refractory heart failure on optimal medical treatment and moderate left ventricular dysfunction with recurrent hospitalization, he was advised upgrading of his PPM to CRT-P.

**Clinical Status during PPM Implantation**

| | |
|---|---|
| NYHA class | II |
| ECG | CHB, Ventricular escape |
| Echocardiography | Mild LV systolic dysfunction with EF: 45% |
| Indication of PPM | Class I |

**Clinical Status during CRT Implantation**

| | |
|---|---|
| NYHA class | IV |
| ECG | Dual chamber paced rhythm, LBBB morphology |
| Echocardiography | EF: 35%, LVIDd: 58mm |
| CAG | Normal Coronaries |
| Indication of CRT | Class I |

In this case, RA & RV lead was already placed. Only LV lead implantation was required for bi-ventricular (Bi-V) pacing. Coronary sinus was engaged with 5F EP catheter and subsequently a 7F MB2 delivery sheath was advanced deep into the body of the coronary sinus. Venography was done in LAO 30° and RAO 30° views which revealed absence of lateral vein. A 0.014 inch extra support BMW coronary guide wire with LV lead was attempted to be negotiated over this wire. However, due to extreme tortuosity and multiple angulations of the vein, the lead could not be advanced to the posterolateral site despite several attempts. Then 5F guide catheter was passed over the wire into posterior vein but LV lead negotiation into the vein was not possible. Finally, 5F Judkin's Right catheter over the PTCA wire was introduced in the tortuous posterior vein which crossed the angulation & LV lead was placed at the desired location with good lead stability and pacing parameters (Figure 2). ECG after CRT-P showed narrow QRS. In-hospital stay of the patient was uneventful and he was discharged after five days. On follow-up after 3 months, the patient showed functional improvement to NYHA Class II and an improved LVEF of around 40% on Echocardiography. Three months after the procedure, chest X-Ray P/A view showed stable LV lead position with excellent parameters.

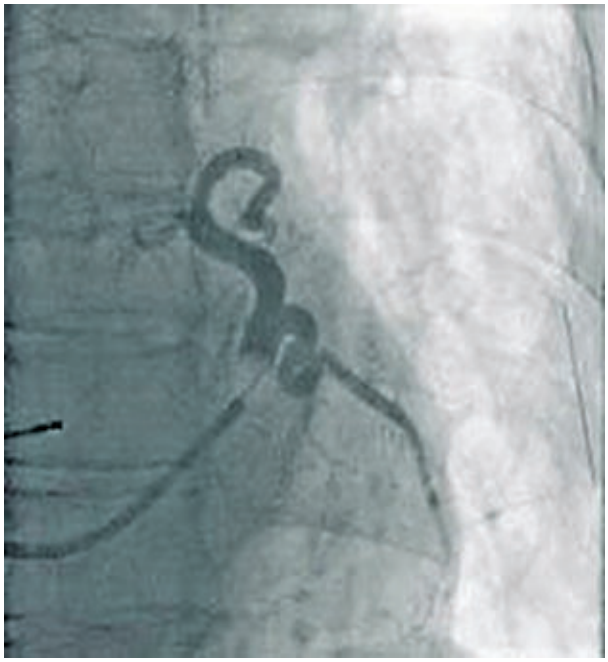

**Fig.-1:** *CS venogram*

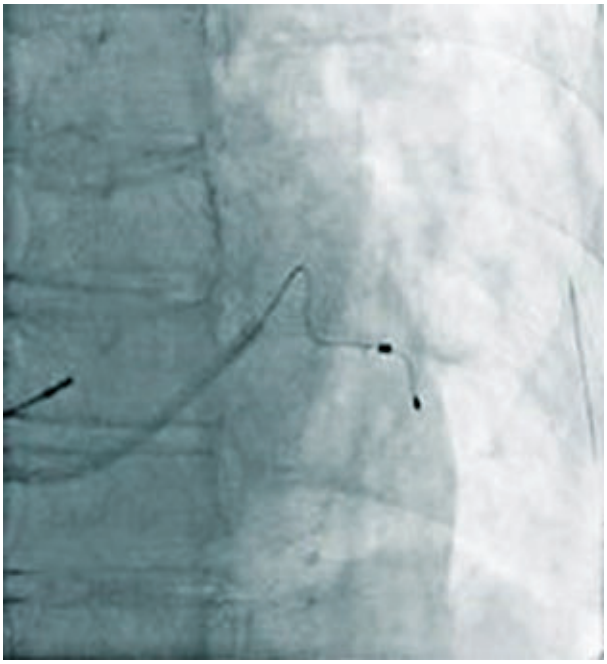

**Fig.-2:** *LV lead*

**Discussion:**

Heart failure (HF) is associated with substantial mortality and morbidity and remains the most common hospital discharge diagnosis in patients e"65 years of age.[7] Development of HF is characterized by progressive left ventricular (LV) remodeling and deteriorating function. Cardiac resynchronization therapy (CRT) is now established as an effective treatment for moderate-to-severe HF patients having ventricular dyssynchrony. Still some of the patients do not show expected response following CRT implantation. One of the major determinants of CRT response is implantation of the left ventricular (LV) pacing lead in coronary sinus.[8] The final positioning of LV pacing lead is crucial for proper activation of left ventricle in order to obtain effective resynchronization. Due to the highly variable anatomy of the coronary sinus and its tributaries, LV lead placement has several challenging technical issues. Thus the observed heterogeneity of response even among those who would appear to be excellent candidates for CRT may result from suboptimal lead location.[9]

The abnormal anatomy of coronary sinus includes congenital presence of Thebesian, Vieussens valves, acute angle of the vein, excessive tortuosity, small size of the vein, epicardial course of the vein or coronary sinus stenosis.[10]

Successful lead placements using various modified techniques are described. The buddy wire technique is one of them. Yoshimitsu Soga et al. have described a case of an obstructed coronary sinus where LV lead placement was done through a collateral pathway.[11] William G. De Voogt et al have also reported a case using a collateral branch for LV lead re-implantation.[12] Another case report described use of the double-wire technique (a second parallel guidewire) as effective way of implanting left ventricular electrodes in patients with anatomical difficulties.[13] Harinder K. Bali et al described a case of CRT implantation where left ventricular lead implantation was done using anterolateral vein where middle cardiac vein was functionally occluded.[14]

In our case, multiple attempts & techniques were required to place LV lead in the highly tortuous posterior vein for optimum lead position, stability & pacing thresholds.

**Conclusion:**

We report this case as there are few case reports regarding abnormal anatomy of coronary sinus & technique required to place LV leads. We also recommend for further studies regarding this topic.

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