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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.

Review Articles:

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.

Case Reports:

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.

D. Editorial Process

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 (except in abstract or poster form) and are not under consideration by another publication or electronic medium. Statements and opinions expressed in the articles published in the Journal are those of the authors and not necessarily of the Editor. Neither the Editor nor the Publisher guarantees, warrants, or endorses any product or service advertised in the Journal. Bangladesh Heart Journal follows the guidelines on editorial independence produced by the International Committee of Medical Journal Editors (ICMJE). All manuscripts correctly submitted to the Bangladesh Heart Journal are first reviewed by the Editors. Manuscripts are evaluated according to their scientific merit, originality, validity of the material presented and readability. Some manuscripts are returned back to the authors at this stage if the paper is deemed inappropriate for publication in the Bangladesh Heart Journal, if the paper does not meet the submission requirements, or if the paper is not deemed to have a sufficiently high priority. All papers considered suitable by the Editors for progress further in the review process, undergo peer review by at least two reviewers. If there is any gross discrepancy between the comments of two reviewers, it is sent to a third reviewer. Peer reviewers' identities are kept confidential; authors' identities are also not disclosed to the reviewers. Accepted articles are edited, without altering the meaning, to improve clarity and understanding. Decision about provisional or final acceptance is communicated within 8 weeks.

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)
2. Statement that the material has not been previously published or submitted elsewhere for publication (this restriction does not apply to abstracts published in connection with scientific meetings.)
3. Transfer of copyright to the Bangladesh Heart Journal upon the acceptance of the manuscript for publication
4. All authors have reviewed the article and agree with its contents
5. Information of any conflicts of interest (of any) of the authors.
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.

F. Manuscript Preparation

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.
- Author names and affiliations. Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower case superscript letter immediately after the author's name and in front of the appropriate address. Provide the e-mail address of each author.
- 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.

b. Abstract

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

Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI. Generic rather than trade names of drugs should be used.

g. Figures and graphics

- For graphics, a digital picture of 300 dpi or higher resolution in JPEG or TIFF format should be submitted.
- Figures should be numbered consecutively according to the order in which they have been first cited in the text, if there is more than 1 figure. Each figure should be cited in the text.
- Each figure/illustration should be provided with a suitable legend that includes enough information to permit its interpretation without reference to the text.
- All photomicrographs should indicate the magnification of the prints.
- When symbols, arrows, numbers or letters are used to identify parts of the illustrations, each one should be explained clearly in the legend.

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.htmArticle

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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Email: bangladeshheartj@yahoo.com

Editorial

Cardiology in the Post-Genomic Era : Road to Personalized Medicine

Zahurul A. Bhuiyan

(Bangladesh Heart Journal 2017; 32(1) : 1-2)

Synchronous action potential of cardiomyocytes lead to rhythmic contraction of the heart. Cardiac action potential is generated by interplay of wide range of cardiac ion channels e.g. Na^+, K^+ and Ca^{++} ion channels.[1] Each ion channel has different functional subunits, which are subdivided in functional domains. Ion channels are supported by different supporting structures, molecules and chaperones, which are required for proper localization of the ion channels and also for their well coordinated function. Cardiac action potentials are propagated from one cardiac cell to its neigbourng cells through the gap junctions located in the intercalated discs. Cardiomyocytes are attached to each other by desmosomal proteins e.g. plakophillin (PKP2), plakoglobin (JUP), desmoglein (DSG2) etc (Bhuiyan et al. 2009).[1] Cardiac sarcomeric proteins are the contractile machineries, which are located inside the cardiomyocytes ; action-potential generated currents lead to contraction of these sarcomeric machineries. All these components in the heart are encoded by a long list of genes ; widely investigated major genes in this list are cardiac Na^+ channel encoding *SCN5A*, K^+ channel encoding *KCNQ1* and *KCNH2*, Ca^{++} channel associated genes *RYR2*, *CASQ2*, *CACNA1C*, *Calm1*, *Calm2*, *Calm3*, and desmosomal proteins encoding genes, *PKP2*, *JUP*, *DSG2*, *TMEM43* etc. Defect (mutation) in these genes are widely known to cause various hereditary cardiac disorders e.g. long and short QT syndromes, Brugada syndrome, Catecholaminergic polymorphic ventricular tachycardia, Arrhythmogenic right ventricular cardiomyopathy/dysplasia, etc.[1] Defects in the cardiac sarcomeric and associated genes e.g. MYBPC3, MYH7, TTN are causal to Hypertrophic and/or Dilated cardiomyopathies.

Address of Correspondence: Zahurul A. Bhuiyan, MBBS, Ph.D, FESC, Head of the Molecular Diagnostic Laboratory, Division of Genetic Medicine, University Hospital Lausanne (CHUV), Lausanne, Switzerland. Email : Z.A.Bhuiyan@CHUV.CH

Structural or non-genetic heart diseases are the predominant cardiac diseases. Ischemic cardiopathy, the more prevalent structural heart disease, is predominantly non-genetic in origin, though individual genetic makeup are considered to play a role in ischemic heart diseases and arrhythmias.[2] Until now these two entities, non-genetic and genetic heart diseases, were kept and dealt separately. Arrhythmias due to genetic defects are causal to specific primary arrhythmias and these diseases are usually familial.[1] In case of primary familial arrhythmias, a genetic defect is usually found in about 70% of patients ; treatment usually depends on the involved gene, mutation location and pathology, family history for the disease, history of syncope, etc.[1] Primary arrhythmia patients usually have no structural heart abnormality : their defect is predominantly in the electrical properties of the heart, which can't be visualized.

But, what we are missing here, is how to deal with a patient who has ischemic heart disease compounded by mutation in a cardiac ion channel gene. Do we know how such a ion channel gene mutation could modify the disease profile in a patient with ischemic heart disease ? Mutation in two different genes are also found in 5-10% of patients with genetic heart diseases, and which could aggravate or worsen the disease.[1] This is not restricted to disease causal pathogenic mutation only as recent studies showed that individual genetic profile could exacerbate post-ischemic arrhythmias.[3] A team led by Prof. Peter J Schwartz conducted a study on patients admitted with myocardial infarction ; their team searched for common variations (polymorphism) in the cardiac repolarization ion channel gene *KCNH2* and investigated their effect on arrhythmia propensity in the subacute phase of myocardial infarction.[3] K897T is a common variation or polymorphism in the *KCNH2* gene : 80% of general population has lysine (K) in the 897th amino-acid position of the *KCNH2* gene, whereas 20-30% population has

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threonine (T) instead of lysine (K). They showed that patients with threonine (T) in 897th position are more prone to develop post-ischemic arrhythmias than those with lysine in that position.[3]

We know that S1103Y is a common variant/polymorphism in *SCN5A* gene in African poulation : individuals who have tyrosine (Y) in the 1103rd position of SCN5A protein are susceptible to develop arrhythmia which can lead finally to sudden cardiac death.[4] *KCNE1* gene encodes for the b-subunit of repolarization curent I_{ks} (encoded by KCNQ1) ; D85N in *KCNE1* is a common variant in Japanese population and individuals with Asparagine (N) at 85th position of *KCNE1* gene are susceptible to drug induced arrhythmia.[5] These studies were conducted mostly in conjunction to genetic heart dieases i.e in patients with primary arrhythmias. But, how would we deal with a patient suffering from potentially dangereous arrhythmias secondary to ischemia or other structural heart diseases ? In addition he /she has single or multiple genetic variants that may influence the disease, positively or negatively. What about the genetic variants with a protective effect that rather attenuates or helps to retard developpement of disease pathology ? What about variants in the drug metabolizing genes acting on cardiac cells, what about the genes and variants that work for ATP generation in heart or during adrenaline induced phosphorylation of I_{ks}?

In the post genomic era, human genome sequence is an open book now as we can sequence the genome of a patient in less than a week. Highthrougput gene sequencing is pretty affordable: whole exome sequencing i.e. DNA sequencing of all the known genes present in a man could be done only with 1000 US Dollar. Intepretation of the genomic data is also becoming less tedious. Studies are now required to look at the combined effect of the genetic and non-genetic aspects of the arrrhythmias. In 10 yrs span to time, we will discover many component of genetics that influences the cardiac diseases, their pathology and evolution. Patients with certain genetic profiles are expected to be more arrhythmia prone than others with different genetic profile or reverse. Individual genetic and epigenetic makeup (imprinting) will be evaluated while consulting a patient. Further, at present, drug treatment for arrhythmia is primarily focused to relieve symptoms and lower the risk of sudden cardiac death, or is targeted to few ion channels or receptors ; present therapy does not target the molecular basis for arrhythmogenesis in an individual patient.

Precise genetic data will lead to the development of individually adapted, targeted therapy for arryhthmia treatment, focused to personalized needs. One such example is excessive SCN5A derived Na^+ causing long QT syndrome type 3 : a drug (e.g. Mexiletine) that reduces this excessive Na^+ in heart would treat the exact pathology and thereby treat the disease by eliminating the pathology process.[6] Similarly cellular loss or diminution of K^+ causes long QT syndrome : a drug that targets the cardiac K^+ channels and normalizes their property will be effective in treating long QT syndrome caused by reduced K^+ current in the heart.

So, it is imperative that we are proceeding toward a new direction in personalized medicine. Individual genetic profile will be necessary to evaluate each patient and his/her disease. All future cardiologists will be required to have an excellent understanding about genetics in their bedside medicine practice. We are on the road to a new era of personalized genomic medicine.

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1. Bhuiyan Z.A. Clinical and genetic spectrum of hereditary cardiac arrhythmia syndromes. Ph.D thesis. University of Amsterdam. ISBN: 9789090243184.
2. Bezzina CR, Pazoki R, Bardai A, Marsman RF, de Jong JS, Blom MT, et al.Genome-wide association study identifies a susceptibility locus at 21q21 for ventricular fibrillation in acute myocardial infarction. Nat Genet. 2010;42:688-91.
3. Crotti L, Hu D, Barajas-Martinez H, De Ferrari GM, Oliva A, Insolia R, et al. Torsades de pointes following acute myocardial infarction: Evidence for a deadly link with a common genetic variant. Heart Rhythm. 2012;9:1104-12.
4. Plant LD, Bowers PN, Liu Q, Morgan T, Zhang T, State MW, et al. Common Cardiac Sodium Channel Variant Associated With Sudden Infant Death in African Americans, SCN5A S1103Y. J Clin Invest. 2006; 116: 430–5.
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Original Article

Association between Peripheral Arterial Disease and Coronary Artery Disease among Tobacco User Diabetic Patients

Syed Dawood Md. Taimur[1], M Maksumul Haq[2], MA Rashid[3] SM Keramat Ali[4], Md. Shahjahan[5], Farzana Islam[6]

Abstract:

Background: Peripheral arterial disease (PAD) is a marker of increased risk for cardiovascular events and of poorer prognosis in patients with coronary artery disease (CAD). The prevalence of unknown PAD amongst patients with ACS varies between studies according to the mode of diagnosis.

Aims: To evaluate the prevalence of peripheral arterial disease (PAD) in diabetic ACS patients with or without tobacco user by using ankle brachial index (ABI).We also assess the probable predictors of PAD among these patients.

Methodology: This prospective observational study was conducted in the Department of Cardiology, Ibrahim Cardiac Hospital and Research Institute, Dhaka, Bangladesh starting from 1st January 2016 to 30th April 2016 over a period of four months. A total of 60 patients were studied. They were grouped on the basis of their smoking habit. Diabetic patients with ACS and tobacco user (smoke and smoke less) in group I and without tobacco user in group II.

Results: The mean age of the studied patients was 56.63 ± 8.95 years, range from 25-90 years. 73.30% was male and 26.70% was female. Twenty three patients of tobacco user in group-I (n=30) had peripheral artery disease and ten patients of group-II (n=30) had peripheral artery disease. It was statistically significant (p=0.003).

Conclusion: There is correlation between peripheral arterial disease and coronary artery disease. Diagnosis and supervision of patients with PAD is important for preventing the local progression of the disease and effective secondary prevention of future coronary and cerebrovascular events.

Key Words: Peripheral artery disease; Acute coronary syndrome; Coronary artery disease; Tobacco.

(Bangladesh Heart Journal 2017; 32(1) : 3-9)

Introduction:

Peripheral arterial disease is considered to be a set of chronic or acute syndromes, generally derived from the presence of occlusive arterial disease, which cause inadequate blood flow to the limbs. On most occasions, the underlying disease process is arteriosclerotic in nature , mainly affecting the blood supply to the lower limbs. From the physiologic point of view, ischemia of the lower limbs can be classified as functional or critical. Functional ischemia occurs when the blood flow is normal at rest but insufficient during exercise, presenting clinically as intermittent claudication. Critical ischemia is produced when the reduction in blood flow results in a perfusion deficit at rest and is defined by the presence of pain at rest or trophic lesions in the legs. In this situation, precise diagnosis is fundamental, as there exist a clear risk of loss of the limb if adequate blood flow is not reestablished, either by surgery or by endovascular therapy.

PAD is a common disorder but because it is not directly life-threatening, it has not received the same degree of attention or research as coronary heart disease. But PAD

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may be a precursor of coronary heart disease since people with narrowed peripheral arteries are also more likely to have a narrowing of the coronary arteries. PAD mostly occurs in the elderly. In the United Kingdom around 1 in 5 men and 1 in 8 women aged 50-75 years have PAD[1]. PAD affects 8 to 10 million individuals in the United States[2,3] and is associated with reduced functional capacity[4-6] and increased risk for cardiovascular morbidity and mortality[7,8]. About half of all people with PAD have no obvious symptoms and the first indication of peripheral arterial disease may be a coronary artery disease or cerebrovascular accident[1]. Approximately one third of patients diagnosed with PAD will die within five years and about one half die within ten years, primarily due to a coronary artery disease or cerebrovascular accident[1].

Peripheral arterial disease (PAD) is one of the macrovascular complications of type 2 diabetes mellitus. Distribution of atheroma is widespread but patchy. Peripherally it effect femoro-popliteal segment, distal aorta and iliac arteries and lower leg arteries with a tendency to spare the profunda femoris beyond its origin of distal popliteal artery[9]. As global patterns in tobacco use changes, the burden of death can be expected to shift dramatically from the developed world to less wealthy countries. It has been estimated that over the next two decades, 70% of tobacco deaths will be in developing countries[10]. About 80% of the world's smokers now live in low and middle income countries, at least in part due to a lack of adequate tobacco controls[11]. In Bangladesh 43.3% of adults (41.3 million) currently use tobacco in smoking or smokeless form. Among them 26.4% of men, 28% of women and 27.2% overall (25.9 million adults) currently use smokeless tobacco[12] in different form like jorda, gul, hooka etc.

The most effective treatment for PAD is to stop tobacco use. This single measure reduces the risk of disease progression amongst patients with peripheral arterial disease and dramatically reduces the need for limb amputation and the risk of premature death.

Methodology:

Study population and design

This prospective observational study was conducted in the Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Dhaka for a period of 4 months starting from January, 2016 to April, 2016. A total of 60 ACS patients who were diabetic with and without tobacco user followed up during hospital period. Patients were categorized into two groups on the basis of tobacco use. Group I (diabetic ACS with tobacco user) had 30 patients and Group II (diabetic ACS without tobacco user) had 30 patients.

Diagnostic criteria

Cardiovascular risk factors

Subjects were defined as having hypertension if they were taking an anti-hypertensive agent, had been clinically diagnosed with hypertension (HTN), or had either a systolic blood pressure (SBP) ≥140 mm Hg or a diastolic blood pressure (DBP) ≥90 mm Hg. Subjects were defined to have dyslipidaemia if they met one of the following requirements: diagnosis of hyper-cholesterolemia or a medication history of hyper-cholesterolemia or Total Cholesterol >200 mg/dL or LDL-C >130 mg/dL. The following body mass index (BMI) categories were recognized: normal (18.5≤BMI<24.9), overweight (25≤BMI<30) and obese (BMI≥30). A patient who had smoked within a year prior to the study was defined as a smoker.

Ankle Brachial Index

The ankle-brachial pressure index (ABPI) or ankle-brachial index (ABI) is the ratio of the blood pressure at the ankle to the blood pressure in the upper arm (brachium). Compared to the arm, lower blood pressure in the leg is an indication of blocked arteries due to peripheral artery disease (PAD). The ABPI is calculated by dividing the systolic blood pressure at the ankle by the systolic blood pressure in the arm[13].

$$ABPI_{Leg} = \frac{P_{Leg}}{P_{Arm}}$$

Where P_{Leg} is the systolic blood pressure of dorsalis pedis or posterior tibial arteries

And P_{Arm} is the highest of the left and right arm brachial systolic blood pressure

The ABPI test is a popular tool for the non-invasive assessment of PVD. Studies have shown the sensitivity of ABPI is 90% with a corresponding 98% specificity for detecting hemodynamically significant (Serious) stenosis >50% in major leg arteries, defined by angiogram[14]. ABPI value of under 0.50,is considered as severe arterial disease[15].

Statistical analysis

The age and gender differences and hypertension, diabetes, dyslipidaemia, smoking habit, family history of IHD,CKD, peripheral artery and coronary artery profile were statistically analyzed to find if they influenced in any way the incidence of standard deviation (SD). Data were entered in computer using SPSS for windows version 16.0 (SPSS Inc., Chicago, IL). Results were cross-

tabulated to find out the relationships between the variables. Statistical analysis was performed using χ^2-square for test of association and Fisher's exact test as appropriate. A p-value of less than 0.05 was considered significant in all statistical analysis.

Result:

Mean age of group I patients were 55.57±9.601 years and mean age of group II patients were 55.47±8.224 years. No significant difference was observed between the two groups (0.428). Among the group I highest number of patients (73.3%) were in age group 46-65 years followed by 25-45 years (16.7%). Among the patients of group II, highest number of patients (80%) in age group 46-65 years followed by age group of 66-75 years (16.5%). 93.33 % patients of group I was male and 6.67 percent was female where as in group- II 73.30 percent was male and 26.70 percent was female was observe.No statistically significant difference was observed the sex distribution of two groups (p=0.531) (Table-I).

Table-I

Age & Sex distribution of the group-I & II study population (n=30x2)

Age & Sex distribution	Group-I (n=30)	Group-II (n=30)	p-value
Age			
25-45 years	5(16.7)	1(3.3)	
46-65 years	22(73.3)	24(80.0)	
66-75 years	2(6.7)	5(16.5)	
76-90years	1(3.3)	0(0.0)	
Mean age	55.57±9.601	55.47±8.224	0.428 NS
Sex			
Male	28 (93.3)	22(73.3)	0.531 NS
Female	2(6.7)	8(26.7)	

NS=Non significant

Twenty three (76.7%) patients of group-I and twenty four (80%) patients of group-II had hypertension. There was no statistically significant difference in hypertension between the two groups (p=0.120).Twenty five (83.3%) patients of group-I and twenty four (80%) patients of group-II had dyslipidaemia. There was no statistically significant difference in dyslipidemia between the groups (p=0.254).Nineteen (63.3%) patients of group-I and twenty five (83.3%) patients of group-II had positive family history of IHD. There was statistically significant difference in positive family history between the groups (p=0.003).No statistically significant difference were observed between two groups of patients (p>0.05) regarding the risk factors like obesity (Table-II).

Table-II

Risk Factors of the study population

Risk Factors	Group-I (n=30) diabetic with tobacco user n(%)	Group-II (n=30) diabetic without tobacco user n(%)	p-value
Hypertension			
Present	23 (76.7)	24 (80)	0.120 NS
Absent	7(23.3)	6(20)	
Dyslipidaemia			
Present	25(83.3)	24 (80)	0.254 NS
Absent	5 (16.7)	6 (20)	
Family History			
Present	19(63.3)	25(83.3)	*0.003 S
Absent	11(36.7)	5(16.7)	
BMI (Obesity)			
Obese(30-34.9kg/m²)	5(16.7)	1(3.3)	0.093 NS
Overweight(25-29.9kg/m²)	12(40.0)	18 (60)	
Normal(18.5-24.9kg/m²)	13(43.3)	11(36.7)	

S= Significant ; NS=Not significant, *p value reached from χ^2 test, p value significant d"0.05

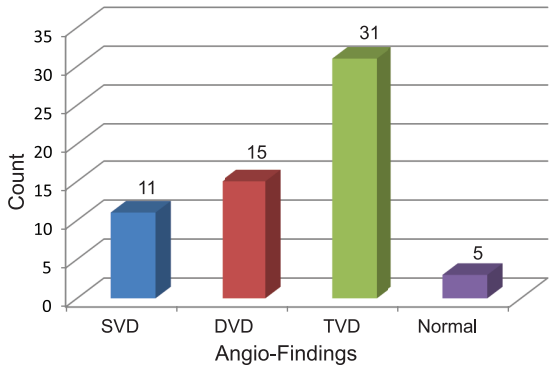

Fig.-1: *Coronary Angiogram findings of the study population (n=60).*

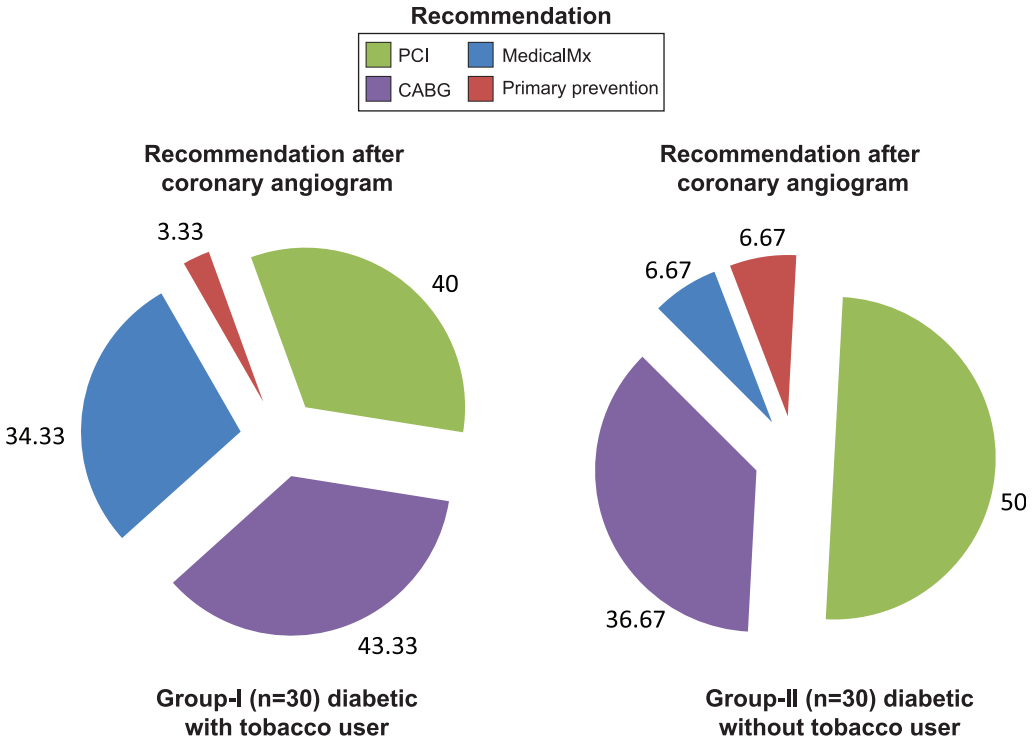

Fig.-2: *Recommendation after coronary angiogram*

Coronary angiogram findings of the study population revealed 31patients had triple vessel disease(TVD),15 patients had double vessel disease(DVD), 11 patients had single vessel disease(SVD) and rest of the patients had normal epicardial coronary arteies.(Fig:1)

After coronary angiogram 40% patients was recommended for PCI in group I and 50% patients was recommended for PCI in group II. 43.33% patients of group I was recommended for CABG and 36.7% patients of group II was recommended for CABG.13.34% patients of group I was recommended for medical management and 6.66% patients of group II was recommended for medical management. Rest of the patients of group I (3.3%) and group II (6.67%) were advised for primary prevention (Fig.-2).

80% patients of group I and 46.7% patients of group II had mild form of ABI value. 3.3% of group II patients had severe form of ABI value. There was no statistical significant difference between the two group of patients (p=0.053) (Table-III).

Table-III

The distribution of ankle brachial index values of both lower limbs and their relation to severity of peripheral artery disease.

Severity (ABI value)	Group-I (n=30) diabetic with tobacco user n(%)	Group-II (n=30) diabetic without tobacco user n(%)	p-value
Mild(0.80-0.89)	24(80%)	14(46.7%)	0.053 NS
Moderate(0.50-0.79)	0	0	
Severe(>0.50)	0	1(3.3%)	
Normal	6(20%)	15(50%)	

Over three quarters (76.7%) of group I patients developed PVD as compared to 33.3% of group II. The risk of developing PVD in diabetic smokers was observed to be more than 6 fold (95% CI: 2.109-20.479) higher than that in non diabetic tobacco user.(Table-4).

Twenty three patients of tobacco user group (n=30) had peripheral artery disease and ten patients of tobacco non user group (n=30) had peripheral artery disease which was statistically significant (p=0.003)(Table-5).

Table-IV

Association between Peripheral arterial disease and DM with or without tobacco user

PAD	DM with or without tobacco user		Odds Ratio	95% CI for OR	p- value	Fisher's Exact Test
	DM with tobacco user (Group I)	DM without tobacco user (Group II)				
Yes	23 (76.7%)	10 (33.3%)	6.571	2.109-20.479	0.001 S	0.002
No	7 (23.3%)	20 (66.7%)				

S= Significant, p value reach from χ^2 test, p value significant d"0.05
OR= Odds Ratio, CI=Confidence interval

Table-V

Association between tobacco use and peripheral artery disease

Tobacco Habit	PAD		p- value
	yes	no	
Smoking habit	18	6	*0.003 S
Smokeless tobacco	5	1	
Nonsmoker or without tobacco user	10	20	

S= Significant ; NS=Non significant
*p value reach from X^2 test, p value significant d"0.05

Thirty three (55%) patients had peripheral artery disease in study population (n=60) and fifty seven patients had coronary artery disease. Out of thirty three patients who had diagnosed PVD, thirty two patients had coronary artery disease which was not statistically significant (p=0.424)(Table-6).

Table-VI

Association between coronary artery disease and peripheral artery disease

	PVD	p value	Fisher's Exact Test	OR	95% CI for OR	
CAD	Yes	No	0.424 NS	0.583	2.560	0.219-29.869
Yes	32	25				
No	1	2				

S= Significant, p value reach from χ^2 test, p value significant $\leq$0.05
OR= Odds Ratio, CI=Confidence interval

Discussion:

The presence of peripheral arterial disease (PAD), even in the absence of overt coronary artery disease (CAD), confers the same relative risk of death from a cardiovascular cause as in patients with a previous cardiovascular event. The mean age of studied patients was 56.63±8.95 years. The commonest age group of study patients was 45-65 years in both groups (48.9% and 53.3 % in group I and group II respectively). Mean age difference was not statistically significant (p=0. 428). Nearly similar pattern of age distribution was reported by Sarangi S, et al.[16] in their study in India. This observation was being consistent with the findings of different studies done in different countries[17-19].

Out of sixty patients twenty three patients of tobacco user group I (n=30) and ten patients of tobacco non user group II (n=30) had peripheral artery disease which is statistically significant (p=0.003) between the two groups of patients. Univariate regression analysis of Gulf RACE 2009 revealed diabetes, family history of ischemic heart disease and tobacco use were independent variable for PAD(p=0.001). DM with tobacco user group showed strong association with PAD & adjusted odds ratio(OR) was 6.571 (CI 2.109-20.491). Out of 33(55%) patients who had PVD, coronary artery disease was found in 32 patients and it was statistically significant (p=.018). 80% male and 15% female had coronary artery disease, which was statistically insignificant. 51.3% male and 0.0332% female had peripheral artery disease which was statistically significant (p=0.018) and OR=6.526 (95%CI for OR 1.252-34.029) Sarangi S, et al.[16] and Al Thani, HA, et al.[20] was found statistically significant.

Various epidemiologic studies have shown that up to 50% of patients with PAD also have symptoms of cerebrovascular or heart disease[21]. In the PARTNERS study[22] of all the patients who were screened for vascular disease, only 13% had isolated PAD with no other manifestation of cardiovascular disease. Thirty two percent of the patients also had either coronary disease or cerebrovascular disease, and 24% had involvement in all 3 territories. The main cause of death in patients with PAD is ischemic heart disease (up to 50% of deaths in patients with PAD). Inversely, the prevalence of PAD in patients diagnosed with coronary disease reaches 30% [21]. The mortality in this group of patients is 2.5 times

greater than that of the group with no clinical symptoms of PAD.

In overall ACS and STEMI, patients with PAD developed worse in-hospital outcomes in terms of greater rate of death, heart failure, recurrent ischemia, stroke, and major bleeding when compared to their non-PAD counterparts. There was only one death in group who presented as STEMI and death due to ventricular septal rupture. Two patients of both groups was suffered acute left ventricular failure. Two patients of group I had diabetic foot ulcer due to peripheral artery disease. Significant difference was found in Al Thani HA, et al.[20].

Conclusion

Prevalence of PAD in ACS Bangladeshi population is low in comparison to western population.Certain traditional risk factors are independent predictors for PAD necessitates aggressive preventive measures. Screening with ABI would allow the identification of a subgroup of CAD patients at particularly high risk and who could benefit from an aggressive medical treatment strategy. Detection of PAD in ACS patients might be a useful simple bedside tool for early detection of the risk stratification.

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Original Article

Association of Increased $T_{peak\text{-}to\text{-}end}$/QT ratio with Malignant Ventricular Arrhythmias in Acute Anterior ST-Segment Elevation Myocardial Infarction

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Abstract::

Background: **Increased $T_{peak\text{-}to\text{-}end}$/QT ratio on 12 lead surface electrocardiogram (ECG) has been shown to be the predictor of arrhythmogenesis in various cardiac disorders. There is limited data regarding association of these two parameters with malignant ventricular arrhythmias (MVA) in acute ST-segment elevation myocardial infarction (STEMI) patients.** ***Objectives:*** **This study was conducted to evaluate association of increased $T_{peak\text{-}to\text{-}end}$/QT ratio with MVAs in acute anterior STEMI.** ***Methods:*** **178 patients with acute anterior STEMI admitted within 12 hours of onset of chest pain into the Coronary Care Unit, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, were enrolled from November 2015 to October 2016. $T_{peak\text{-}to\text{-}end}$/QT ratio was calculated from surface ECG at the time of admission. The patients were divided into two groups, group I and II according to normal (≤0.25) and increased $T_{peak\text{-}to\text{-}end}$/QT ratio (>0.25). Each group was monitored for development of MVAs for the first 48 hours of myocardial infarction.** ***Results:*** **MVAs were significantly higher in group II than group I (19.5% vs 3.1%, p<0.001). Multivariate regression analysis showed significant association (p=0.002) of increased $T_{peak\text{-}to\text{-}end}$/QT ratio with MVAs (Odds Ratio, 3.845).Receiver operating characteristic (ROC) curve analysis showed that $T_{peak\text{-}to\text{-}end}$/QT ratio <0.25 had a negative predictive value of 96.88% for the prediction of MVAs.** ***Conclusion:*** **The study demonstrated that there was significant association of increased $T_{peak\text{-}to\text{-}end}$/QT ratio with malignant ventricular arrhythmias in acute anterior STEMI patients. Thus analysis of 12 lead surface ECG on admission may help predict malignant ventricular arrhythmias in the first 48 hours of acute anterior myocardial infarction and close monitoring with prompt management may be ensured in high risk patients.**

Key words:Acute anterior ST-segment elevation myocardial infarction, malignant ventricular arrhythmia, $T_{peak\text{-}to\text{-}end}$/QT ratio.

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Introduction:

Sudden cardiac death (SCD) causes approximately 800,000 deaths each year in the world[1]. It is often the first manifestation and responsible for 50% of the mortality of cardiovascular disease[2]. It is often caused by malignant ventricular arrhythmias (MVA). Among patients admitted with acute ST-segment elevation myocardial infarction (STEMI), 2-20% suffer from MVAs during first few hours of a sustaining myocardial infarction (MI) [3, 4]. In most cases, MVAsconsist of ventricular fibrillation (VF), or less frequently, by monomorphic or polymorphic ventricular tachycardia (VT) and Torsades de Pointes[5].

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Anterior myocardial infarction (MI) carries the worst prognosis of all infarct locations, mostly due to larger infarct size. A study comparing outcomes from anterior and inferior MI found that on average, patients with anterior MI had higher incidences of in-hospital mortality (11.9 vs 2.8%), total mortality (27 vs 11%), heart failure (41 vs 15%) and significant ventricular ectopics (70 vs 59%) compared to patients with inferior MI[6].

Various electrocardiographic(ECG) indices have been proposed as risk predictors in patients with MI e.g. T wave alternans[7], heart rate (HR) turbulence[8], decreased HR variability[9], prolonged QT interval (QT), increased QT dispersion[10]. But these ECG markers have prognostic values usually 6-8 weeks after acute MI.

$T_{peak\text{-}to\text{-}end}$/QT ratio ($T_{p\text{-}e}$ /QT ratio) has been suggested as more accurate measure for the dispersion of ventricular repolarization compared to other parameters and is independent from heart rate alterations[11, 12]. This ratio is a novel index to predict cardiac arrhythmias[13]. It includes the values of transmural dispersion ($T_{p\text{-}e}$) and spatial dispersion (QT) of ventricular repolarization. $T_{p\text{-}e}$ /QT ratio measured in healthy population in precordial lead V6 which best reflects the trasmural axis of left ventricle has a mean value of 0.21 ±0.03 and a range of value from 0.15 to 0.25[11].

Increased $T_{p\text{-}e}$ /QT ratio represents a period of potential vulnerability to reentrant ventricular arrhythmias[14]. Underlying mechanisms to explain modification ofthis indicators in acute myocardial ischemia include an expression of cardiac M cells properties. Activation of Mcells determines an increase in the action potentialin the heart and subsequently QT interval and $T_{p\text{-}e}$ prolongation[15, 16, 17].Other proposed mechanisms arethe reduction in epicardial temperature[18], acidosis[19] and changes in sodium and potassium currents[20].

In the past years, some studies have shown $T_{p\text{-}e}$ /QT ratio as predictors of malignant ventricular arrhythmias in patients with ST-segment elevation myocardial infarction (STEMI)[21,22,23].

There is no data in our country regarding association of this ECG parameter with malignant arrhythmia in acute anterior STEMI setting till date.

Methods:

178 patients with acute anterior ST-segment elevation myocardial infarction (STEMI) admitted within 12 hours of onset of chest pain into the coronary care unit (CCU) of National Institute of Cardiovascular Diseases (NICVD), Dhaka and receiving thrombolyticswere studied from November 2015 to October 2016. Patients with prior MI, acute left ventricular failure and cardiogenic shock; valvular heart disease, congenital heart disease and cardiomyopathy; prior pacemaker implantation; previous

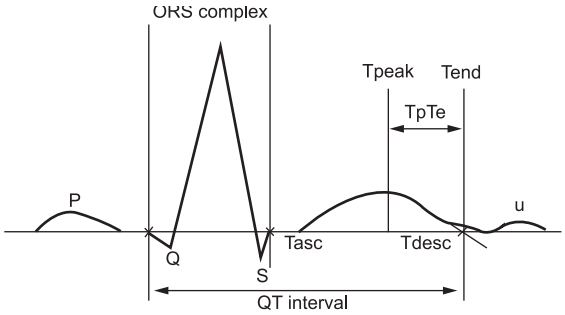


Fig.-1: *Electrocardiographic parameters measured when assessing the QT interval and $T_{p\text{-}e}$ interval*

history of any arrhythmias, abnormal electrolyte values, bundle branch block, patients on medications affecting QT and $T_{p\text{-}e}$ intervals such as antibiotics, tricyclic antidepressants, antihistaminics, antipsychotics and antiarrhythmics; family history of sudden cardiac death and ECGs without clearly analyzable $T_{p\text{-}e}$ interval and QT segment were excluded from the study. Study population were divided into two groups on the basis of $T_{p\text{-}e}$ /QT ratio: Group I: Normal $T_{p\text{-}e}$ /QT ratio &Group II: Increased $T_{p\text{-}e}$ /QT ratio. In the study, group I consisted of 96 subjects and group II consisted of 82 subjects.

Informed written consent and meticulous history were taken and detailed clinical examination was done and recorded in pre designed data collection sheet. Demographic data profile was recorded: age, sex. Cardiovascular risk factors were determined e.g. smoking, hypertension (HTN), diabetes mellitus (DM), dyslipidemia and family history of premature CAD. Clinical profile: pulse, blood pressure, respiratory rate, precordial examination findings were recorded. Baseline investigations like blood sugar, serum creatinine and serum electrolytes were done.

12 lead resting ECG was done at a paper speed of 25 mm/s and 10mm standardization on admission with subject in supine position by Fukuda Denshi Cardimax FX-2111 Electrocardiograph, Fukuda Denshi Co., Ltd., Japan.The resting heart rate was measured from the ECG data. ECG measurements of QT and $T_{p\text{-}e}$ intervals were performed manually by the investigator, using slide calipers and a magnifying glass to decrease measurement errors. In case of a difference of >20 ms in each measurement, an agreement was obtained after consulting an electrophysiologist who was blinded to the patients.The average value of three examinations was calculated.The QT interval was measured from the earliest onset of the QRS complex to the point at which the tangent of the maximal downslope of the descending limb of the T wave crossed the isoelectric baseline.

The QT interval was corrected for heart rate using Bazett's formula. The QT_{peak} (QT_p) interval was measured from the onset of the QRS complex until the maximal deflection

of the T wave. The T_{p-e} interval was calculated as the difference between the corresponding lead QT interval and the QT_p interval. The T_{p-e} /QT ratio was calculated as the ratio of T_{p-e} in that lead to the corrected QT interval.

If a U wave followed the T wave, the nadir between the T wave and the U wave was considered T-wave offset. The precordial lead V6 was selected because it best reflects the transmural axis of the left ventricle. If lead V6 was not suitable, leads V5 and V4 were measured. If the T-wave amplitude was < 1.5 mm in a particular lead, then that lead was excluded from the analysis. Increased T_{p-e} /QT ratio was defined as T_{p-e} /QT ratio ≥0.25.

The patients were followed up for the first 48 hours of MI with continuous monitoring in coronary care unit (CCU) & serial ECGs, for any development of malignant ventricular arrhythmias or symptoms. The continuous ECG monitorings of the study subjects were saved in the central monitoring system (model: Hypervisor VI, V-38108371, 2013-11, ver 1.3, Shenzhen Mindray Bio-Medical Electronics Co., Ltd., China). The recorded data was reviewed to note down any arrhythmic events. The patients were treated as per hospital protocol of treatment of acute STEMI.

The numerical data obtained from the study were analyzed and significance of differences were estimated by using statistical methods. The SPSS Statistical Software categorical (23.0 version, IBM SPSS Corporation, Armonk, New York, USA) was used for data analysis. Continuous variables were expressed in mean & standard deviation and categorical variables as frequency and percentage. Quantitative variables were analyzed by Student's t-test and Categorical variables were analyzed by Chi-square test and Fisher's exact test. Multiple logistic regression analysis was performed to establish T_{p-e} /QT ratio as the determinant of malignant ventricular arrhythmias. P value of less than 0.05 was considered as significant. Receiver operating characteristic (ROC) curve analysis was performed to assess sensitivity and specificity of T_{p-e} /QT ratio as a predictor of malignant ventricular arrhythmias.

Results:

Among 178 patients, 96 patients belonged to group-I and 82 patients belonged to group-II. The mean age of group I was 52.60±11.29 years and group II was 51.59±11.17 years. Male patients were predominant (80.2% vs 93.9%) in both groups. The highest percentage of study population had history of smoking (76% vs. 84%), followed by hypertension (47% vs. 48%), diabetes mellitus (38% vs. 28%), family history of premature CAD (29% vs 33%) and dyslipidemia (17% vs 18%) in group I and group II respectively. Among group I subjects, pulse was 86.61±12.49 beats per minute, systolic and diastolic blood pressure were 118.07±21 mmHg and 76.04±10.76 mmHg respectively. Among group II, pulse, systolic blood pressure and diastolic blood pressure were 89.26±16.99 beats per minute, 108.48±22.07 mmHg and 73.54±12 mmHg respectively.The mean T_{p-e}/QT ratio was 0.196±0.029 in group I and 0.309±0.053in group II. There was statistically significant difference between both groups regarding T_{p-e}/ QT ratio (p<0.001). Sustained VT (7.9%) occurred more than VF (2.8%) among those having malignant ventricular arrhythmias (10.7%). The mean T_{p-e}/QT ratio was 0.297±0.067 in arrhythmic patients and 0.242±0.068 in non-arrhythmic patients and difference was statistically significant between those two groups (p=0.001). Multivariate logistic regression analysis for characteristics of factors likely to cause malignant ventricular arrhythmia revealed, T_{p-e}/QT ratio was the independently significant predictors of malignant ventricular arrhythmia with odds ratio (OR) being 3.845.Receiver operating characteristic (ROC) curve for the relationship ofT_{p-e}/QT ratio with malignant ventricular arrhythmias showed, the value of the area under the curve (AUC) was 0.730 (95% confidence intervals (CI), 0.621–0.839). Sensitivity of T_{p-e}/QT ratio was high (78.95% vs 84.21%). Negative predictive value of T_{p-e}/QT ratio at value ≤0.25 was 96.88%.

Table-I

Age distribution of the study population (n=178).

Age in years	Group I (n=96)		Group II (n=82)		Total(n=178)		p value
	Number	%	Number	%	Number	%	
21-30	04	4.2	03	3.7	07	7.9	
31-40	13	13.5	10	12.2	23	25.7	
41-50	31	32.3	33	40.2	64	72.5	
51-60	28	29.2	23	28.0	51	57.2	
61-70	17	17.7	12	14.6	29	32.3	
>70	03	3.1	01	1.2	04	4.3	
Mean ± SD (Range)	52.60(±11.29)		51.59(±11.17)		52.13(±11.13) (25-85)		0.71^{ns}

Group I: Acute Anterior STEMI patients with normal T_{p-e} /QT ratio
Group II: Acute Anterior STEMI patients with Increased T_{p-e} /QT ratio
ns= not significant (p>0.05)
p value reached from unpaired t-test.

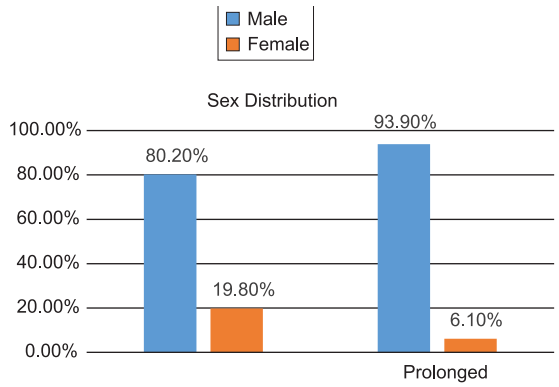


Fig.-2: *Sex distribution among the study population.*

Table-II

Distribution of risk factors of the study population (n=178).

Risk Factors		Group I(n= 96)		Group II(n=82)		Total(n=178)		p value
		Number	%	Number	%	Number	%	
Smoking								
	Yes	73	76.0	69	84.0	142	80.0	0.47^{ns}
	No	23	24.0	13	16.0	36	20.0	
Hypertension								
	Yes	45	47.0	39	48.0	84	47.0	0.92 ^{ns}
	No	51	53.0	43	52.0	94	53.0	
Diabetes mellitus								
	Yes	36	38.0	23	28.0	59	33.0	0.20^{ns}
	No	60	62.0	59	72.0	119	67.0	
Dyslipidemia								
	Yes	16	17.0	15	18.0	31	17.0	0.84 ^{ns}
	No	80	83.0	67	82.0	147	83.0	
Family H/o of premature CAD								
	Yes	28	29.0	27	33.0	55	16.0	0.62^{ns}
	No	68	71.0	55	67.0	123	84.0	

Table-III

Distribution of the study population according to clinical examination (n=178).

Parameters	Group I(n= 96)	Group II(n=82)	p value
	Mean ± SD	Mean ± SD	
Pulse/minute	86.61(±12.49)	89.26(±16.99)	0.235^{ns}
Systolic blood pressure (mmHg)	118.07 (±21)	108.48(±22.07)	0.003^{s}
Diastolic blood pressure (mmHg)	76.04 (±10.76)	73.54(±12)	0.148^{ns}

Table-IV

Distribution of ECG parameters of the study population (n=178).

ECG parameters	Group I (n= 96)	Group II (n=82)	p value
	Mean ± SD	Mean ± SD	
Heart rate (beats per minute)	91.41(±19.53)	89.09 (±20.82)	0.444
QT interval (millisecond)	444.99 (±60.52)	450.33 (±86.72)	0.631
T_{p-e}/QT Ratio	0.196(±0.029)	0.309(±0.053)	<0.001^{s}

Table-V

Distribution of occurrence of malignant ventricular arrhythmias among the study population (n=178).

Malignant Ventricular	Group I(n=96)		Group II(n=82)		Total		p value
Arrhythmia	No.	%	No.	%	No.	%	<0.001[s]
Present	03	3.1	16	19.5	19	10.7	
Absent	93	96.9	66	80.5	159	89.3	

Table-VI

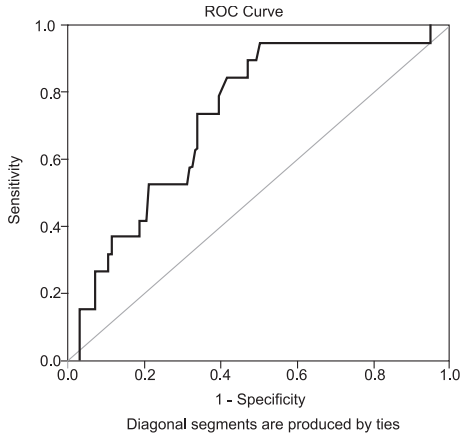
Distribution of ECG parameters of the study population depending on occurrence of malignant ventricular arrhythmias (n=178).

Parameters	Malignant ventricular arrhythmia		p value
	Yes(n=19) Mean ±SD	No(n=159) Mean ±SD	
Heart Rate (beats per minute)	90.32 (±28.05)	90.34 (±19.06)	0.996[ns]
QT interval (ms)	436.53 (± 77.25)	448.76 (73.27)	0.495[ns]
T_{p-e} /QT ratio	0.297 (±0.067)	0.242 (±0.068)	0.001[s]

Table-VII

Multivariate logistic regression analysis for determinants of malignant ventricular arrhythmias.

Variables of interest	Multivariate	
	OR (95% CI)	P value
Age (>45 years)	0.577 (0.218-1.526)	0.268[ns]
Sex	0.733 (0.158-3.393)	0.691 [ns]
Smoking	1.470(0.151-2.118)	0.998[ns]
Hypertension	2.086 (0.755-5.763)	0.156 [ns]
Diabetes mellitus	2.90(0.810-10.381)	0.102 [ns]
Dyslipidemia	1.896 (0.415-8.665)	0.409 [ns]
Family history of premature CAD	1.284 (0.439-3.762)	0.648 [ns]
Heart rate	0.995 (0.338-2.930)	0.993 [ns]
QT interval	0.576 (0.216-1.539)	0.271[ns]
T_{p-e}/QT ratio	3.845(1.321-11.193)	0.002[s]



Null hypothesis: true area = 0.5

Fig.-3: *Receiver operating characteristic (ROC) curve for the relationship of T_{p-e}/QT ratio with malignant ventricular arrhythmias.*

Table-VIII

Sensitivity, specificity, positive and negative predictive value and accuracy of T_{p-e}/QT ratioas predictors of malignant ventricular arrhythmias.

Performance	T_{p-e}/QT ratio(>0.25)
Sensitivity	84.21%
Specificity	58.49%
Positive predictive value	19.51%
Negative predictive value	96.88%
Accuracy	61.24%

Discussion:

An electrocardiogram (ECG) is a cost effective, easily available, non-invasive and bedside diagnostic tool that may be obtained within 10 minutes after arrival of patients with a history of chest discomfort consistent with acute

coronary syndrome[24]. Increased T_{p-e}/QT ratio have been associated with increased risk of ventricular arrhythmias in congenital as well as in acquired long-QT syndromes[25], in hypertrophic cardiomyopathy with troponin I mutations[26] and in patients with the Brugada syndrome[27].

In this study, the mean age of the study population was 52.13±11.13 years ranging from 25 to 85 years. Chowdhury et al[28] found that among 4500 cases of first MI admitted into NICVD, mean age of the patients was 53±10 years.Male patients were predominant among the study population. This was consistent with previous studies in Bangladesh by which the percentage of male patients were 85-92 %[29,30].

In the study, smoking was the most prevalent risk factor (76% vs 84%) in group I and group II study population. The second most prevalent risk factor was hypertension (47% vs 48%), followed by diabetes mellitus (38% vs 28%), positive family history of premature CAD (29% vs 33%) and dyslipidemia (17% vs 18%) between group I and II. Rahman and Zaman[31] have reported that, 79.7% cases of CAD were either current or past consumers of some form of tobacco.

Among the group I patients, the pulse, systolic blood pressure and diastolic blood pressure in mmHg were 86.61±12.49 per minute, 118.07±21mmHg and 76.04±10.76 mmHg respectively. Among group II, the pulse, systolic and diastolic blood pressure in mm of Hg were 89.26±16.99 per minute, 108.48±22.07 mmHg and 73.54±12 mmHg respectively. Abu Sayeed et al[32] have reported that mean systolic blood pressure and diastolic blood pressure in mm of Hg were 128±29 mmHg and 80±15 mmHg respectively among patients with coronary artery disease. The difference of blood pressures can be explained by the presence of an acute state in the study population.

There was no significant difference regarding heart rate (91.41±19.53 vs. 89.09±20.82 per minute) and QT interval (444.99±60.52ms vs. 450.33±86.72 ms) between group I and II. Mugnai et al[23] have found mean heart rate among anterior STEMI patient was 82 ± 18 beats per minute and mean QT interval 453 ± 39 ms, which were consistent with findings of this study.

The mean T_{p-e}/QT ratio was 0.196±0.029 in group I and 0.309±0.053 in group II. There was significant difference between the two groups regarding T_{p-e}/QT ratio (p<0.001). Malignant ventricular arrhythmias occurred in 19 patients (10.7%) out of 178. There was significant difference regarding occurrence of MVA between the groups I and II (p <0.001). MVA occurred in 03 (3.1%) subjects of group. In group II, 16 (19.5%) subjects developed MVA.

The mean T_{p-e}/QT ratio was 0.297±0.067 in arrhythmic patients and 0.242±0.068 in non-arrhythmic patients (p=0.001). Shu et al[21] have observed Tp-e/QT ratio was significantly increased (0.32±0.07 *vs.* 0.26±0.05) in those patient with STEMI having arrhythmia compared to those having no arrhythmia.Mugnai et al[23] have reported mean T_{p-e} was 149 ±41ms in subjects with MVA and 123 ± 34 msin subjects without MVA. The mean T_{p-e}/QT Ratio was 0.38 ± 0.10 in arrhythmic patients and 0.31 ± 0.08 in subjects without arrhythmia. Shenthar et al[22] have found mean T_{p-e}/QT Ratio0.41±0.09 in arrhythmic patients and 0.26±0.02 in subjects without arrhythmia.In another study, Zhao et al[33] have reported T_{p-e}/QT ≥0.29 was able to independently predict both in-hospital death (21.9% vs. 2.3%, p<0.001) and main adverse cardiac events (48.1% vs. 15.3%, p<0.005) in a population of 338 patients with STEMI treated by PCI and also after discharge. T_{p-e} /QT was significantly higher in patients with life-threatening arrhythmias compared with those without major arrhythmic events (0.38±0.10 and 0.31±0.08, p=0.02). Gupta et al[11] have found increased T_{p-e} /QT among in leads with ST elevation to be prolonged in a cohort of 32 patients with acute STEMI as compared with normal subjects. The difference of T_{p-e} and T_{p-e}/QT ratio in this study with other studies may be explained by difference in extent of myocardial injury and severity of MI in different study populations and different settings.

Multivariate logistic regression analysis revealed that after adjusting the individual risk factors, T_{p-e}/QT ratio have significant association with malignant ventricular arrhythmias (p=0.002). Odds ratio for T_{p-e}/QT was 3.845 with 95% confidence interval (1.321-11.193).

Receiver Operating Characteristic (ROC) curve showed that area under ROC curve was 0.730 (95% CI=0.621–0.839) in predicting the major arrhythmic events.

The sensitivity, specificity and negative predictive value for T_{p-e}/QT ratio at >0.25 was84.21%, 58.49% and 96.88%. Mugnai et al[23] have found T_{p-e}/QT ratio of 0.31 showed the best combined sensitivity and specificity (69.7% and 63.7%), respectively, along with negative predictive value of 92%. Shenthar et al[22] have found that T_{p-e}/QT ratio<0.3 had a negative predictive value of 100%.

Thus the results of the study suggested that there was significant association of increased T_{p-e} /QT ratio with malignant ventricular arrhythmias in acute anterior STEMI population.

Conclusion:

The study demonstrated that increased$T_{peak-to-end}$/QT ratio were associated with malignant ventricular arrhythmias in acute anterior ST-segment elevation myocardial infarction. This parameter may represent simple and useful marker in predicting increased risk of in-hospital malignant arrhythmias among patients with anteriorST-segment elevation myocardial infarction and to take prompt measures to prevent arrhythmias. But the study had limitations e.g. number of study population was limited to generalize the results, sampling method was purposive, so there was risk of selection bias.It was conducted in a single center. ECG was assessed by visual observation and despite repeated measurements, there was a few chance of intra observer variation.The study excluded patients hospitalized after 12 hours of chest pain, patients not receiving thrombolytics and patients undergoing primary PCI. Thus association of this ECG parameters with malignant ventricular arrhythmias could not be established in all patients with acute anterior STEMI.Further prospective, randomized andmulti-center studies are needed to confirm these resultsand to define optimal cut-offs of $T_{peak-end}$ and $T_{peak-end}$ /QT ratio. Other studies are also required to evaluate role of urgent revascularization in patients with prolonged $T_{peak-end}$ and increased $T_{peak-end}$ /QT ratio.

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Original Article

Gender Differences in In-Hospital Outcome in Non ST-Elevation Myocardial Infarction

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Abstract:

Among the different types of acute coronary syndrome (ACS), non ST-elevation MI (NSTEMI) is about 25%. Women with ST-segment-elevation myocardial infarction have a worse prognosis than men. However, information about the prognosis of women with non-STEMI is scarce. There are several studies regarding gender difference in NSTEMI. Almost all of these studies were done in western & European countries. Though in third world countries like Bangladesh the patients of NSTEMI are found in large number, limited data are available in this situation. The aim of the study is to determine difference in effect between the genders, in real life patients, with non-invasive treatment. So that definite measures can be formulated to the patients properly of that gender specific group.

Key word: Non-ST segment elevation myocardial infarction, Gender, ACS

(Bangladesh Heart Journal 2017; 32(1) : 18-22)

Introduction:

The myocardial infarction (MI) mortality has decreased markedly during recent decades, a decrease that has multiple causes. In spite of improvements, the incidence of acute MI has remained high and cardiovascular disease is still the leading cause of death, afflicting almost 50 % of both men and women. Coronary heart disease accounts for most of the cardiovascular events, and MI is the single most important contributor to the mortality and morbidity[1].

Historically, fewer women than men have been included in studies on coronary heart disease (CHD). Whether this is caused by lower incidence in women, especially at younger age, or actual exclusion of women from the trials have been debated[2]. The consequence is that evidence base for several treatments are fewer firms for women than for men. Lack of gender-specific knowledge has emerged as an important issue in the management of non ST-elevation acute coronary syndromes where some data have indicated a difference in benefit from a routine invasive strategy according to gender[3-6].

There are also reports that women have been managed less intensively, with worse outcome, compared to men. For example, women have less often received reperfusion therapy, early antithrombotic therapy and antiplatelet therapy at discharge[7,8]. Moreover, men have more often been referred for coronary angiography. There are several important differences in background characteristics between a female and a male population with acute coronary syndromes (ACS); for example, females are older and have more co-morbid conditions[9].

Today, ACS is the leading cause of death in both gender of the western world and during the last two decades there has been an ongoing debate about women and ACS and whether women and men suffering from this syndrome differ in baseline characteristics, clinical presentation, treatment and outcome[10].

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Early mortality among patients hospitalized with an acute MI has been consistently reported to be higher among women than men . An important question has been whether women tend to be treated less vigorously than men although current knowledge from a couple of studies strongly indicates that women in most aspects benefit as much as men from recommended therapies. In contrast to these studies, FRISC II and RITA 3 trials reported worsening outcomes among women with ACS who were treated invasively. This finding has raised doubt as to whether treatment in women and men should be similar[11].

Other studies investigating age-sex differences in short-term mortality beyond the hospital stay support higher long-term mortality rates among women, particularly younger women, compared with men at same ages. In a study from 2001. Vaccarino *et al* observed that women younger than 60 years of age had a higher mortality rate than men and the mortality risk for women compared with men decreased with increasing age, to the point where women in the oldest age groups showed a lower 2 year mortality rate than men of similar age[12,13].

Studies comparing management and outcome in men and women are, for obvious reasons, not randomized why fair comparisons rely on statistical methods to adjust for observed differences in background characteristics[14,15]. To decide whether it is gender per se or other characteristics that account for observed differences in management and outcome between the genders, large study populations, with information on potential confounders, are needed to perform proper adjustments[16-17].

To improve the individual management of NSTEMI patients it is important to clarify if we, in real life clinical practice, treat women differently than men. It is also important to evaluate if there are differences in effect of treatments between the genders, and if observed differences are due to gender per se.

Methodology:

A hospital-based cross-sectional study. It was done on one year duration (July 2014 – June 2015) in the coronary care unit (CCU) of Sir Salimullah Medical College & Mitford Hospital , Dhaka. Study population were patients attending at hospital having Non ST-elevation MI screened out by clinical examination and electro-cardiography (ECG) and biochemical marker (S.Troponin I). Considering the inclusion and exclusion criteria a total number of 115 patients presented with NSTEMI were included in the study.

After collection all the data were checked and edited. Then data were entered into computer with the help of software SPSS for Windows programmed version 16. After frequency run, data were cleaned and frequencies were checked. An analysis plan were developed keeping in view with the objectives of the study.

Results:

The 115 Non ST Elevated patients were included in the study comprising 50 women and 65 men. The study population consisted of 51 patients (16 women, 35 men) aged under 50 years and 64 patients (34 women, 30 men) aged 50 years or older. The mean age of NSTEMI in study population is 52.45 years and the mean age of women in the study is 55.70 years and the mean age of men in the study is 49.49 years.

Table-I

Distribution of risk factors according to sex

Risk factors	<50 years		p value	≥50 years		p value
	MaleN=35	FemaleN=16		MaleN=30	FemaleN=34	
HTN	12(34.3)	11(68.7)	0.02	15(50)	27(79.4)	0.01
DM	06(17.1)	09(56.2)	0.007	14(46.7)	11(32.4)	0.24
CKD	—	—	—	02(6.7)	02(5.9)	1.0
Dyslipidemia	12(34.3)	03(18.7)	0.33	05(16.7)	03(8.8)	0.45
Smoking	27(77.1)	01(6.3)	< 0.001	16(53.3)	05(14.7)	0.001
Family history of coronary heart disease	07(20.0)	06(37.5)	0.18	04(13.3)	08(23.5)	0.29

HTN – Hypertension, DM – Diabetes Mellitus, CKD – Chronic kidney disease

Table-II

In hospital outcome according to distribution of gender

Outcome	Sex		Total	p value
	Male (n=65)	Female (n=50)		
Persistent chest pain	16	23	39	0.030
Heart failure	2	3	5	0.035
Cardiogenic shock	2	3	5	0.34
Arrhythmia	1	1	2	0.043
Reinfarction	2	1	3	0.49
Major bleeding	2	1	3	0.49
CVD/Stroke/TIA	2	1	3	0.49
Death	2	1	3	0.49

CVD – cerebro-vascular disease, TIA – transient ischemic attack

Most patients have no changes in ECG. Commonly ST depression and T wave inversion are significantly seen in women. Other ECG changes include atrial fibrillation, LBBB or RBBB pattern but all of these changes have no significance differences in relation to sex .

Younger women <50 years were significantly more frequently diagnosed with arterial hypertension and diabetes than men, and they were significantly less frequently current smokers. Older women > 50 years more often were hypertensive, while men more often had a history of smoking. Apart from smoking, the frequency of cardiovascular risk factors was similar in both female age groups, while the incidence of arterial hypertension , diabetes was higher in older than in younger men .

Regarding in hospital outcome there is persistent chest pain in 23 (46%) women and 16 (24.6%) men heart failure is present in 3 (6%) women and 2 (3.1%). The differences in incidence of persistent chest pain and heart failure are statistically significant between the two genders.

Discussion:

The debate on the reasons for the differences in mortality and morbidity between women and men with NSTEMI is still ongoing and no full agreement has been reached so far. Many researchers associate poorer outcomes in women with co-morbidities, clinical manifestation and adverse events.

Risk factors and baseline characteristics

In the present study, there were more men in the age group of <50 years, while in the older group the percentage of men and women were practically the same. Women tend to live longer and develop cardiovascular disease at a later age, which means that both in younger and older age groups women are older than men and they have additional risk factors. In the general population of patients with NSTEMI, there is a discrepancy in the prevalence of conventional risk factors (arterial hypertension, diabetes, dyslipidemia, smoking , obesity, prior MI) between sex .

Women <50 years tend to have hypertension, diabetes and family history of coronary heart diseases more often, while smoking and dyslipidemia are more frequent in men. The incidence of hypertension increases with age in both sexes. It seems that the frequency of diabetes mellitus is more in women than men of age < 50 years but it is reverse in age >50 years patients . There is no significant differences in women and men regarding chronic kidney disease (CKD), dyslipidemia and family history of coronary heart disease.

Electrocardiographic changes:

A negative prognostic value of ST-segment depression and T-wave inversion in the index ECG is well established. In our study, there was significant difference in ST-segment depression and T -wave inversion between men and women <50 years age groups; however, atrial fibrillation was observed more frequently in older men >50 years.

Echocardiographic changes:

In this study we have found that women <50 years have significant echocardiographic changes. There were only significant wall motion abnormalities in case of inferior and lateral wall which was more in female patients. The mean ejection fraction was found more in men (EF=57.97%) than women (EF=55.48%) . But it was not significant.

Regarding diastolic dysfunction there was no significant difference in women and men.

In-hospital management

In our study we have found that women were more likely to be treated with beta-blockers, angiotensin converting enzyme inhibitor (ACEi) and diuretics which may reflect the higher rate of hypertension and heart failure. After age adjustment there was no difference between the gender in treatment with heparin/low molecular weight heparin (LMWH), statins, nitrates were used infrequently in both men and women in our data, but less often in women.

Complications:

In our observation 24.6% men experienced persistent chest pain in comparison to 46% women and it was statistically significant. The incidence of heart failure increases with age and reaches 12.5% in patients younger than 65 years and 22% to 41% in patients over 65 years. In many registries, and also in our study, no differences between young men and women were observed, while women had developed heart failure (6.0%) more than men (3.1%) and it is statistically significant. Another important finding was arrhythmia, statistically significant in men (20%) than women (8.0%). Other complications like cardiogenic shock, re-infarction, cerebro-vascular events were not found to differ significantly between the groups.

Mortality

In our study we have found that in hospital death occurred only in 2 men (3.1%) and 1 women (2%) and the difference was not significant.

Conclusion:

In the present study men represent a large population of patients with NSTEMI than women. Smoking is the most alarming risk factors in young male while diabetes and hypertension in young female. There are substantial differences in baseline characteristics between a male and a female population with NSTEMI. Women are older and more likely to have a history of diabetes, hypertension and heart failure. Men are more likely to have a history of NSTEMI. Women are less likely to be admitted to coronary care units. Women receive more diuretics, beta-blockers and angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) in relation to men. Women show worse prognosis regarding heart failure and persistent chest pain.

Risk factors identification, early diagnosis and management are very crucial in the primary and secondary prevention in young patient with CAD. Adoption and application of new knowledge regarding sex differences will hopefully lead to improve outcomes.

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Original Article

Disparity in Coronary Artery Diameter in Diabetic and Non-diabetic Subjects undergoing Percutaneous Coronary Intervention in Bangladesh: A 2-Year Retrospective Analysis

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Abstract:

Objective: Coronary arteries in diabetic patients were found to be narrower than in non-diabetic subjects. The aim of the study was to compare the coronary arteries diameter between diabetic and non-diabetic patients undergoing percutaneous coronary intervention (PCI) using stent diameter for greater accuracy.

Methods: This was a randomized observational study. From a dedicated database, we retrospectively analysed all consecutive patients of both gender who underwent PCI in the cardiac catheterization laboratory of Ibrahim Cardiac Hospital and Research Institute, Dhaka, Bangladesh, from January 2011 to December 2012. Patients who required left main coronary artery stenting were excluded from this study. Patients were divided into two groups; diabetics and non-diabetics. We calculated the coronary artery diameter according to the diameter of the stent, achieved at the final pressure at which the stent was deployed. The diameter which was achieved at a given atmospheric pressure was taken from the attached booklet provided with the stent packaging. If post dilatation was required then the diameter achieved by the non-compliant balloon after post dilatation was taken as the reference diameter of the artery.

Results: A total of 571 patients, 333 in diabetic and 238 in non-diabetic group were included in the study. Proximal segments of left anterior descending (LAD) coronary artery in diabetics and non-diabetics were 2.99±0.44 vs 3.14±0.50 mm (p=0.00) while mid and distal segments were 2.90±0.38 vs 3.10±0.42 mm (p=0.00) and 2.25±0.39 vs 2.42±0.45 mm (p=0.00) respectively. Various segments of proximal left Circumflex (LCx) coronary artery in diabetics and non-diabetics were 2.98±0.21 vs 3.01±0.25 mm (p=0.39) while distal circumflex were 2.35±0.40 vs 2.49±0.43 mm (p=0.00) respectively. Proximal segments of right coronary artery (RCA) in diabetic and non-diabetics were 3.0±0.28 vs 3.28±0.25 mm (p=0.00) while mid and distal segments were 2.97±0.26 vs 3.19±0.25 mm (p=0.00) and 2.43±0.51 vs 2.87±0.32 mm (p=0.00) respectively. The number of stents (1.34±0.87 vs 1.30±0.65; p=0.40) and type of stent utilized (DES & non DES: 87.3 & 12.7% vs 85.2 & 14.8%; p=0.50) between diabetic & non-diabetic groups were not significantly different; however the total stent length (23.1±13.3 vs 21.5±9.52 mm; p=0.03) in diabetic group was significantly longer.

Conclusions: The diameter of LAD, distal circumflex and right coronary arteries were significantly narrower in diabetic than non-diabetic subjects.

Key words: Diabetes mellitus, Coronary arteries, Percutaneous coronary intervention.

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Introduction:

The association between diabetes mellitus (DM) and cardiovascular disease is well-known, and DM is associated with a 2–4 fold increased incidence of Coronary Artery Disease (CAD).[1]. A world-wide non-communicable disease, DM has affected an estimated **387 million** people **globally in 2014,[2] with** Bangladesh having the second highest prevalence of diabetes in the South East Asia region at 10.6%.[3]

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It is estimated that more than 50% of adult diabetics have significant coronary atherosclerosis, a prevalence 10 times greater than that of the general population.[4] Diabetics have high prevalence of subclinical CAD with more diffuse lesions and accelerated progression in frequently smaller native vessels.[5,6]

Angiographic comparison of different segments of the coronary vessel tree has, in the vast majority of cases, revealed a tendency towards narrower coronary artery diameters among diabetic patients with CAD.[7] Most authors from different countries have found the Right coronary artery (RCA) to be significantly more frequently involved in diabetics, in terms of narrower diameter.[8-11.] There is also evidence of smaller luminal diameter of the Left anterior descending (LAD) artery among diabetics,[8,10-12] and distal left circumflex (LCx).[11] In contrast, some investigators have found similar angiographic profiles between non-insulin dependent diabetics (NIDDM) and non-diabetics.[13]

Most of these have been based on measurement of diameters by means of Quantitative Coronary Angiography (QCA). However QCA, which was developed to overcome the limitations of visual interpretation, is in turn limited in that observational variations can occur owing to the use of different frames. In the present study, we investigated diabetic patients undergoing PCI and applied a different method of measurement of coronary vessel diameter by means of the stent size, in order to avail a more objective measurement and overcome observer bias. We sought to study the disparity of vessel diameters among diabetics and non-diabetics, and in particular, the respective segments of vessels affected greatest among diabetics.

Materials and Methods:

This was a randomized observational study. From a dedicated database, we retrospectively analysed all consecutive patients of both gender who underwent PCI in the cardiac catheterization laboratory of Ibrahim Cardiac Hospital and Research Institute, Dhaka, Bangladesh from January 2011 to December 2012 for a total period of 2 years. The aim of the present study was to compare the coronary artery diameters between diabetic and non-diabetic patients undergoing PCI. Prior approval had been taken for the study protocol by the hospital ethical committee. Diabetes mellitus was defined as fasting plasma glucose of 7.0 mmol/L or above or random 2 hours post-prandial plasma glucose of 11.1 mmol/L or above following oral glucose tolerance test or A1C $\geq$6.5%.[14]

Informed written consent was taken from each patient prior to PCI. Patients who required left main coronary artery stenting were excluded from this study. Demographic data such as age, sex, height (cm), weight (kg), and BMI (kg/m^2) were noted. Risk factors were recorded for all patients. Patients were divided into two groups; diabetics and non-diabetics. All interventions were performed according to standard techniques. Unless contraindicated, all patients were given a pre-load of aspirin 300 mg & clopidogrel 600 mg prior to the procedure.

Angiographically, LAD is divided into 3 portions: Proximal, Mid and Distal. Proximal LAD is the portion from its origin from the LMCA to its first diagonal (D1) branch. Mid LAD is the portion between first diagonal (D1) and second diagonal (D2) branches. Distal LAD is the portion of the LAD beyond (D2) branch.[15]

Similarly, LCx is angiographically divided into 2 portions: Proximal and Distal. Proximal LCx is the portion from its origin from the LMCA to the origin of the first obtuse marginal (OM) branch. Distal LCx is the portion of the LCx beyond first OM branch.[15]

Angiographically, RCA is divided into 3 parts: Proximal, Mid and Distal. Proximal RCA is the portion of the RCA from its origin from the right anterior coronary sinus to the origin of its RV branch. Mid RCA is the portion of RCA between its RV branch and its PDA branch. Distal RCA includes PDA and PLV branches.[15]

We analyzed the coronary artery diameter according to the diameter the stent achieved at the final pressure at which the stent was deployed. The diameter which was achieved at a given atmospheric pressure was taken from the attached booklet given with stent packaging. If post dilatation was required then the diameter achieved by the non-compliant balloon after post dilatation was taken as the reference diameter of the artery.

Mean±standard deviation (SD) was calculated for numerical variables while categorical variables were presented as frequencies and percentages. Comparison between two groups was performed by using student's *t*-test for numerical variables and Chi-Square test for categorical variables. A p-value of <0.05 was considered significant. Data were analysed using computer based Statistical Programme for Social Science (SPSS) version 16.0.

Results:

A total of 571 consecutive patients who underwent PCI, 333 in diabetic and 238 in non-diabetic group were included in the study. Mean age in diabetic and non-diabetic groups was 58.6±7.5 vs 59.9±6.7 years (p=0.91) respectively (Table I). Male patients in diabetic and non-diabetic group were 260(78%) vs. 209(87.8%); p=0.00 respectively (Figure 1). Hypertension among diabetics and non- diabetics were 47% vs 42.4% (p=0.39)

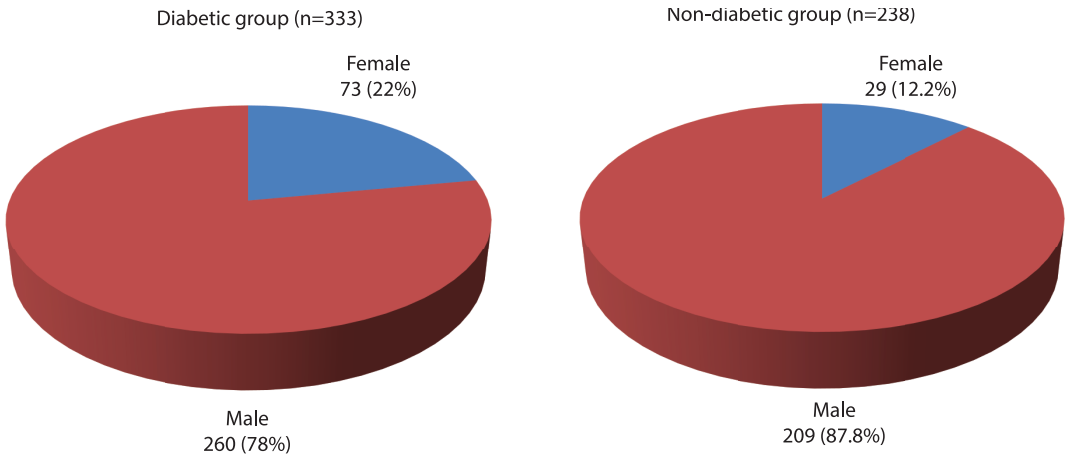

Fig.-1: *Sex distribution of the study population*

respectively. Mean BMI in diabetic and non-diabetic groups was 26.2±2.5 vs.26.8±2.7kg/m^2 (p=0.31) respectively. These baseline characteristics were shown in Table I.

Proximal segments of LAD coronary artery in diabetics and non-diabetics were 2.99±0.44 vs 3.14±0.50mm (p=0.00) while mid and distal segments were 2.90±0.38 vs 3.10±0.42 mm (p=0.00) and 2.25±0.39 vs 2.42±0.45 mm (p=0.00) respectively (Table II).

Various segments of proximal LCx coronary artery in diabetics and non-diabetics were 2.98±0.21 vs 3.01± 0.25mm (p=0.39) while distal circumflex were 2.35±0.40 vs 2.49±0.43mm (p=0.00) respectively (Table III).

Proximal segments of right coronary artery in diabetic and non-diabetics were 3.0±0.28 vs 3.28±0.25mm (p=0.00) while mid and distal segments were 2.97±0.26 vs 3.18±0.25 mm (p=0.00) and 2.43±0.51 vs 2.87±0.32 mm (p=0.00) respectively (Table IV).

Procedural data were presented in Table V. The mean number of stent deployed per patient (1.34±0.87 vs 1.30±0.65; p=0.40) and type of stent utilized (DES & non DES: 87.3 & 12.7% vs 85.2 & 14.8%; p=0.50) between diabetic & non-diabetic groups were not significantly different; however the total stent length (23.1±13.3 vs 21.5±9.52 mm; p=0.03) in non-diabetic group was significantly shorter than diabetic group.

Table-I

Baseline Characteristics of diabetic and non-diabetic patients

Characteristics	Diabetic Group (n=333)	Non-diabetic Group (n=238)	p-value
Mean age (y)	58.6±7.5	59.9±6.7	0.91
Hypertension	156(47%)	101(42.4%)	0.39
BMI (kg/m^2)	26.2±2.5	26.8±2.7	0.31

Table-II

Comparison of LAD artery diameters among diabetics and non-diabetics

	Diabetes	Mean±SD	p-value
Proximal LAD	Yes (n=101)	2.99±0.44	0.00
	No (n=75)	3.14±0.50	
Mid LAD	Yes (n=113)	2.90±0.38	0.00
	No (n=96)	3.10±0.42	
Distal LAD	Yes (n=126)	2.25±0.39	0.00
	No (n=111)	2.42±0.45	

Table-III

Comparison of LCx artery diameters among diabetics and non-diabetics

	Diabetes	Mean±SD	p-value
Proximal LCx	Yes (n=111)	2.98±0.21	0.39
	No (n=125)	3.01±0.25	
Distal LCx	Yes (n=133)	2.35±0.40	0.00
	No (n=118)	2.49±0.43	

Table-IV

Comparison of right coronary artery diameters among diabetics and non-diabetics

	Diabetes	Mean±SD	p-value
Proximal RCA	Yes (n=129)	3.0±0.28	0.00
	No (n=103)	3.28±0.25	
Mid RCA	Yes (n=123)	2.97±0.26	0.00
	No (n=100)	3.19±0.25	
Distal RCA	Yes (n=133)	2.43±0.51	0.00
	No (n=106)	2.87±0.32	

Table-V

Procedural characteristics of the study population

Characteristics	Diabetic Group (n=333)	Non-diabetic Group (n=238)	p-value
Mean number of stents per patient	1.34±0.87	1.30±0.65	0.40
Proportion of DES used (%)	87.3%	85.2%	0.50
Mean total length of stent(s) per lesion (mm)	23.1±13.3	21.5±9.52	0.03

Discussion:

There is a greater incidence of CAD among diabetic patients. CAD in diabetic patients is more severe and diffuse than non-diabetics.[8,9] This could be attributed to various pathophysiological mechanisms among diabetics, including hyperglycemia, hyperinsulinemia and insulin resistance.[8] In addition, a smaller coronary artery diameter should also be viewed as an important factor in the increased prevalence of CAD among diabetics.

Although a number of prior studies have concluded that the disparity in coronary artery diameters between diabetics are non-diabetics is significant, there have been contradictory opinions regarding this concept as well. Most of these studies have been QCA based. The alternative we adopted in this study was to measure the vessel diameters according to stent size.

Our study found no significant difference in the mean ages between the diabetic and non diabetic groups, being 58.6±7.5 vs 59.9±6.7 years (p=0.91) respectively. Melidonis et al. found that among their subjects, there was no statistical significance in the age of male versus female among diabetics.[8]

Male patients in diabetic and non-diabetic group were 260(78%) vs. 209(87.8%); p=0.00 respectively, indicating that the vast majority of patients diagnosed with CAD and undergoing PCI in both groups were male, with a significantly higher number of patients being from the diabetic group, a finding that was also statistically significant. This is consistent with the observations of other studies by Faridullah et al.[12] and Melidonis et al.[8] Hypertension among diabetics and non- diabetics were 47% vs 42.4% (p=0.39) respectively, indicating that it was an important risk factor for the development of CAD among both groups, a finding that has been established in studies done by Melidonis et al.[8] and Gui et al.[9] Mean BMI in diabetic and non-diabetic groups was 26.2±2.5 vs. 26.8±2.7kg/m^2 (p=0.31) respectively, which was also found to be insignificant statistically by Gui et al.[9]

This study found that the disparity in vessel diameters between the two groups of all segments of the LAD coronary artery were statistically significant. Proximal segments of LAD coronary artery in diabetics and non-diabetics were 2.99±0.44 vs 3.14±0.50 mm (p=0.00) while mid and distal segments were 2.90±0.38 vs

3.10±0.42 mm (p=0.00) and 2.25±0.39 vs 2.42±0.45 mm (p=0.00) respectively. In a QCA- based study, Faridullah et al and Adil et al. found very similar vessel diameters among Pakistani populations, all values of which were significant.[11,12] In contrast, however, in a Greek Caucasian population, Melidonis et al. found no statistically significant difference in vessel diameters between diabetics and non-diabetics for all segments of LAD.[8] It is notable to mention that the vessel diameters obtained in our study as well as the study by Faridullah et al. has found greater width for both diabetic and non-diabetic subjects in an Asian population, in comparison to the numbers obtained by Melidonis et al. among a Caucasian population.

As for LCx coronary artery, our study found that the measurements for the distal segment were statistically significant among diabetics and non-diabetics, being 2.35±0.40 vs 2.49±0.43 mm respectively. These findings were consistent with the findings of Faridullah et al.[12] The proximal LCx in diabetics and non-diabetics were 2.98±0.21 vs 3.01±0.25 mm (p=0.39); both Faridullah et al.[12] and Melidonis et al.[8] found no statistically significant difference among the diameters of the two groups for proximal LCx, as in our study.

Our study found that diameters of all segments of the right coronary artery were reduced among diabetic patients undergoing PCI, with statistical significance. Proximal segments of right coronary artery in diabetic and non-diabetics were 3.0±0.28 vs 3.28±0.25 mm (p=0.00) while mid and distal segments were 2.97±0.26 vs 3.19±0.25 mm (p=0.00) and 2.43±0.51 vs 2.87±0.32 mm (p=0.00) respectively. Coincidentally, a Pakistani study conducted by Adil et al.[11] found almost identical vessel diameters. Melidonis et al. however did not find a statistically significant difference in the sizes of the coronaries, although it found that the RCA was more affected with coronary disease in terms of stenosis.[8] Gui et al. who studied the angiographic profiles of diabetic and non-diabetic patients with CAD in a Chinese population, also found that the RCA was more frequently involved among diabetics than non-diabetics (66.4% vs. 52.6%, p=0.002).[9] They postulated this predominance of stenosis is RCA to the low blood flow which coexists in RCA in comparison to other vessels, and the increased plasma viscosity among diabetics.[8,9]

Reference data derived from the literature for standard luminal diameters of normal coronary arteries as derived from literature are as follows: LAD 2-5.0mm (mean 3.6mm), LCx 1.5-5.5 mm (mean 3 mm) and RCA 1.5-5.5mm (mean 3.2mm). LAD and LCx generally taper in diameter as they extend from the LMCA, while RCA maintains a fairly constant diameter till it gives rise to PDA.[16] In comparison to this data derived the diameters measured from our study for non-diabetic patients were similar albeit lesser than the diameters quoted above. Diabetic patients demonstrated significant lesser artery diameter. However, these reference data could not be applied for comparison totally, as they only gave a single average diameter for the whole vessel, as opposed to segments which we measured; in practice, the diameters of the coronary tree changes throughout its length giving rise to different vessel widths.

In summary, our study found that the artery diameters of specific segments of the coronary tree among diabetic patients undergoing PCI were significantly narrower than non-diabetic subjects, particularly the right coronary artery (all segments), proximal and mid LAD and distal LCx. These are consistent with the findings of QCA based measurements of vessel diameter, as well as other studies comparing angiographic profiles between diabetic and non-diabetic populations. Although the exact diameters of the vessels were not measured, these studies reiterate our findings, by showing similar segment and vessel involvement being more predominant among diabetics.

Thus, the smaller diameter of coronary artery segments comes with important therapeutic implications, especially in terms of revascularization, both CABG and PCI. A smaller coronary arterial diameter even after dilatation by PCI/balloon implies that a lower atheroma burden would be required to develop critical stenosis, leading to more frequent occurrence of CAD among diabetics. Consequently, this has an impact in both treatment options as well as outcome, with the incidence of PCI being more frequent among diabetics, as evidenced by our study and others.[4,6]

Due to the more diffuse coronary involvement, diabetics have also been known to require greater stent length due to longer and more diffuse lesions[1,5,6] as reflected in our study with the mean total stent length among diabetic subjects being significantly longer, i.e. 23.1±13.3 vs 21.5±9.52 mm; p=0.03 among diabetics and non-diabetics respectively. However, this study did not find any statistical significance in the number of stents used between the two groups (1.34±0.87 vs 1.30±0.65 mm; p=0.40 for diabetics and non-diabetics respectively).

Smaller vessel reference diameter before the procedure and greater stented length of the vessel have been found to be independent predictors of restenosis in patients with diabetes, leading to poor outcome following PCI.[17]

As restenosis is the major limitation of BMS use in patients with diabetes, DES are considered to be the standard of care for patients with diabetes undergoing PCI, and likely to significantly improve outcome after PCI.[4] DES reduce angiographic restenosis and need for repeat revascularization procedures amongst all patients, with similar benefit among diabetics.[6]

In terms of the type of stent used, our study found no difference in the frequency of the use of DES among diabetic and non-diabetic populations (87.3% vs 85.2%; p=0.50 respectively); given the increasing evidence of better outcome in diabetic following DES, further studies to assess the effects of stent implantation with BMS versus DES stent among diabetics may be warranted.

Conclusion:

Coronary arteries in diabetic patients were found to be narrower than in non-diabetic subjects. The diameter of LAD, distal circumflex and right coronary arteries were significantly narrower in diabetic than non-diabetic subjects. The diabetic subjects needed longer stent lengths than non diabetics.

Limitations:

This study is a retrospective analysis performed on a relatively small number of consecutive patients. Stent size may not reflect the vessel size. IVUS utilization has an additive effect on correcting the appropriate size. Our study also does not take into account potential differences between male and female patients.

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Original Article

Effects of Early Development of Hyponatremia on In-hospital Outcomes in Acute ST- Elevation Myocardial Infarction

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Abstract:

Background: Coronary heart disease is a major cause of death and is a global health problem and reaching epidemic in both developed and as well as in developing countries. In patients with acute myocardial infarction baroreceptor mediated hormonal activation has a prognostic value. Clinical importance of hyponatraemia in ST-elevation acute myocardial infarction has not been fully understood. Hyponatremia which developed in early phase of AMI has been recently advocated as an important prognostic factor in several studies. Objectives: The aim of the study was to investigate the impact of hyponatremia on in-hospital outcomes in patients with ST-elevation acute myocardial Infarction treated by thrombolysis. Methods: Hyponartaemia was defined as a sodium concentration <135 mmol/L. Hyponatremia which developed at 72 hours after admission was defined as early developed hyponatraemia. This study is a prospective observational study. A purposive sampling technique was used to select the sample. In this study data on 100 patients with ST-elevation acute myocardial infarction were analyzed. This study was done in the department of Cardiology Mymensingh Medical College Hospital from July 2014 to June 2015. Patients admitted in the department of Cardiology MMCH with acute ST-elevation myocardial infarction and treated with thrombolysis were evaluated for serum sodium level at admission and at 72 hours after admission. Total 100 patients were studied. Fifty patients with hyponatraemia were Group-I and fifty patients with normal sodium level were Group-II. Then the in-hospital outcome variables were analyzed. Results: Among the study population 85% were male and 15% were female. Age range was 25 years to 74 years. Mean age was 52.88±11.88. Risk factors such as smoking, hypertension, diabetes mellitus, dyslipidemia and F/H of CAD were evaluated. Highest percentage of study population had hypertension (52%) followed by dyslipidemia (49%), smoker (46%), diabetes mellitus (39%) and F/H of CAD had (24%) of study population. There were five outcome variables such as heart failure, cardiogenic shock, arrhythmia, duration of hospital stay and death. Total 12 patients died. 10 patients died in Group-I and 2 patients died in Group-II. Among the outcome variables death, heart failure and hospital stay was more in Group-I and was statistically significant. Conclusion: Early developed hyponatremia in patients with ST-elevation acute myocardial infarction was an independent predictor of prognosis. Heart failure, duration of hospital stay and death was more in hyponatraemic patients and Prognosis worsen with increasing severity of hyponatremia. Plasma sodium level may serve as a simple marker to identify patient at high risk.

Keywords: Hyponatraemia, In- hospital outcome, Acute STEMI, Thrombolysis.

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Introduction:

Coronary heart disease is a major cause of death and is a global health problem reaching epidemic in both developed as well as in developing countries[1]. It is the highest killer in developed countries and is rapidly assuming a similar role in developing ones. Globally, of those dying from cardiovascular diseases, 80 percent are in developing countries and not in the Western world. Coronary heart disease has been classified as chronic stable angina, acute coronary syndrome, (ACS) and sudden death. ACS encompasses different clinical

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entities associated acute myocardial ischemia including ST segment elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA).[2]

Acute STEMI continues to be a significant public health problem in industrialized Countries and is becoming an increasing by significant problem in developing countries[3].

Hyponatremia is a well-known electrolyte disorder in hospitalized patients and it can make the prognosis worse depending on their backgroundt { v . In congestive heart failure (CHF), hyponatremia is associated with exaggerated activation of baroreceptor-mediated hormones, including arginine vasopressin (AVP), catecholamines and the renin angiotensin-aldosterone systemv { [11]. In particular, the primary mechanism is dilutional hyponatremia triggered by osmolality independent secretion of AVP. Baroreceptor mediated hormonal release reflects the severity of heart failure, worsens cardiac remodeling in it-self, and thus could be one of the independent prognostic factors in CHFy.[9,12-17]

In patients with acute myocardial infarction (AMI), successful thrombolysis after acute STEMI, baroreceptor-mediated hormonal activation is similar to that in patients with CHF and has a prognostic value[1]x { [2]p . Hyponatremia, which developed in the early phase of AMI, has also been recently advocated as an important prognostic factor in several studies[18,21]

The prevalence and importance of hyponatremia in patients with ST elevation AMI (STEMI), however, have not yet been fully established. The present study had the aim to investigate the impact of hyponatremia on in hospital outcomes in patients who received successful thrombolysis after acute STEMI.

Materials and Methods:

This prospective observational study was carried out in the department of Cardiology, Mymensingh Medical College Hospital, Mymensingh during the period of July 2014 to June 2015, availing the laboratory facilities of the Mymensingh Medical College, Mymensingh. Purposive sampling was done using a structured case record form.

All patients with chest pain who were admitted into the Department of Cardiology of MMCH examined. With brief clinical history, target physical examination, ECG and Troponin-I the patients with first attack of Acute ST- segment elevation myocardial infarction were selected and thereby one hundred (100) patients who were eligible for thrombolysis were selected. Serum electrolyte of those patients were measured. The sample population was divided into two groups. Group-I: Patients with first attack of acute ST-Elevation myocardial infarction who developed hyponatraemia at 72 hours after admission. Group-II: Patients with first attack of Acute Myocardial Infarction who had normal sodium level at 72 hours after admission.

Group-I was further divided into 04 sub-groups according to the serum sodium levels. Group-Ia: Sodium level 130-134 mm/L, Group-Ib: sodium level 125-129 mm/L, Group-Ic: Sodium level 120-124 mm/L, Group-Id: Sodium level <120 mm/L.

Selection of the study population was done on the basis of history taking and clinical examination of the patients and on some inclusion and exclusion criteria.

Inclusion Criteria:

Patients admitted into the Department of Cardiology with first attack of acute ST – elevation myocardial infarction treated by thrombolytic (Streptokinase).

Exclusion Criteria:

- Patient with valvular heart disease, congenital heart disease and cardiomyopathy.
- Patients who have major non cardiovascular disorder which causes hyponatraemia such as severe renal impairment, diarrhea and vomiting.
- Any systemic infection.
- Patient not willing to enroll in study.
- Patients who are not treated with thrombolytic agent after acute STEMI.
- Clinical conditions which causes syndrome of inappropriate ADH secretion (SIADH).
- Patients who have already hyponatraemia on admission.

Before examination a detailed briefing about the purpose of the study was given to the subjects and written consents were taken for all of the study population.

Variables studied:

Age, Sex, Smoking, Hypertension, Diabetes Mellitus, Dyslipidemia, F/H of CAD, Serum Electrolytes, Troponin-I, Heart failure, Arrhythmia like Atrial fibrillation, Ventricular tachycardia, Ventricular fibrillation, Cardiogenic Shock, Death.

The data were processed and analyzed by computer software SPSS (Statistical package for social science) Version 20. Level of significance was considered as p value less than 0.05 ($p < 0.05$).

Statistical Method and analysis:

Continuous data were expressed as mean ± SD. Categorical data were analyzed with x^2 test. Student's t" test

was used for analysis of continuous variables. Comparison between groups was done by unpaired t-test.

Results:

This was a prospective observational study conducted in the Cardiology department of Mymensingh Medical College Hospital for a period of one year from 1st July 2014 to 30th June 2015. The main objective is to ascertain in-hospital outcome of early developed hyponatraemia in a setting of acute ST-elevation myocardial infarction treated by thrombolysis. Total sample population were 100. Group-I (n=50) acute STEMI patient with hyponatraemia. Group-II (n=50) Acute STEMI patient with normal sodium level.

Total of 100 patients were studied. The mean age of patient was 52.88±11.81 ranging from 25 to 74 years. Majority of the patients were in 50 to 69 years of age but 12% patients were below 40 years. There was no statistically significant difference between the study groups (p=0.765).

This table shows 85% patients were male and 15% were female. There was no statistically significant differences between the sex among the study population (p= 0.652).

The above table shows that HTN and Dyslipidaemia are the most prevalent risk factors among the study groups. Although smoking, diabetes and family history of CAD also had high prevalence but all were not statistically significant (p>0.05).

Group-I Hyponatraemia (sodium level <135 mmol/L), Group –II (normal sodium level). Group -I further divided into 4 sub-groups.

Group-Ia: Sodium level 130-134 mmol/L, Group- Ib: Sodium level 125-129 mmol/L, Group-Ic: Sodium level 120-124 mmol/L and Group-Id: Sodium level <120 mmol/L.

Table-4 shows division of Group-I patients according to plasma sodium level. Twenty eight patients (56%) had sodium level 130-134 mmol/L, fifteen patients (30%) had sodium level 125-129 mmol/L, five patients(10%) had sodium level 120-124 mmol/Land two patients (4%) had sodium level <120 mmol/L.

Table 5 shows outcome of study population according to serum sodium level. Heart failure occurred in 2o% patients (p= .003), arrhythmia developed in 23% patients (p=0.107), cardiogenic shock occurred in 12% patients (p=0.254) and death occurred in 12% patients (p=0.002).

P-Value of heart failure and death was statistically significant.

Table 6 shows hospital stay /days of the study population according to serum sodium level. Group-I: two days 16%, three days 36%, four days 28% and five days were 20% patients. Group-II: 2 days 28%, 3 days 56%,4 days 12% and 5 days were 4% patients (p=0.001). It was statistically significant.

Table-I

Distribution of subjects by age (n=100)

Age in years	Group				Total		p- Value
	Group-I (n=50)		Group-II (n=50)				
	No.	%	No.	%	No.	%	
<30	3	6.0%	1	2.0%	4	4.0%	
30-39	3	6.0%	5	10.0%	8	8.0%	
40-49	8	16.0%	14	28.0%	22	22.0%	
50-59	18	36.0%	12	24.0%	30	30.0%	
60-69	13	26.0%	12	24.0%	25	25.0%	
e”70	5	10.0%	6	12.0%	11	11.0%	
Total	50	100.0%	50	100.0%	100	100.0%	
Mean ± SD	53.52±11.58		52.24±12.11		52.88±11.81		0.765

Table-II

Sex Distribution of the study group (n=100)

Sex	Group				Total		p- Value
	Group-I (n=50)		Group-II (n=50)				
	Frequency	%	Frequency	%	Frequency	%	0.652
Male	42	84.0	43	86.0	85	85.0	
Female	8	16.0	7	14.0	15	15.0	

Table-III

Distribution of the study subject by risk factors (n=100)

	Group I		Group II				
	Frequency	%	Frequency	%	Total	P –value	Sig
Smoking	24	48%	22	44%	46	0.455	NS
HTN	27	54%	25	50%	52	0.547	NS
DM	22	44%	17	34%	39	0.222	NS
Dyslipidemia	26	52%	23	46%	49	0.382	NS
Family F/H of CAD	14	28%	10	20%	24	0.300	NS

Group-I: Patients with hyponatraemia.
Group-II: Patients with normal sodium level.
P-value obtained by Chi-square test

Table-IV

Distribution of Group-I by serum sodium level (n=50)

Na^+ Level	Group-I	
	Frequency	%
Group Ia (Na^+ 130-134 mmol/L)	28	56.0
Group Ib (Na^+ 125-129 mmol/L)	15	30.0
Group Ic (Na^+ 120-124 mmol/L)	5	10.0
Group Id (Na^+ <120 mmol/L)	2	4.0
Total	50	100.0

Significant at 1% level of probability (p<0.01)

Table-V

Distribution of the subject by in-hospital outcome (n=100)

Outcome		Na^+ Level												
		(Na^+ 130-134 mmol/L)		(Na^+ 125-129 mmol/L)		(Na^+ 120-124 mmol/L)		(Na^+ <120 mmol/L)		(Na^+ >135 mmol/L)				
		Frequency	%	Frequency	%	Frequency	%	Frequency	%	Frequency	%	Total	P value	Sig.
Heart Failure	Yes	6	21.4	5	33.3	2	40.0	1	50.0	6	12.0	20	0.003	**
	No	22	78.6	10	66.7	3	60.0	1	50.0	44	88.0	80		
Arrhythmia	Yes	7	25.0	5	33.3	2	40.0	1	50.0	8	16.0	23	0.107	NS
	No	21	75.0	10	66.7	3	60.0	1	50.0	42	84.0	77		
Cardiogenic shock	Yes	4	16.6	3	20.0	2	40.0	1	50.0	2	4.0	12	0.254	NS
	No	24	83.3	12	80.0	3	60.0	1	50.0	48	96.00	88		
Death	Yes	2	7.1	5	33.3	2	40.0	1	50.0	2	4.0	12	0.002	**
	No	26	92.9	10	66.7	3	60.0	1	50.0	48	96.0	88		

** = Significant at 1% level of probability (p<0.01)
NS = Not significant (p>0.05)

Table-VI

Distribution of study subject by duration of hospital stay (n=100)

Hospital Stay/day	Na^+ Level										P value	Sig.
	(Na^+ 130-134 mmol/L)		(Na^+ 125-129 mmol/L)		(Na^+ 120-124 mmol/L)		(Na^+ <120 mmol/L)		(Na^+ >135 mmol/L)			
	Frequency	%	Frequency	%	Frequency	%	Frequency	%	Frequency	%		
2.00	5	17.9	3	20.0	0	0.0	0	0.0	14	28.0		
3.00	13	46.4	2	13.3	3	60.0	0	0.0	28	56.0	0.001	**
4.00	7	25.0	6	40.0	1	20.0	0	0.0	6	12.0		
5.00	3	10.7	4	26.7	1	20.0	2	100.0	2	4.0		
Total	28	100.0	15	100.0	5	100.0	2	100.0	50	100.0		

Discussion:

Total 100 patients of acute ST-Elevation Myocardial Infarction were selected for the study. Patients admitted in CCU in MMCH with first attack of acute STEMI were evaluated for hyponatraemia.

Among the base line characteristics age range were 25 to 74 years, mean age 52.88 ±11.81 years. The difference between the age groups were statistically non-significant. 85% were male and 15% were female. The difference between the age groups were statistically non-significant. Male and female ratio was 5.6: 1. Rahman et al., 1999 found in their study that 13.3% were female. The observations of our study was quite similar to the other studies.

Among the important risk factors the prevalence of smoking (46%), hypertension (52%), diabetes mellitus (39%), dyslipidemia (49%) and family history of coronary disease (24%). But they were statistically non-significant.

In hyponatremic patients (Group -I) 44% patients were diabetic, where as diabetes was 34% among the patients with normal sodium level (Group-II). In Group-I patients 48% had history of smoking habit. In a previous study smoking habit was found 37% among the patient with hyponatraemia in setting of acute ST-Elevation MI. Hypertension were present 54% among the study population. In previous study it was 44%[21].

In this study total of 12 patients (12%) died. Another study in 1999 it was found that hospital mortality was 22.5%. A study in 1982 found 20% mortality rate in their study with MI. In patient with normal sodium level death occurred in 2 patients (4%) and death occurred in patient with hyponatraemia 10 patients (20%), (P= 0.002) [22]. In this study mortality decreases may be due to early detection and management of hyponatraemia.

Hyponatraemic patients were categorized in to four groups, one patient (50%) out of 2 patients died with plasma sodium level <120 mmol/L. In patients with plasma sodium level 120-124 mmol/L death occurred in 2 patients (40%) out of 5 patients in this group. 5 patients (33.3%) died out of 15 patients in sodium level 125-129 mmol/L. Death occurred in 2 patients(7.1 %)out of 28 patients having serum sodium level 130-134. So mortality increased with increasing severity of hyponatraemia compared with patients having normal sodium level. Chi –square test and multivariate regression analysis on mortality was significantly higher among Group-I compared with Group- II.

A study in 1979 showed in their study that relation of mortality and plasma sodium level. 7% died with normal plasma sodium level, 17% with sodium level 135- 130 mmol/L and 22% died with plasma sodium level less than130 mmol/L[23].

In acute STEMI patients without hyponatraemia had a mortality rate 6.2%[22]. Patients with hyponatraemia on admission mortality rate were 19.8% and 16.8% in patients who developed hyponatraemia after admission. After logistic regression analysis and adjustment for other important co-variants they concluded that both hyponatraemia on admission and hyponatraemia developing after admission remained strong independent predictor of 30 –day mortality.

In our study adverse hospital outcome other than mortality included heart failure, arrhythmia, cardiogenic shock and duration of hospital stay. Heart failure developed in 20% patients. Another study found that 22.7% patients developed heart failure[2]t . Sixteen (32%) developed heart failure in Group-I and Six patients (12%) in Group-II. Heart failure developed in highest percentage in patients with sodium level <120 mmol/L. So there was a relation between hyponatraemia and developing heart failure that was increasing with increased severity of hyponatraemia.

Arrhythmia developed in this study was 23%. Rahman et al., 1999 found occurrence of arrhythmia increased with increasing the degree of hyponatraemia

A study found that episodes of ventricular fibrillation occurred in relation to sodium level. They got significant ventricular fibrillation in patient with sodium level 132 mmol/L and got no arrhythmia in patients with normal sodium level[23].

Cardiogenic shock occurred in twelve patients (12%) of study population, 10 patients (20%) in hyponatraemic and 2 patients (4%) in patients with normal Sodium level. p-value was 0.254, was statistically non- significant.

Duration of hospital stay of the study population according to serum sodium level was statistically significant.

Total 12 patients died, among them 10 patients died in Group-I and 2 patients died in Group-II. Mortality increased with increasing severity of hyponatraemia. It was statistically significant. Other study also concluded that mortality increased with degree of hyponatraemia[22].

Limitations

Several limitations of our study must be acknowledged:

- Study population was small.
- Study was single centered.

Conclusion:

This study was done to find out the prognostic implication of hyponatraemia in the setting of STEMI. Observations

were done to find out the in-hospital outcome of hyponatraemic patients and patients with normal sodium level at 72 hours after acute ST-elevation myocardial infarction treated by thrombolysis. Among the parameters of outcome, heart failure, hospital stay and death was statistically significant but arrhythmia and cardiogenic shock was not significant. This study concluded that heart failure, hospital stay and death occur more in hyponatremic patients than patients with normal sodium level and increasing disease severity with increasing severity of hyponatraemia. So early developed hyponatraemia in patients with ST-elevation acute myocardial infarction treated by thrombolysis considered to be an important predictor of prognosis.

Recommendations

Early developed hyponatraemia in patients with acute ST-elevation myocardial infarction is an important predictor of prognosis. Prognosis worsen with increasing severity of hyponatraemia. Facilities of plasma sodium measurement is available in most of the hospitals and is a non-invasive procedure. By early detection of serum sodium level we can identify the patients at high risk.

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Original Article

Association of Visceral Adiposity Index Score with the Severity of Coronary Artery Disease in Patients with Ischemic Heart Disease

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Abstract:

Background: Ischemic Heart Disease (IHD) is the leading cause of death throughout the world and obesity especially visceral adiposity (central obesity has significant influence for its development & progression. Visceral adiposity index (VAI) is a novel sex specific index which had significant correlation with visceral adiposity. Objectives: To evaluate the impact of cut-off points of VAI defining visceral adipose dysfunction (VAD) on the angiographic severity of coronary artery disease in patients of IHD. Methods: A total of 100 patients with IHD were divided into Case (of which 50 patients of IHD with VAD positive) and Control group (of which 50 patients of IHD with VAD negative). Then clinical, biochemical, echocardiographic and coronary artery angiographic indexes (determined by Gensini score) were acquired in relation to VAI. Results: VAD positive group had more significant form of coronary artery disease in term of Gensini score than VAD negative group.The mean level of Visceral Adiposity Index (VAI) was observed 3.1±0.9 and 2.1±0.6 in significant CAD (Gensini score ≥36) and insignificant CAD (Gensini score<36) respectively. The difference of mean VAI between the significant and insignificant CAD groups were statistically significant (p=<0.001). First group (VAD positive) also had more CAD risk factors like hypertension, diabetes mellitus and dyslipidemia which were significantly higher than second group (VAD negative) (p=0.02, 0.002, 0.01). Univariate and multivariate analysis revealed that out of the 8 variables hypertension, dyslipidemia, diabetes mellitus, waist circumference and visceral adiposity index were found to be the independently significant predictors of severe CAD patients with ORs being 1.61 vs. 1.52, 1.97 vs. 1.36, 2.19 vs. 1.97, 1.94 vs. 1.61 and 3.89 vs. 3.49 respectively. Thus the VAI was found to be more strong predictor of the severity of CAD. Conclusion: VAI is a simple indicator of visceral adipose mass & was markedly associated with the severity of coronary artery disease in IHD patients.

Key words: Coronary artery disease, Viscereal, Adiposity.

(Bangladesh Heart Journal 2017; 32(1) : 36-39)

Introduction:

Obesity, a worldwide epidemic in recent years and around 2.1 billion people-nearly one-third of the world's population are overweight or obese & it is one of the important modifiable risk factor.[1]Apart from CVD it also increases type 2 diabetes, Obstructive sleep apnea, certain types of Cancer, Osteoarthritis, Depression, Sexual dysfunction, Alzheimer's.[2]

However, not every obese patient develops cardiovascular diseases. In this regard, visceral adiposity has been found to play a key role in cardio metabolic risk and it is the central obesity which is the main culprit for our body.[3]Abdominal adiposity, is a reflection of central body fat distribution, is associated with significant metabolic abnormalities including insulin resistance, hyperinsulinemia, elevated triglycerides, glucose

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intolerance, DM, as well increased incidence of hypertension (HTN), atherosclerosis and stroke[4], & obesity is as much risk as smoking to (replace by for) developing heart disease.[5] It is striking that South Asian people are more susceptible to develop central obesity than others as because their primary subcutaneous compartment is small results(resulting) in more visceral fat accumulation in response to positive energy balance, which leads to early development of metabolic syndrome and adverse cardiovascular event.[5] The precise measurement of the total amount of body fat and its regional distribution is possible by using computed tomography (CT) or Magnetic resonance imaging (MRI)[6], but they are costly and not routinely available. Accordingly, there is a need for simple technique that can identify visceral adiposity & there are different parameter (parameters) exist like BMI, WC, Waist/Hip ratio but none of these can accurately identify the exact impact of visceral adiposity on IHD. In this regard Amato, et al., (2010) have developed a novel sex-specific index based on WC, body mass index (BMI), triglyceride (TG), and high-density lipoprotein (HDL) cholesterol and termed it visceral adiposity index (VAI), and observed that VAI had significant correlation with visceral adiposity. And VAI showed a strong independent association with cardiovascular risk[7]& it has an optimal cut-off pointsaccording to age. Optimal VAI cut-off points are: 2.52 (age < 30 years), 2.23 (age ≥30 and < 42 years), 1.92 (age ≥42 and < 52 years), 1.93 (age ≥52 and < 66 years) and 2.00 (age ≥ 66 years). Patients with VAI scores greater than these cut-off points were arbitrarily defined as visceral adipose dysfunction (VAD) and this dysfunctional fat is very much deleterious for our body & this dysfunctional fat is very much deleterious for our body.[8]

Objective of the study:

To find out the correlation of Visceral adiposity index score with the angiographic severity of coronary artery disease in patients with Ischemic Heart Disease.

Materials and Methods:

This was a cross sectional (not cross-sectional, but case-control study)analytical study, carried out in the Department of National Institute of Cardiovascular Diseases, Dhaka, Bangladesh during the period of August 2015 to July 2016. Meticulous history, detailed clinical examination and necessary investigations were done.Considering the inclusion and exclusion criteria, consecutive 100 patients of IHD who had undergone CAG were recruited and divided into two group depending on the VAD.In group I 50 patients of IHD with VAD positive &In group II 50 patients of IHD with VAD negative. Following equation showing calculation of VAI where WC

$$\text{Males: VAI} = \left(\frac{\text{WC}}{39.68 + (1.88 \times \text{BMI})}\right) \times \left(\frac{\text{TG}}{1.03}\right) \times \left(\frac{1.31}{\text{HDL}}\right)$$

$$\text{Females: VAI} = \left(\frac{\text{WC}}{36.58 + (1.89 \times \text{BMI})}\right) \times \left(\frac{\text{TG}}{0.81}\right) \times \left(\frac{1.52}{\text{HDL}}\right)$$

is expressed in cm, BMI in Kg/m2, TG in mmol/L, and HDL in mmol/L. After CAG the severity of coronary artery were assessed through Gensini score & 36 points was chosen as an appropriate cut-off value and patients were divided into two groups, those with a Gensini score ≤36 points were considered as absent or mild coronary artery disease and those with a Gensini score >36 points were considered as moderate to severe coronary artery disease (Sun and Lu, 2011).

Results:

A total of 100 patients of IHD underwent CAG were studied. In table I shows the severe form of CAD were higher in group I than group II and the difference is statistically significant. Again group II had higher no. of less severe form of CAD than group II and the difference is also statistically significant.

Table-I

Distribution of the study population according to CAD severity (n=100).

CAD severity (by Gensini Score)	Group I (n= 50)		Group II(n=50)		p value
	Number	%	Number	%	
Moderate to severe disease (≥36 points)	39	78.0	11	22.0	<0.001[s]
No to mild disease (<36 points)	11	22.0	39	78.0	<0.001[s]

s = Significant, p value reached from Chi Square test. CAD= coronary artery disease

Table-II

Mean status of VAI of the study population according to significant CAD defined by Gensini Score (n=100).

VAI	Significant CAD (n=50)(≥36)	Insignificant CAD (n=50) (<36)	p value
Mean ± SD	3.1±0.9	2.1±0.6	<0.001[s]

s=Significant, p value reached from unpaired t test.

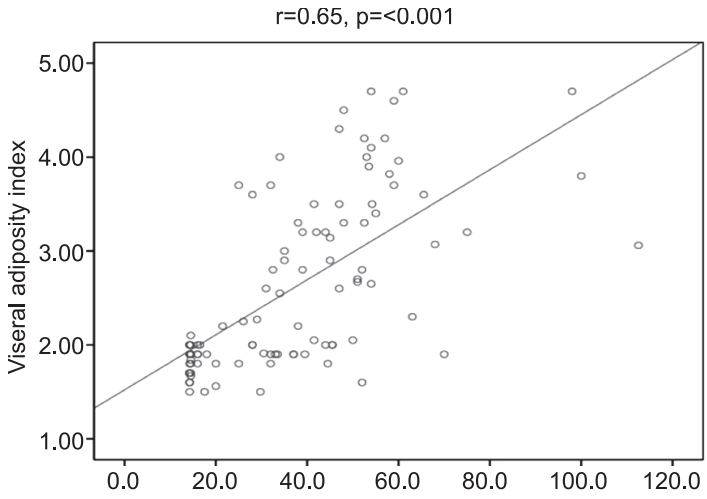

Fig.-1: *Correlation between Visceral Adiposity Index and Gensini score*

Table-III

Variables of interest	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Advance age (>50yrs)	1.40 (0.299 – 2.928)	0.26^{ns}	1.22 (0.119 – 2.101	0.40^{ns}
Smoking	1.27 (0.180 – 2.119)	0.22^{ns}	1.10 (0.112 – 2.001)	0.31^{ns}
Hypertension	1.61 (1.155 – 3.404)	0.02^{s}	1.52 (1.120 – 2.691	0.03^{s}
Dyslipidemia	1.97 (1.182 – 4.691)	0.01^{s}	1.36 (1.105 – 3.109)	0.02^{s}
Diabetes mellitus	2.19 (1.728 – 6.578)	0.003^{s}	1.97 (1.596 – 5.241)	0.005^{s}
Waist Circumference (WC)	1.94 (1.121 – 4.112)	0.001^{s}	1.61 (1.211 – 3.520)	0.003^{s}
Increased BMI	1.51 (0.212 – 2.219)	0.28^{ns}	1.44 (0.121 – 2.106)	0.32^{ns}
VAI	3.89 (1.611 – 9.320)	0.003^{s}	3.49 (1.410-8.654)	0.007^{s}

OR= odds ratio, CI=confidence interval
The scattered diagramme shows the significant moderate positive correlation between Gensini score & VAI.

Table II shows the mean value of VAI in group I is more than group II and the mean difference is statistically significant.

Table III shows VAI has the highest independent prediction of causing CAD as it has the highest OR and it is statistically significant.

Discussion:

In the present study, the mean mean FBS level was 8.2±2.8 mmol/l in group I and 6.1±2.0 mmol/l in group II and the mean difference was statistically significant between the two groups (p=0.001). In consistent with the present study, Han, et al. also observed the same result. The mean BMI of group I was 26.3±4.4 (kg/m2) and that of group II was 22.5±2.3 (kg/m2). Waist circumference was found in group I and group II 93.0±8.0 vs 80.6±4.4 cm. Above two characteristics were significantly (p=<0.001) higher in group I than group II & supported by the study done by Han and colleagues [10]& Khondker R[11.] The mean level of Visceral Adiposity Index (VAI) was observed 3.1 ±0.9and 2.1 ±0.6 in significant CAD and insignificant CAD respectively. The difference of mean VAI between the significant and insignificant CAD groups were statistically significant (p=<0.001) and it was compatible with the study of Han and colleagues study[10]. Regarding correlation coefficient of different anthropometric measurement with the severity of CAD as assessed by Gensini score, it was found that VAI (r=0.65) had highest positive correlation followed by WC (r=0.54) and then BMI (0.46) and it was supported by the study of Han and colleagues[10]. Coronary artery disease (CAD) severity of the study patients were assessed by Gensini score and it was found that moderate to severe form of CAD (Gensini score e" 36 points) was 78% and 22% in group I and group II respectively. No to mild form of CAD (Gensini score <36) was found 22% and 78% in group I and group II respectively. Moderate to severe form of CAD patients were significantly more in group I than

group II (p=<0.001) and no to moderate form of CAD patients were significantly more in group II than group I (p=<0.001). Study done by Han and colleagues[10] also found that the mean difference of severity of CAD in relation to Gensini score between the two group was statistically significant (p=<0.001). Univariate and multivariate analysis revealed that hypertension, dyslipidemia, diabetes mellitus, waist circumference and Visceral Adiposity Index were found to be the independently significant predictors of severe CAD patients with ORs being 1.61 vs. 1.52, 1.97 vs. 1.36, 2.19 vs. 1.97, 1.94 vs. 1.61 and 3.89 vs. 3.49 respectively. Thus the VAI was found to be more strong (stronger) predictor of the severity of CAD. An important study was done by Han and colleagues [10] in 95 patients of CAD & showed that VAI (OR 18.257 [95% CI 6.038-30.475]; P = 0.005) was independently associated with Gensini score and it supports our present study.

Conclusion:

From this study it may be concluded that, Visceral Adiposity Index Score act as asimple indicator of visceral adipose mass and is significantly associated with the severity of Coronary Artery Disease in patients with Ischemic Heart Disease. So, overweight or central obesity or increased visceral adiposity, as evidenced by increased Visceral Adiposity Index Score may be considered as an emerging parameter of severe form of coronary artery disease, among the patients of Ischemic Heart Disease.

Study limitations:

Sampling method was not random rather purposive, so there was a risk of selection bias. It was conducted in a single center. Coronary angiography was assessed by visual observation, so there was every chance of inter observer variation.

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Original Article

Study on Risk Factors and Pattern of Coronary Artery Involvement in Young Acute Coronary Syndrome Patients

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Abstract:

Aims: To compare the risk factors and pattern of coronary artery involvement in young acute coronary syndrome patients with that of the elderly.

Methods: This was a cross sectional analytic study done in the Department of Cardiology, Sir Salimullah Medical College and Mitford Hospital during November 2015 to October 2016.

Results: Study population was divided into two subgroups, those 18-40 years were considered as young and those >40 years were considered as elderly. Young patients had greater prevalence of smoking, dyslipidemia and positive family history of Ischemic Heart Disease (IHD), whereas hypertension was more prevalent in the elderly. Younger patients mainly presented with STEMI and predominantly had single vessel disease (SVD), whereas elderly patients frequently presented with NSTEMI and Unstable angina and had higher incidence of double vessel disease (DVD) and triple vessel disease (TVD).

Conclusion: Younger patients had a different pattern of risk factors and coronary artery involvement in comparision to the elderly.

Keywords: Young adult, Acute Coronary Syndrome, Coronary Angiography, Bangladesh.

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Introduction:

Coronary artery disease is a global health problem reaching an epidemic proportion in both developed and developing countries and is the leading cause of mortality and morbidity worldwide.[1, 2] In 1990 coronary artery disease accounted for 28% of world's 50.4 million deaths and 9.7% of the 1.4 billion lost disability adjusted life years. By 2020 the world's population will grow to 7.8 billion and 32% of all deaths will be caused by coronary artery.[3]

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The South Asian countries have among the highest incidence of coronary artery disease globally.[4] Estimates from the global burden of disease study suggests that by the year 2020, this part of the world will have more individuals with atherosclerotic coronary artery disease than in any other region.[4, 5] Data related to different aspects of CAD in Bangladesh are inadequate but it is highly prevalent in Bangladesh.[6]

South Asian populations have an increased risk and 5-10 years earlier onset for acute myocardial infarction compared to the western population. In recent years the frequency of acute myocardial infarction in young individuals is increased.[4, 7, 8] Like other South Asians, Bangladeshis are unduly prone to develop CAD, which is often premature in onset.[6]

Methods:

This was a cross sectional analytical study, done in the Department of Cardiology, Sir Salimullah Medical College and Mitford Hospital, Dhaka during November 2015 to October 2016. All patients 18 yrs and above with acute

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coronary syndrome admitted in CCU during the specified period were included in this study considering the inclusion and exclusion criteria. Inclusion criteria were ACS patients ≥18 yrs and in whom CAG could be done. Exclusion criteria were patients withconcurrent valvular or congenital heart disease, cardiomyopathy, CKD, cerebro-vascular disease and old MI.

They were further divided into 2 groups based on their age. Patients 18-40 yrs were considered as young and those >40 years were considered as elderly.[4]Informed written consent was taken from the selected patients. Initial evaluation of patients was done by history taking and clinical examination and were duly recorded. Demographic data, such as, age, sex and anthropometric data like height (cm) and weight (kg) were recorded. Presence of risk factors of ACS or risk factors reported were also noted. Pulse, BP and other vital parameters were recorded.

Troponin I level was measured at admission but not before 6 hrs from the onset of chest pain. Blood for screening DM was taken with patients fasting at least 8 hrs before giving the blood sample and 2 hrs after 75 gram oral glucose load (in patients not confirmed by FBS and RBS), but for screening dyslipidemia fasting only for 8 hrs would do suffice. To evaluate renal status serum creatinine was assessed. Echocardiography was done after admission of the patient. The mode of ACS presentation in both the groups were noted. Coronary angiogram was done during admission or on follow up (within 14 days) regardless of patient receiving thrombolysis or not and was recorded.

Data were processed and analyzed using SPSS (Statistical Package for Social Science) for Windows Version 16. The test statistics used to analyze the data were descriptive statistics, Chi-square ($Ç^2$) and unpaired t-test. While the categorical data were compared between groups using Chi-square Test, the data presented on continuous scale were compared between groups using unpaired t-test. The level of significance was set at 5% and $p < 0.05$ was considered significant

Results:

The present study intended to compare the risk factors and coronary artery involvement between younger and elder ACS included a total of 110 patients. Of them 58 were £40 years and considered as young (case) and 52 were above 40 years were older (control). Males and females were 83 and 27 respectively. The mean ages of the younger and the elder group were 36.6 ± 4.3 and 56.9 ± 8.7 years respectively, while the mean ages of the males and females 47.0 ± 12.7 and 43.9 ± 10.4 years respectively.

Table-I
Comparison of sex distribution of the study groups (N=110)

Sex distribution	Group		p value*
	Case (≤ 40 years) (n = 58)	Control (>40 years) (n = 52)	
Male	41(70.7)	42(80.8)	0.220
Female	17(29.3)	10(19.2)	

*Data were analyzed using Chi-square test.

Table I shows that over 70% of the case group and 80% of the control group were male with no significant intergroup difference (p = 0.220).

Table-II
Comparison of lifestyle and BMI of the study groups (N=110)

Variables	Group		p value*
	Case (≤ 40 years) (n = 58)	Control (>40 years) (n = 52)	
Lifestyle	0.952		
Active	12(20.7)	11(21.2)	
Sedentary	46(79.3)	41(78.8)	
BMI (kg/m^2)	0.240		
Under weight	3(5.2)	2(3.8)	
Normal BMI	19(32.8)	23(44.2)	
Over weight	20(34.5)	21(40.4)	
Obese	14(24.1)	6(11.5)	
Morbidly obese	2(3.4)	0(0.0)	

*Data were analyzed using Chi-square test.

Table II shows majority of the patients in both case and control groups (79.3 and 78.8% respectively) were accustomed to sedentary life-style, the difference was not statistically significant (p = 0.952). Over half of the patients in both case and control groups were overweight or obese (58.6 and 51.9% respectively). The groups were almost identical in terms of BMI (p = 0.240).sedentary lifestyle was defined as daily engagement of at least 30 minutes or more in moderate to severe exercise[9]

Table-III
Comparison of clinical presentation of the study groups (N=110)

Clinical Presentation	Group		p value*
	Case (≤ 40 years) (n = 58)	Control (>40 years) (n = 52)	
STEMI	28(48.3)	12(23.1)	
NSTEMI	16(27.6)	19(36.5)	0.021
UA	14(24.1)	21(40.4)	

*Data were analyzed using Chi-square (test).

Table III shows while STEMI was considerably higher in the case group compared to the control group, NSTEMI

Table-IV

Comparison of risk factors of the study groups (N=110)

Cardiovascular risk factors	Group		p value*
	Case (≤ 40 years) (n = 58)	Control (>40 years) (n = 52)	
Smoking*	34(58.6)	20(38.4)	0.035
DM*	17(29.3)	19(36.5)	0.420
HTN*	25(43.1)	36(69.2)	0.006
Dyslipidemia*	41(70.7)	24(46.1)	0.009
Family H/o IHD*	30(51.7)	12(23.1)	0.002

*Data were analyzed using Chi-square test.

Table-V

Comparison of biochemical findings of the study groups (N=110)

Biochemical variables#	Group		p value*
	Case (≤ 40 years) (n = 58)	Control (>40 years) (n = 52)	
FBG (m.mol/L)	7.1 ± 3.7	6.0 ± 1.7	0.054
RBG (m.mol/L)	7.4 ± 3.2	7.3 ± 1.8	0.776
Serum creatinine (mg/dl)	0.98 ± 0.7	0.97 ± 0.1	0.945
Total cholesterol (mg/dl)	200.6 ± 49.3	200.2 ± 28.8	0.957
Serum LDL-C (mg/dl)	130.3 ± 42.2	114.6 ± 28.8	0.026
Serum HDL-C (mg/dl)	36.6 ± 4.2	37.0 ± 4.3	0.646
Serum TG (mg/dl)	227.0 ± 134.8	176.3 ± 65.2	0.015

#Data were analyzed using unpaired t-test and were presented as mean ± SD.

Table-VI

Comparison of angiographic profile of the study groups (N=110)

Angiographic profile	Group		p value*
	Case (≤ 40 years) (n = 58)	Control (>40 years) (n = 52)	
Site of lesion*			
LM	3(5.2)	2(3.8)	0.739
RCA	28(48.3)	38(73.1)	0.008
LAD	28(48.3)	45(86.5)	<0.001
LCX	16(27.6)	42(80.8)	<0.001
Severity of lesion#			
Occlusion in LM (%)	67.2 ± 29.5	69.6 ± 29.5	0.919
Occlusion in RCA (%)	86.4 ± 15.5	79.3 ± 23.2	0.165
Occlusion in LAD (%)	80.5 ± 18.9	85.34 ± 14.0	0.209
Occlusion in LCX (%)	83.1 ± 16.1	80.4 ± 23.5	0.657
No. of vessels involved*			
SVD	24(41.4)	12(23.1)	<0.001
DVD	10(17.2)	20(38.5)	
TVD	7(12.1)	20(38.5)	
None	17(29.3)	0(0.0)	

*Data were analyzed using Chi-square; figures in the parentheses denote percentage.
#Data were analyzed using unpaired t-test and were presented as mean ± SD.

and unstable angina were much higher in the latter group, this difference was statistically significant (p = 0.021).NSTEMI was differentiated from UA by having elevated Troponin-I.

Table IV shows risk factors distribution in younger ACS patients had significantly higher prevalence of smoking, dyslipidemia and family history of IHD compared to the elder group (p = 0.035, p = 0.009 and p = 0.002 respectively).In contrast, hypertension demonstrated their significant presence in the latter group compared to that in the former group (p = 0.006).

Table V shows comparison of pertinent biochemical variables reveals that FBS was relatively high in the case group than that in the control group (p = 0.054). The level of serum LDL and serum triglycerides were significantly elevated in the former group than those in the latter group (p = 0.026 and p = 0.015 respectively).

Table VI shows that in younger patients RCA and LAD were commonly involved (48.3% cases) than the LCX (27.6%), where as in elder patients all the major coronary arteries were almost equally involved. Site of lesions were more in elder group than that in younger group. However, in terms of percentage of occlusion, no significant difference was observed between the groups with respect to any of the major coronary arteries. While SVD was common in the case group, DVD and TVD were prevalent in the control group which was statistically significant (p < 0.001).

Discussion:

In the present study majority of the ACS patients in either group were male although earlier studies reported that ACS occurs more in males than in females in younger age.[10,11] CAD is much less frequent in premenopausal women due to the effect of estrogen; as the protection from CAD is much less evident after menopause, the disease affects both sexes equally.[12]In a recent study however, researchers have found that young women who are current smoker and obese are more likely to suffer from ACS.[13]

Among the conventional risk factors smoking, dyslipidemia and positive family history of IHD were the most prevalent cardiovascular risk factors (CVRFs) in the younger patients (58.6, 70.7 and 51.7% respectively) which was statistically significant (p = 0.035, p = 0.009 and p = 0.002 respectively). Whereas hypertension was the most prevalent established CVRF in the elderly group (69.3%) which was statistically significant (p = 0.006).

In terms of clinical presentation, STEMI was the most common form of ACS in younger group (48.3%), whereas NSTEMI and UA were significantly higher in the older group (36.5 and 40.4% respectively) (p = 0.021).Several studies have shown that STEMI is the most common form of ACS in young. Bhattacharjee et al. 2014.[14] in a recent study found that STEMI is significantly more common in younger patients. In a Thai ACS Registry study, 67% young ACS patients had STEMI.[15]On the other hand, NSTEMI and UA have been reported to be more common in the elderly.[16,17] Similar finding has been observed by another group where majority (70%) of the young patients with ACS presented with STEMI.[18]

Mean FBG was relatively high in the case group than that in the control group (p = 0.054). Serum LDL-C and serum triglycerides levels were significantly higher in the former group than in the latter group (p = 0.026 and p = 0.015, respectively).The study demonstrates that younger patients have lesser number of coronary artery involvement and less severe disease (in terms of percentage of occlusion and number of vessels involved) compared to elderly(p = <0.001). They also have fewer complications than the older cohorts in terms of cardiogenic shock and recurrent angina than their older counterparts (p = 0.023 and p < 0.001 respectively).

This study showed that younger patients have lesser number of coronary artery involvements and less severe disease (in terms of percentage of occlusion and number of vessels involved) compared to the elderly. They also have less complications than their older counterparts. Consistent with these findings Bhattacharjee showed prevalence of no. of vessels involvement and SVD to be significantly higher in younger ACS patients while multi-vessel disease is more common in the elderly. Similar findings have been reported by other authors.[19,20] The less extensive CAD observed in younger patients in our study might suggest that premature CAD is associated with rapid disease progression rather than with a gradually evolving process. This is in agreement with the finding that ACS is the common first presentation in younger patients.[21]

The study had few limitations including small sample size and a single center study. Syntax orGensini scores indicating severity of the involvement of the coronary arteries and Medina Classification indicating the type of lesion have not been included in the study as a variable. Because of resource constraint we could not include the emerging cardiovascular risk factors like serum homocystine, high sensitivity C-reactive protein, serum Lp(a), Chlamydia pneumoniae IgG antibody, Vitamin D level.

Conclusion:

Younger ACS patients had significantly higher prevalence of smoking, dyslipidemia and family history of IHD compared to the elder group, whereas elderly ACS patients were more prone to be associated with hypertension. Young ACS patients frequently presented with STEMI and single vessel disease whereas elderly

patients frequently presented with NSTEMI and UA with more severe and extensive CAD.

At the end of this study we recommend early risk stratification, identification of the disease and its management may prevent fatal outcomes in a large number of cases. Particularly smoking cessation in the younger population is strongly advocated to lower the ACS risk, further large-scale multicenter study is needed to elucidate the roles of these risk factors so that appropriate policy making and public health measures can be taken to prevent premature CAD in the young people.

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Original Article

Effect of Successful Percutaneous Transvenous Mitral Commissurotomy on Pulmonary Function

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Abstract:

A total of 58 patients of severe mitral stenosis with Wilkins score < 10 were studied, all of them underwent PTMC. Spirometry and peak expiratory flow rate were done before and after PTMC. A follow up echocardiographic assessment of successful PTMC and pulmonary artery systolic pressure were taken. Two patients died of PTMC related procedural complications. There was no dropout. Hemodynamic measurements obtained by echocardiography showed improvement of mean mitral valve area from 0.764 ± 0.1257 cm^2 to 1.404 ± 0.1194 cm^2 after PTMC (p < 0.001). Transmitral peak pressure gradient decreased from 26.43 + 5.62 mmHg to 11.36 + 2.40 mmHg after PTMC (p < 0.001). Pulmonary artery systolic pressure was decreased from 57.73 ± 17.03 mmHg to 31.27± 8.30 mmHg after the procedure (p < 0.001). pulmonary functions - The mean FEV_1 was increased from 60.18 ± 13.054 to 78.32 ± 11.874 after PTMC (p<0.001). The mean FVC was 53.80+ 12.313 before PTMC, which significantly improved to 68.57 + 11.662. PEF also showed an improvement from 223.75 + 62.3215 to 372.05 + 62.2. (p<0.001).

Key Words: Mitral stenosis, PTMC, Pulmonary function test

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Introduction:

Many patients of mitral stenosis in Bangladesh present with respiratory symptoms, and are often treated as bronchial asthma or chronic obstructive airway disease. Impaired pulmonary function may be an important contributor to overall morbidity and mortality in our country, where the patients often present late. In a more recent community based study on 5925 rural Bangladeshi children aged 5-15 years, the prevalence of rheumatic fever and rheumatic heart disease was found to be 1.2 per 1000 for rheumatic fever defined by Revised Jones Criteria and 1.3 per 1000 for Doppler echocardiography-defined rheumatic heart disease.[1]

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Although the pathogenesis of pulmonary function abnormality in mitral stenosis is not fully known, it is certain that the chronic changes in pulmonary circulation secondary to increased pulmonary venous pressure and reflex pulmonary artery vasoconstriction cause alterations in pulmonary vessels and in the composition of lung tissue.[2] Accumulation of water, proteins, and proteoglycans in the interstitium has been acknowledged in this condition. These interstitial changes are the basis of the clinical manifestations of mitral stenosis and can be detected by pulmonary function tests.[3] Several propositions are known to contribute to the pathogenesis of airflow obstruction in patients with mitral valve disease. Hypertrophied and hyperplastic airway smooth muscle and increased wall thickness are also heightened along with bronchial hyper-reactivity.[4]

Thus, the effect is completely mechanical one and depends on the degree of stenosis of mitral valve. The major act of affray comes into account from several studies are reduction in pulmonary compliance ventilation-perfusion mismatch,

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reduction in diffusion capacity, increased "pulmonary capillary blood volume" and hyperventilation in exercise in relation to the oxygen uptake.[2,4,5]

Majority of ventilatory functions impairment caused by hemodynamic alteration are mainly reversible.[2] In the present study, the pulmonary functions and echocardiography were done before and after PTMC in an order to observe the effect of PTMC on lung function test in severe mitral stenosis patients.

Materials and methods:

58 patients with severe mitral stenosis eligible for percutaneous transvenous mitral commissurotomy (PTMC) were enrolled with informed written consent. Concomitant mild aortic stenosis was taken under consideration. Exclusion criteria included chronic obstructed airway disease (COPD), bronchial asthma (BA), interstitial lung disease, smoker, left ventricular EF <55%, neurological disease and other valvular heart diseases, spinal deformities, age >40 years. Lung causes were excluded by taking history, chest x-ray and pulmonary function test and high resolution computed tomography of chest where needed. Demographic data such as, age, sex, height (cm), weight (kg) and BMI (kg/m^2) were also recorded. Symptoms were assessed by New York Heart Association (NYHA) functional status.

Transthoracic M-mode, two-dimensional and Doppler echocardiography was done in all patients before and after PTMC. Diagnosis was confirmed by two-dimensional surface area and Doppler ultrasound-derived pressure half-time methods. Wilkins score was applied to assess the Mitral valve morphology, the degree of mitral regurgitation was assessed by Doppler study. Patients with favorable morphology of mitral valve were selected, and a transesophageal echocardiography was performed to exclude the presence of left atrial thrombus in selected patients. Pulmonary arterial systolic pressure was measured.

Spirometry and measurement of peak expiratory flow rate was done in every patient, 2 to 3 days before and 7 days after PTMC. Spirometry was performed according to the American Thoracic Society recommendations. The following parameters were recorded: FVC, FEV_1, FEV_1/FVC, and peak expiratory flow (PEF). FVC and FEV_1 was expressed as percentage predicted and PEF expressed as liter/min.[5,6,7,8]

Only mitral stenosis patients with favorable valve morphology (Wilkins score ≤10) were selected for PTMC; PTMC was done by a transseptal antegrade technique using the Inoue balloon.

Successful commissurotomy was considered as an MVA >1.5 cm^2 or >50% increase in mitral valve area in absence of complications including severe mitral regurgitation (>grade II) and/or a large atrial septal defect (<1.5:1 left-to-right shunt) which was confirmed by both auscultatory method and Doppler echocardiography.[9]

Results:

58 patients were enrolled in this study but 2 patients died due to procedural complications. So, calculation was done on 56 patients. The majority of the respondents were female 46 (82.14%), and the remaining 10 (17.86%) were male. Among the female patients, maximum were > 20 year age group (n=34, 60.71% of total). The majority of the male subjects (n=8, 14.29%) were above 20 years. (Table I)

Table-I

Distribution of the study subjects by age and sex. (n=56)

Age group	Sex		Total
	Male	Female	
<20 years	23.57%	1221.43%	1425%
>20 years	814.29%	3460.71%	4275%
Total	1017.86%	4682.14%	56100.0%
Mean + SD			28.76 ± 7.2

Before PTMC, 36 patients (64.3%) patient were in NYHA class II, 19 patients (33.9%) were in NYHA class III. After successful PTMC, majorities (37 patients, 66.1%) switched over to NYHA class I and remaining 18 patients (32.1%) were in NYHA function class II. (Table II)

Table-II

Distribution of patients by NYHA functional class (n = 56)

NYHA	Before PTMC		After PTMC	
class	Frequency	Percentage	Frequency	Percentage
I	0	0	37	66.1
II	36	64.3	18	32.1
III	19	33.9	1	1.8
IV	1	1.8	0	0
Total	56	100.0	56	100.0

The mean mitral valve area increased from 0.764 ± 0.1257 cm^2 to 1.404 ± 0.1194 cm^2 after PTMC ($p < 0.001$). Transmitral peak pressure gradient decreased from 26.43 + 5.62 mmHg to 11.36 + 2.40 mmHg after PTMC ($p < 0.001$). Mean left atrial diameter (mm) before and after PTMC were 47.23 ± 5.35 mm and 40.18 ± 5.557 mm respectively ($p < 0.001$). Pulmonary artery systolic pressure increased from 57.73 ± 17.03 mmHg to 31.27± 8.30 mmHg after the procedure ($p < 0.001$). (Table III)

Almost all the patients had restrictive type of pulmonary function and only 2 patients showed obstructive pattern. The mean FEV_1 was 60.18 ± 13.054% before PTMC, which increased to 78.32 ± 11.874% after PTMC ($p < 0.001$). The mean FVC improved from 53.80+ 12.313% to 68.57 + 11.662% ($p < 0.001$). PEF also showed an improvement from 223.75 + 62.3215 l/min to 372.05 + 62.2 l/min. The statistics shows that, changes of FVC and PEF after PTMC were highly significant ($p < 0.001$). It is noted that, the effect of PTMC on FEV_1/FVC was insignificant ($p = 0.33$). (Table IV)

There was no significant correlation between pulmonary artery systolic pressure and FVC before and after successful PTMC. (Figure 1 and 2)

Table-III

Comparison of echocardiographic findings before and after PTMC (n=56).

Echocardiographic findings	Group		*p* value
	Before PTMC	After PTMC	
Mitral valve area (square cm)	0.764 ± 0.1257	1.404 ± 0.1194	<0.001
Transmitral peak pressure gradient (mmHg)	26.43 ± 5.62	11.36 ± 2.4000	<0.001
Left atrial diameter (mm)	47.23 ± 5.350	40.18 ± 5.557	<0.001
Pulmonary artery systolic pressure (mmHg)	57.73 ± 17.03	31.27± 8.30	<0.001

Paired t- test was done to analyze the data and presented as mean ± SD.

Table-IV

Comparison of pulmonary function test findings before and after PTMC. (n=56)

Pulmonary function test findings	Group		p value
	Before PTMC	After PTMC	
FEV_1	60.18 ± 13.054	78.32 ± 11.874	<0.001
FVC	53.80 ± 12.313	68.57 ± 11.662	<0.001
FEV_1/FVC	112.64 ± 16.292	114.98 ± 12.714	0.330
PEF	223.75 ± 62.3215	372.05 ± 62.200	<0.001

Paired t- test was done to analyze the data and were presented as mean ± SD.

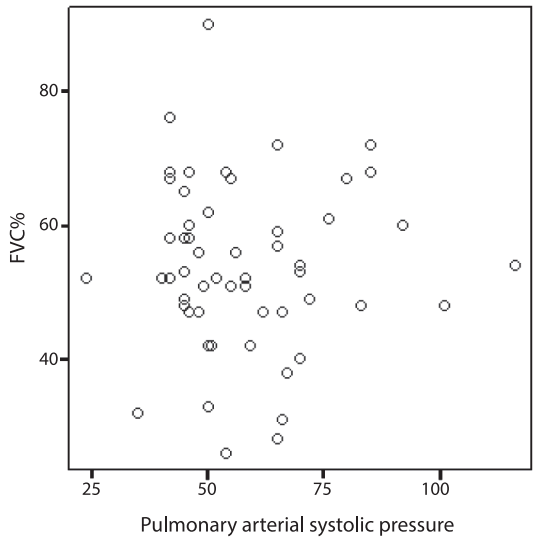

Fig.-1: *Correlation between FVC and PASP before PTMC. (r=000; p>0.05).*

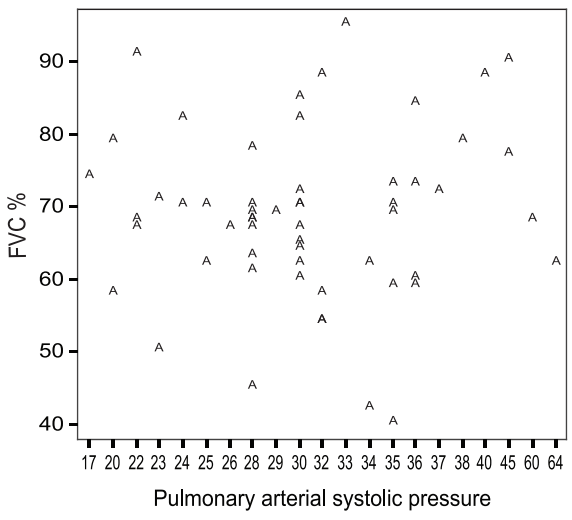

Fig.-2: *Correlation between FVC and PASP after PTMC. (r=0.028; p>0.05)*

Discussion:

Pulmonary function deterioration in mitral stenosis patients has been elucidated previously and certain reversible effects were also demonstrated.[1]

In the present study, young age and female preponderance were observed. All patients had severe mitral stenosis. Seven days after the procedure a dramatic improvement in functional status of all the patients were demonstrated. Patients felt significant relief of dyspnea which was assessed by NYHA class stratification. All hemodynamic parameters including Pulmonary artery systolic pressure (PASP), mitral valve gradient, mitral valve area significantly improved after PTMC those are also supported by other studies.[2,9] A greater reduction of pressure gradient across mitral valve was observed due to increase in mitral valve area.[10]

Different parameters of lung function improved after PTMC. FEV_1 improved significantly post PTMC. FVC and PEF also increased significantly after the procedure. The changes of these parameters were highly significant ($p<0.001$). However, the changes in FEV_1/FVC did not reach statistical significance ($p=0.33$). In another study, there was significant improvement in FVC after PTMC, but FVE_1/FVC change was not significant statistically.[2] In their study, GÌmez-Hospital et al. found significant improvement in FVC and FEV_1, but not in FEV_1/FVC and PEF.[3]

In the current study, out of 56 non-smoker patients, 2 cases had obstructive type airway flow limitations and rest of the patients had restricted type of features on pulmonary function before PTMC. Previous studies found mostly obstructive pattern of defect in pulmonary function, but those involved mostly moderate mitral stenosis patients.[3,11] The restrictive features which are encountered in the chronic stages of lung congestion are attributed to increased interstitial fluid, increased pulmonary blood volume, muscle fatigue, decreased lung compliance, and fibrosis from chronic congestion.[12] Both obstructive and restrictive type of lesions in pulmonary function test were demonstrated in patients with congestive heart failure, as well as, in those with mitral stenosis.[13,14] Simkova and Urbanova found restrictive, as well as, obstructive ventilatory disturbance in patients with mitral stenosis.[11]

Almost all patients got improvement of their ventilatory function after PTMC which is due to alteration of reversible pulmonary haemodynamics. This study showed significant increase in FVC and FEV_1 (percent predicted) and PEF after successful PTMC but there is no significant change in FEV_1/ FVC ratio after PTMC. As a result of improvement on pulmonary hemodynamics, increase in FVC and FEV_1 (percent predicted) may be due to improvement on pulmonary compliance which might be derived from improvement in pulmonary hypertension and decrease in pulmonary venous congestion. It is suggested that the increase in distribution of cardiac output after PTMC to respiratory muscle might change the force of diaphragm and other respiratory muscle causing increase in value of FEV_1 and FVC.[4] In a study, post procedural pulmonary function tests revealed significant improvement of FVC and TLC, i.e. disappearance of restrictive pattern on long term follow up.[11]

Lack of correlation is observed in the present study between FVC and PASP before and after PTMC whereas one study found correlation between the FVC and PASP before PTMC but no correlation after PTMC, probably due to noncorresponding improvement of vital capacity in relation to PASP. There is no striking relationship between cardiac defect and respiratory abnormality and the closest being the inverse one between vital capacity and PASP after PTMC.[5] Maximum breathing capacity correlated poorly with mean pulmonary artery pressure and explanation in favour of this that many of these patients were on prolonged bed rest and thus induced muscular fatigue probably introduced an independent variable factor in the reduction of maximum breathing capacity.

Patients sensed relief of dyspnea immediately after dilatation of the valve corresponding with hemodynamic changes. Significant decrease of NYHA class was detected early after correction of mitral stenosis except in 2 cases where patients died due to procedural complications. Almost all studies mentioned above found symptomatic improvement and decrease in NYHA functional class.

Conclusion:

From this study, it may be concluded that patients with severe mitral stenosis have impaired pulmonary function which is of restrictive type. Symptom often does not correlate with the severity of the disease. Successful PTMC improves pulmonary function, as well as, clinical status. So, PTMC should be done in suitable cases to reduce morbidity in mitral stenosis. Also, assessment of lung function in patients with mitral stenosis may aid in timely decision-making before adopting the interventional strategy of treatment.

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Original Article

Age Distribution of Aortic Sclerosis among Bangladeshi Population

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Abstract:

Aortic sclerosis (ASc) is defined as thickening or calcification of the aortic valve without significant obstruction of blood flow. Aortic sclerosis is diagnosed when in echocardiography, thickening and calcification of one or more cusps of a tricuspid aortic valve is manifested, whereas in aortic stenosis, cusp separation is restricted and the velocity through the aortic valve is > 2.5 m/s. Its prevalence increases with age. Aortic valve stenosis is associated with systemic endothelial dysfunction, and it carries a 50% increase in risk of cardiac death or myocardial infarction. As aortic sclerosis has proved to be more and more relevant in recent days, it has been important to identify epidemiological data and demographic information of aortic sclerosis in Bangladeshi population. This study tried to determine age distribution of aortic sclerosis in Bangladehsi population.

Median age of aortic sclerosis patients was 65 years (mean 67 ± 12 years), most of the patients (17.2%) were in 56-60 years of age group. The same statement holds correct for females, where highest number of patients (7.7% of total patients) were in the same age group. For the males, the highest number of patients (11% of total patients) were in 61-65 years of age group. The minimum age was 45 years for both males and females. Although the minimum age is same for both sex, females are affected a bit earlier than males, and statistically significant difference was found between mean ages of two sexes. Most of the aortic sclerotic patients are below the usually used age cut off of 65 years. There is significant difference between mean age of presentation of aortic sclerosis between males and females. Further study should be undertaken to understand these effects more clearly.

Keywords: Aortic Valve, Cardiology, Sclerosis, Echocardiography, Age distribution.

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Introduction:

Aortic sclerosis (ASc) is defined as thickening or calcification of the aortic valve without significant obstruction of blood flow.[1] Aortic sclerosis is diagnosed when in echocardiography, thickening and calcification of one or more cusps of a tricuspid aortic valve is manifested, whereas in aortic stenosis, cusp separation is reduced and the velocity through the aortic valve is > 2.5 m/s.[2] Its prevalence increases with age.[1,3] In the Monica-KORA study of 935 European adults aged 35 to 84 years, the prevalence of aortic sclerosis increased across the age distribution from 7 percent in those age 35 to 44 years to 65 percent in those age 75 to 84 years.[4] Aortic valve sclerosis is associated with systemic endothelial dysfunction,[5] and it carries a 50% increase in risk of cardiac death or myocardial infarction.[2] In 2279 middle aged African Americans, the presence of aortic sclerosis conferred a hazard ratio of 3.8 for myocardial

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infarction or fatal coronary heart disease after adjustment for multiple risk factors.[6] It is also found that AV sclerosis is associated with several CV risk factors and predicted CV events independently of prevalent CV disease and traditional CV risk factors, including LV mass and ejection fraction.[7] Sui et.al. found that there were significant similarities in clinical risk factors, histopathological alterations of AVS and coronary atherosclerosis.[8] Kim et.al. found that aortic valve sclerosis on echocardiography is a good predictor of coronary artery disease in patients with an inconclusive treadmill exercise test.[9] As aortic sclerosis has proved to be more and more relevant in recent days, it has been important to identify epidemiological data and demographic information of aortic sclerosis in Bangladeshi population. This study tried to determine the age distribution of aortic sclerosis in Bangladeshi popualtion.

Methods:

Sampling technique

The patients were included from a diagnostic center, by consecutive sampling technique. All the patients that met the criteria of aortic sclerosis were included in this study. Enrollments of patients were done over one-year period.

Two-dimensional transthoracic echocardiography

2D transthoracic echocardiography was performed using a 4 MHz Sequoia C256 probe (Medison Inc,). 2D echocardiographic tests and Doppler tests were performed following the Standard Practical Guideline for 2D echocardiography from the American Society of Echocardiography.[10] The area of the aortic valve orifice on the sternal left margin was measured using a static image in which the 3 cusps were most widely open, while the aortic valve blood flow speed was measured in the apical 5-chamber view using a continuous wave Doppler.[9] These measurements were taken three times and the average was used in analysis.

Aortic valve sclerosis measurement

Using a long axis view of the left sternal margin, valve thickness was defined as the value obtained by enlarging the area of the aortic valve, and measuring the thickest part of the right coronary aortic cusp as well as the non-coronary aortic cusp during the systolic period. Using a short axis view of the left sternum margin, when movements of the right coronary aortic cusp and non-coronary aortic cusp during the systolic period were examined by enlarging the aortic root, a valve opening inward concave was defined as normal, whereas a valve opening inward flat or inward convex was defined as showing restricted motion.[11]

Definition of aortic sclerosis

Patients were included as case of aortic sclerosis if they showed one the following criteria on trans-thoracic echocardiogram (TTE):[9,12,13]

1. Aortic cusp thickness was >2 mm
2. Aortic valve cusps showed restricted motion.

AND,

3. Aortic jet velocity (m/s) $\leq$2.5 m/s.[13,14]

Exclusion criteria

1. Patients who did not meet either of the first two criteria.
2. Patients who did not give consent.

Statistical analysis

Statistical analyses were done with Statistical Package for Social Sciences (SPSS) version 23 (IBM Corporation, USA). Descriptive statistics and graphs are derived, and independent Student's t test and Mann-Whitney U test were employed to determine any significant differences between means.

Result:

A total of 209 patients were selected in this study, among which 135 (64.59%) were male and 74 (35.41%) were female (Figure 1).

Age distribution of the different sex groups are shown in Table 1 and 2 and Figure 2 and 3.

An independent sample t test and Mann-Whitney U test were employed assessing differences between mean age of male and female, both came significant (p=0.014, Table 3).

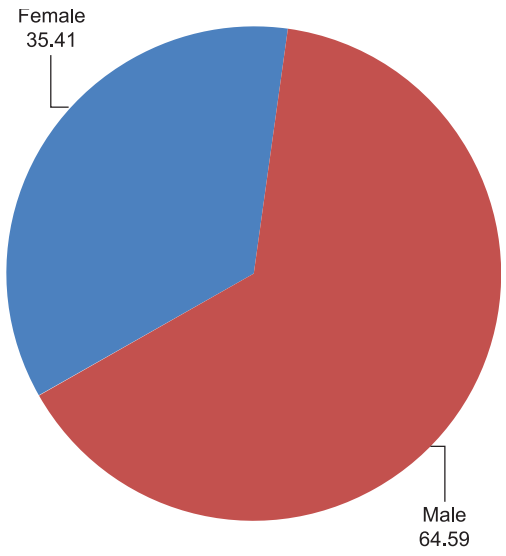

Fig.-1: *Sex distribution*

Table-I

Age distribution of the patients in different sex groups

			Mean	Median	Minimum	Maximum	Standard Deviation
Age	Sex	Male	68	70	45	100	12
		Female	64	65	45	90	11
		Total	67	65	45	100	12

Table-II

Percentage of patients in different age groups

		Sex					
		Male		Female		Total	
		Count of total %	Percentage	Count of total %	Percentage	Count of total %	Percentage
Age Categories	41-45	3	1.4%	1	0.5%	4	1.9%
	46-50	7	3.3%	12	5.7%	19	9.1%
	51-55	12	5.7%	7	3.3%	19	9.1%
	56-60	20	9.6%	16	7.7%	36	17.2%
	61-65	23	11.0%	7	3.3%	30	14.4%
	66-70	22	10.5%	13	6.2%	35	16.7%
	71-75	13	6.2%	9	4.3%	22	10.5%
	76-80	20	9.6%	5	2.4%	25	12.0%
	81-85	8	3.8%	1	0.5%	9	4.3%
	86-90	4	1.9%	3	1.4%	7	3.3%
	91-95	0	0.0%	0	0.0%	0	0.0%
	96-100	3	1.4%	0	0.0%	3	1.4%
	Total	135	64.6%	74	35.4%	209	100.0%

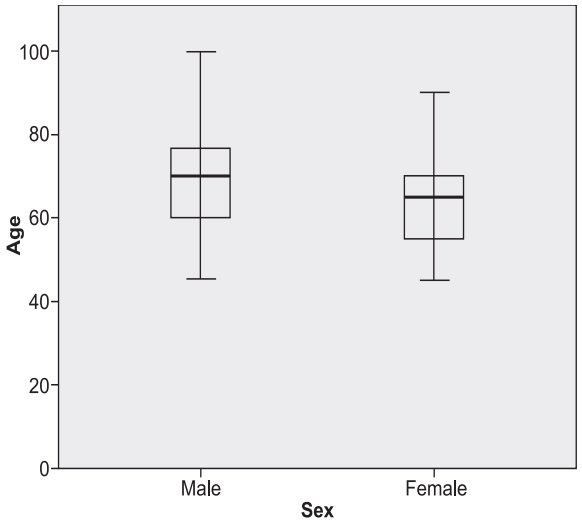

Fig.-2: *Age distribution of the patients in different sex groups*

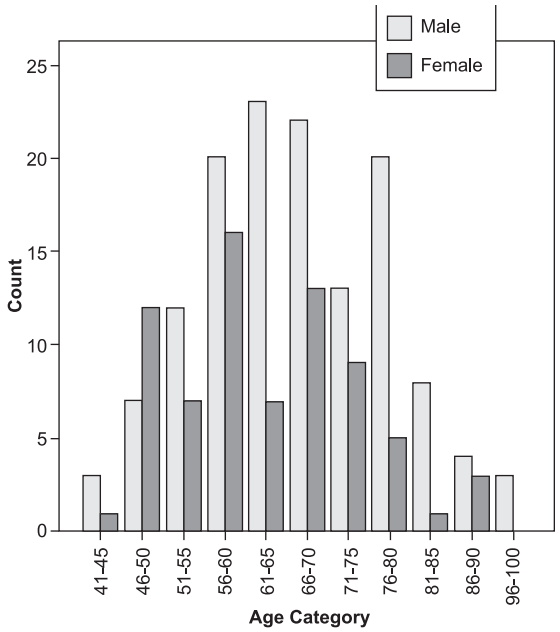

Fig.-3: *Percentage of patients in different age groups*

Table-III

Independent sample t test between two sex groups

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	P value	t	df	P value (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference Lower	Upper
Age	Equal variances assumed	.225	.636	2.468	207	.014	4.063	1.646	.818	7.309
	Equal variances not assumed			2.517	159.097	.013	4.063	1.614	.875	7.252

Discussion:

From the results, it is evident, that although median age of aortic sclerosis patients was 65 years (mean 67 ± 12 years), most of the patients (17.2%) were in 56-60 years of age group (Table 2, Figure 3). The same statement holds correct for females, where highest number of patients (7.7% of total patients) were in the same age group. For the males, the highest number of patients (11% of total patients) were in 61-65 years of age group. The minimum age was 45 years for both males and females irrespectively. From the boxplot (Figure 2), we can see the picture more clearly. Although the minimum age is same for both sex, females are affected a bit earlier than males, and statistically significant difference was found between mean ages of two sexes (Table 3).

In a meta-analysis, collecting information from 22 studies, Coffey et.al. found an increase of 1·5% in prevalence per year of increase in average age of study participants (95% confidence interval 0·75 to 2·25%, p=0·0007, R^2 0·549). This data is consistent with our findings, which shows most of the patients are from geriatric age groups. Völzke et.al. and Stewart et.al. reported age is an independent risk factor for aortic sclerosis.[15,16]

Stewart et.al. reported 5,201 subjects with >65 years of age enrolled in the Cardiovascular Health Study, aortic valve sclerosis was present in 26% and aortic valve stenosis in 2% of the entire study cohort; in subjects > 75 years of age, sclerosis was present in 37% and stenosis in 2.6%.[16] Stewart et. al. also reported in subjects > 75 years of age, prevalence of sclerosis is 37%.[16] But, in our study, 51.7% patients were below or up to 65 years of age, and 21% of patients were above 75 years of age. The reason for this may lie in the fact that many studies have been done where first a specific age group has been selected, and then the prevalence of aortic sclerosis or other CV outcomes statistics are determined in that age group.[17] But we took a different approach and enrolled patients by consecutive sampling which allowed us to determine demographic information including age, etc. not restricted to some specific group. It is clearly seen in this study that most of the aortic sclerotic patients are actually below the usually used age cut off of 65 years.

In the Monica-KORA study of 935 European adults aged 35 to 84 years, the prevalence of aortic sclerosis increased across the age distribution from 7 percent in those age 35 to 44 years to 65 percent in those age 75 to 84 years.[4] But in our study, we had only 1.9% patients in 41-45 years age group, 16.3% in 76-85 years age group.

It is well known that there are sex-related differences in atherosclerosis progression, plaque composition and prevalence of microvascular disease.[18] But the differences of age of presentation of aortic sclerosis in different sexes are not well documented. In our study, there was significant difference between mean age of male and females. This finding contrasts with the results reported by Aksoy et.al. who did not find any such difference.[19]

Conclusion:

Most of the aortic sclerotic patients are actually below the usually used age cut off of 65 years. There is significant difference between mean age of presentation of aortic sclerosis between males and females. Further study should be undertaken to understand these effects more clearly.

List of abbreviations

ASc = Aortic sclerosis

CV = Cardiovascular

LV = Left ventricle

TTE = Trans-thoracic echocardiogram

Conflict of interest: None

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Case Report

A Case Report of Stroke in a Young Recreational Drug Abuser with Left Ventricular Apical Myxoma with Lupus Nephritis, Secondary Antiphospholipid Syndrome and Homocysteinemia

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Abstract:

In young adults 20%-47% cases of stroke is due to cardiac embolism. Cardiac Myxoma is an infrequent cause of embolic stroke in young. We are reporting a case of a ischemic stroke in a young adult of 34 years with a history of recreational drug use who was eventually diagnosed with Left Ventricular Apical Myxoma, Systemic Lupus Erythematous (SLE), Lupus Nephritis, Secondary Anti phospholipid Syndrome, Hyper homocysteinemia, and Dyslipidemia.

Keywords: *Stroke, Young Adult, Myxoma, Lupus Nephritis, Homocysteinemia*

(Bangladesh Heart Journal 2017; 32(1) : 55-61)

Introduction:

Stroke is often considered a disease of older people, but an estimated 10% of patients with stroke are younger than 50 years[1]. Many of them have no risk factors for atherosclerosis and no ultimate clear etiological diagnosis even after a thorough investigation. This diagnostic challenge is one of the main scopes of studying and researching mechanisms of brain ischemia in young adults in addition to the dramatic personal, familial, and socio-economic consequences by affecting individuals at the top of their productive age.

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Cardioembolism and cervicocephalic arterial dissection have been established as principal etiological factors of IS in young adults[2], The proportion of cardioembolic strokes in young adults varies from 20% to one third[3,4].

Considered an unusual cause of IS in the young two decades ago[5], atherosclerosis has gaining projection by recent reports of significant raise in traditional risk factors as hypertension, diabetes, obesity, dyslipidemia and tabagism among hospitalized adolescents and young adults[6].

Only 1-4% of IS are related to acquired and genetic thrombophilias, but these numbers seem higher in young adults[7]. The most common acquired thrombophilia associated to IS in the young is antiphospholipid syndrome. Antiphospholipid antibodies, particularly lupus anticoagulant, are an independent risk factor for IS in young adults[8]. Genetic prothrombotic states play an important role in young patients with cerebral venous thrombosis, but thrombophilia alone rarely causes arterial occlusions[9].

We herein report a case of a young adult male who was diagnosed as having Ischemic stroke with right sided hemiplegia and Left Ventricular Apical Myxoma, as well as multiple other comorbidities, each of which are capable of causing recurrent stroke.

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Case report:

A 34 year old non diabetic, normotensive gentleman presented on 17th, April 2016 with sudden onset right sided weakness and speech difficulty for twelve hours. He had no loss of vision, diplopia or dizziness. He gave no history of headache, vomiting, convulsion or loss of consciousness. On further query, he denied having any rash, arthralgia, chest pain, palpitation, breathlessness, or syncope. He had no relevant family history, but he was a chain smoker (20 pack year) and had a history of Cannabis abuse. Examination revealed he was drowsy with normal vital signs. Neurological examination showed nonfluent aphasia and right hemiplegia .Examination of the other systems revealed no abnormality.

CT scan of the brain (Figure 1) showed early signs of infarction the loss of 'insular ribbon' sign. MRI of the brain (Figure 2) showed an embolic acute large left MCA territory infarct with midline shifting and effacement of the left lateral ventricles.

ECG (Figure 3) showed sinus rhythm with anterolateral ischaemia and Chest X-Ray was normal. CBC: Hb-11.5g/dL, WBC- 9,100/cm^{3-}, Platelet- 1,32,000/cm^{3-}, ESR-42mm in 1st hour. Urine R/M/E revealed Pus cell:1-2/HPF, Epithelial cell:0-3/HPF, RBC: Occasional, Protein: ++. S. electrolytes, renal function tests and liver function tests were within normal range.

Evaluation of the patient by Transthoracic echocardiography (Figure 4) revealed an inhomogeneous, contractile,

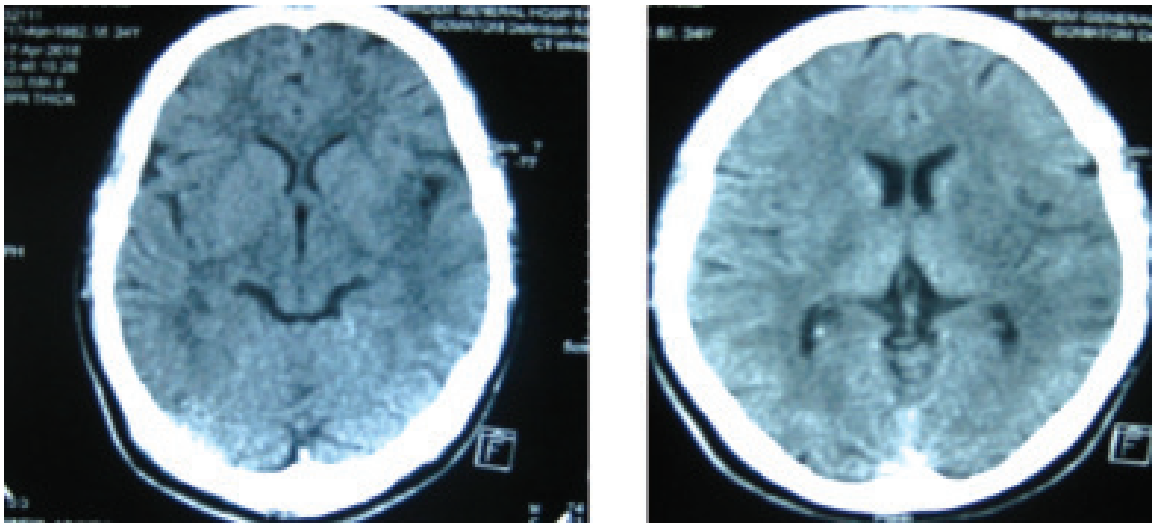

Fig.-1: *CT Scan Brain showing the loss of 'insular ribbon' sign on left cerebral hemisphere*

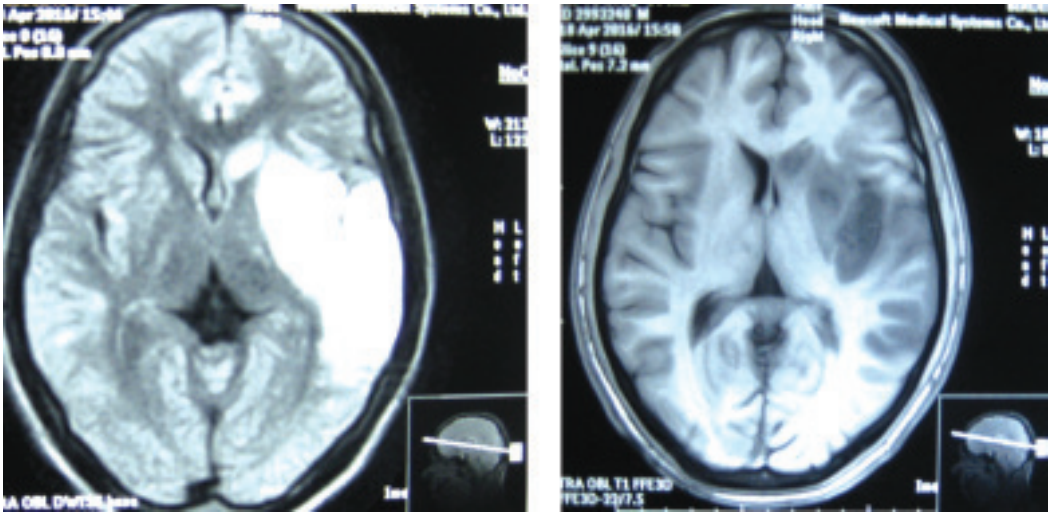

Fig.-2: *MRI of Brain showing acute large left MCA territory infarction with midline shifting and effacement of the left lateral ventricles.*

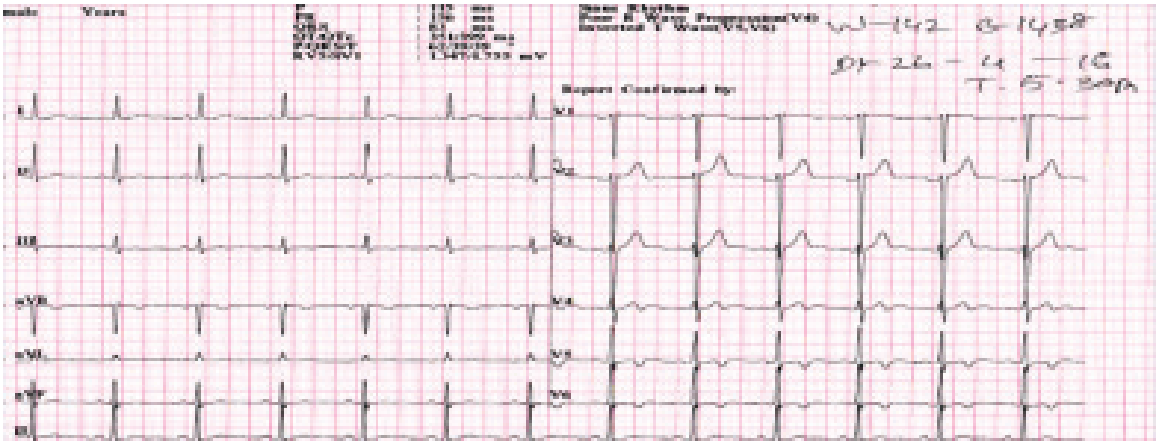

Fig.-3: *ECG showing normal sinus rhythm and anterolateral ischaemia.*

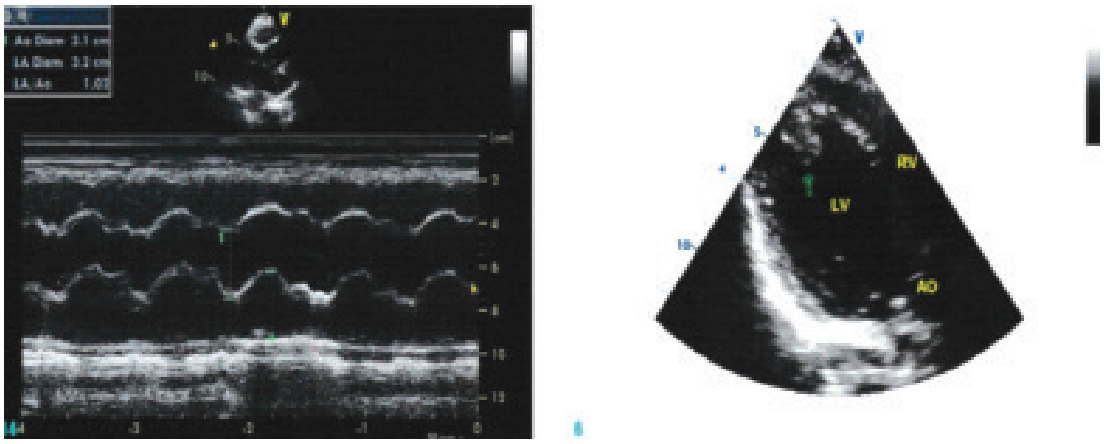

Fig.-4: *Transthoracic echocardiography showing a pedunculated heterogeneous mass (arrow) in the left ventricle.*

pedunculated, echogenic mass (measuring 19 × 16 mm) attached to the apical septum of left ventricle strongly suggestive of Left ventricular Apical Myxoma. No LV regional wall motion abnormality was detected and LV ejection fraction of 65%.

Following a consultation with Cardiac Surgeon, a Transoesophageal echocardiography (TEE) was done which showed the Myxoma with non-organized thrombus or vegetation attached with it (Figure 5).

Investigations to detect risk factors for stroke in young adults done in our patient were S. Homocysteine: 30.1 µmol/l, VDRL: non-reactive, TPHA: non-reactive, Anti phospholipid antibody: 40 U / ml (Positive), ANA: Positive (>1.5), Anti ds DNA: Positive 27 U/ml (>25 U/ml). Toxicology screen for Urine was Positive for Cannabinoids. Further investigations included PBF which showed nonspecific morphology with neutrophilia and thrombocytopenia. Blood culture showed no growth. PT: 13.4 sec; INR: 1.1 . Doppler study of neck vessels revealed: Bilateral mild atherosclerosis with no limitation of flow.The patient was not evaluated for Protien C and ProteinS deficiency.

Macroscopic hematuria and high titre of ANA and positive ds DNA warrented further investigation. Phase contrast microscopy of urine was done and it showed 3-5 RBC/ HPF, (10% dysmorphic). 24 hours urinary total protein estimation was 1.00 gm/day, Ccr: 62 ml/min. USG of whole abdomen showed mild swelling of both kidneys. Renal biopsy (Figure 6) revealed mesangial proliferative lupus nephritis (Class-II Lupus nephritis). Serum C3 and C4 levels were within normal range. Vasculitis markers including c-ANCA and p-ANCA were negative.

The patient was initially treated with I.V Mannitol, Aspirin, Pantoprazole, Losartan Potassium, Folic acid , Vitamin B6, Vitamin B12 combination, Atorvastatin and daily physiotherapy. The final treatment was modified after

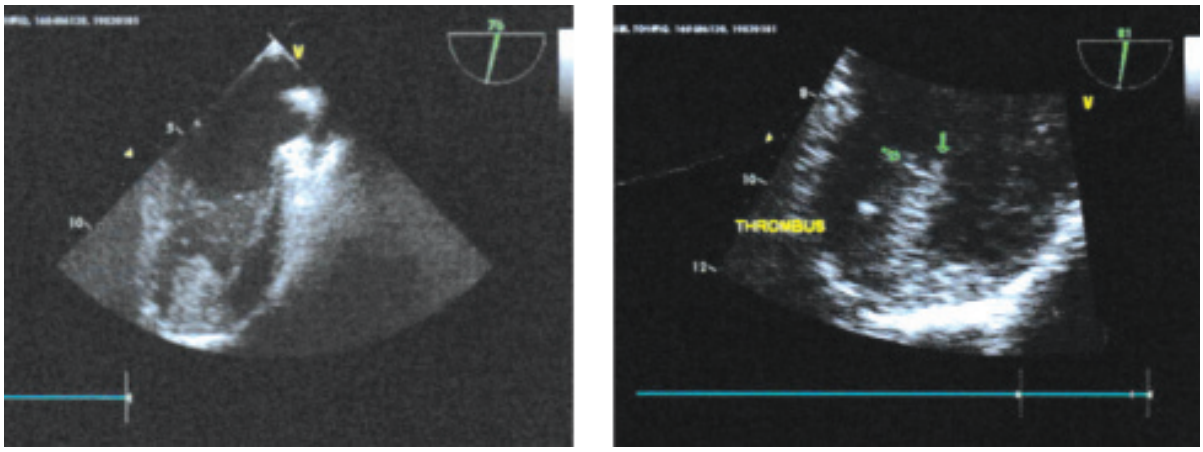

Fig.-5: *Transeosophageal Echo showing Left ventricular apical Myxoma with non-organized thrombus or vegetation.*

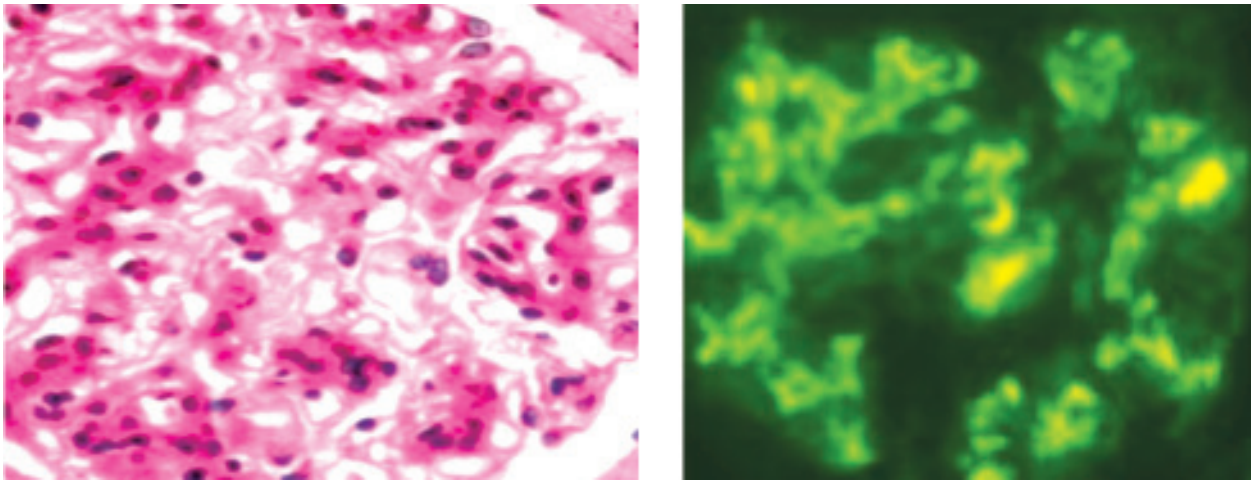

Fig.-6: *Mesangial proliferative lupus nephritis (Class-II lupus nephritis).*

Consultation with Cardiac Surgeon and Nephrologist and it included Warfarin keeping international normalized ratio value between 2 and 3 and Hydroxychloroquine Sulphate (200mg) once daily. After improvement of general condition he was discharged with advice to follow up in the OPD with PT and INR, creatinine and Urine R/M/E.

The patient was discharged home with advice to follow up with Echocardiography, PT and INR, S. creatinine and Urine R/M/E.

Echocardiogram 6 weeks post discharge revealed a sessile LV apical myxoma of 2cm^2 in size (FIGURE 7). Cardiac surgery consultation was taken at that time and the Surgeon advised to follow-up the patient for another 6 months to see the progression of LV mass.

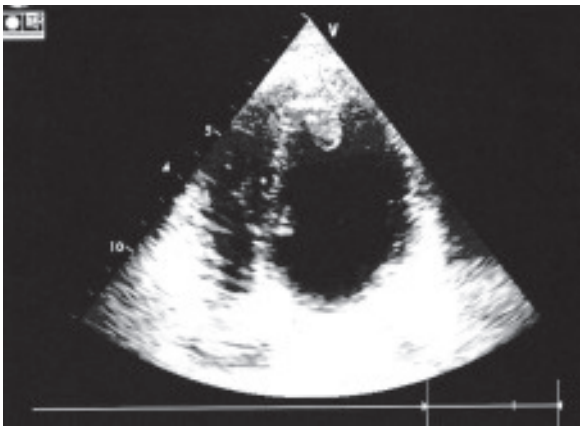

Fig.-7: *Follow up echocardiogram*

Discussion:

Cardiac myxomas, although uncommon are one of commonest primary cardiac tumours and account for ~50% primary benign cardiac tumours.[10] The majority of myxomas are in the left atrium (75%) followed by the right atrium (20%). LV myxomas account for only 2.5% of cases[11] .The first description of a primary intracardiac tumor was in 1559, located in the left ventricle[12] . In a review of literature, Mazer and Harrigan reported the first case of LV myxoma diagnosed by 2D echocardiography in 1982 [13] . Only 37 cases of left ventricular myxomas have been reported up to 1996 [14] and 72 cases up to 2014[15].In this respect ,our case is an extremely rare one.

Myxomas develop in all age groups. Myxomas are found particularly frequently between the 3rd and 6th decades of life[16].

Our patient was a 34 year old male. Patients range from stillborn infants to a 95-year-old woman, with an average age of 24 years[17.]

In a series of 66 sporadic myxomas, the female-to-male ratio was 2.7:118 [15] and 3:1 in one series[19] [1]Cardiac myxomas have no typical presentation. Typically, patients are asymptomatic or present with nonspecific signs and symptoms. Some authors call heart neoplasms the great "masqueraders" [20]. The clinical features of LV myxoma are mostly caused by embolization and obstruction to LVOT and systemic manifestations as components of the classical triad, but rarely are present all. However, at least one of the triad symptoms is present. Arrhythmias, conduction disturbances, and LV dysfunction can also be seen[21,22] .

Embolic phenomena in LV myxoma are more common than LA myxomas, occurring in 64% of patients with LV myxoma[23] .In our case ischemic stroke occurred as embolic phenomenon of myxoma and it was the first manifestation of otherwise asymptomatic myxoma.

Thrombus formation in LV is well-known complication in systolic heart failure (incidence 10-30%) and after acute myocardial infarction (incidence 5-15%) [24] .Hypercoagulable state can lead to ventricular thrombus formation even in the normal heart[25] .Main causes of Inherited thrombophilia are G1691A mutation of factor V gene, G20210A mutation of the prothrombin gene, antithrombin deficiency, protein C and protein S deficiency [26].LV thrombus formation is also associated with antiphospholipid antibody syndrome (APS)and hypereosinophilic syndrome [27,28] .Autoimmune disorders like Adamantiadis-Behcet's disease and Systemic lupus erythematosus(SLE), have been suggested to cause left ventricular thrombus formation [29,30] TEE of our patient demonstrated a thrombus attached to LV myxoma .The co-existence of SLE and Secondary APS could have been the contributing factors.

The most important method in myxoma preoperative diagnostics is transthoracic echocardiography. An additional diagnostic method in unclear diagnostic cases is transesophageal echocardiography [31,32].

Echocardiography plays a key role in establishing the diagnosis of patients with cardiac myxomas and thrombi. The differentiation between myxomas and thrombi is important because of the distinct treatment strategy. But it is often difficult to triage one from the other.In our case the trans thoracic and TEE did not reveal the typical features of myxoma –a mobile mass attached by a stalk to the septum. But treatment with anticoagulation for a prolonged period only caused slight reduction in size of the mass; possibly due to resolution of its overlying thrombus.

In contrast to masses in ventricle masses in the atria were deemed to be thrombi because of associated spontaneous echo contrast, location in the left atrial appendage, mitral valvular disease or prosthesis, atrial fibrillation, congestive heart failure, and enlarged left atrial chamber.[33]

CT and MRI can be used to differentiate the kind of tumor in right parts of the heart. MRI allows determining more specific tumor localization, its size and spread, tumor position to adjacent organs, and also the histological structure as compared to CT.[34]

A pedunculated thrombus moving throughout the cardiac cycle has a high tendency to embolize despite adequate anticoagulation[35] .Treatment for such thrombi has included thrombectomy, anticoagulation, or thrombolysis. Our patient was adequately anticoagulated and is now under the constant supervision of cardiac surgeon for further management.

Echocardiographies of our patient showed that the LV myxoma was sessile smooth surfaced and rounded. Cardiologist and cardiac surgeon both have opted for watchful observation. At present our patient is continuing medical management and is gradually improving neurologically and has not experienced any adverse events.

Most cases obtained complete recovery after tumor resection and histological confirmation can be obtained [36]. Our patient has not yet undergone surgical resection of the cardiac tumour. So histological confirmation of diagnosis has not been done.

Conclusion:

Approximately 15%of all ischemic strokes (IS) occur in young adults and adolescents. The causes of Ischemic Stroke in the young are heterogeneous and can be relatively uncommon. We report a young adult suffering from ischemic stroke diagnosed with an isolated otherwise asymptomatic left ventricular myxoma with thrombus which is an extremely rare finding. Extensive search based on clinical clues also revealed SLE associated with Lupus nephritis and Secondary APS, Homocysteinemia, significant smoking history and history of recreational drug use; which are all contributors to ischemic stroke. But considering our patients clinical presentation and imaging findings LV myxoma seemed to have the major contribution in causation of stroke by embolization. The patient was managed conservatively, attempts were taken to treat modifiable vascular risk factors aggressively and healthy lifestyle especially abstinence from recreational drug use was advised.

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Obituary

Prof. MA Zaman

Professor Md Aktheruzzaman , popularly known as Prof. MA Zaman breathed his last at Dhaka on 19th July, 2016 .He left behind wife, 3 daughters and innumerable number of students.

He had long career in teaching in medical science in the country. He was the registrar at Dhaka Medical College Hospital in mid-sixties before he went to UK for higher studies. After doing MRCP (UK), he returned back in late seventies and joined Dhaka Medical College as the Associate Professor of Cardiology. He organised the Department of Cardiology, the first sub-speciality in medicine in any medical college. He started coronary care unit in early eighties which was the first such unit in any medical college in Bangladesh. For some time he was at Rangpur Medical College . Later he joined Dhaka Medical College as the Professor and Head of Cardiology and worked till 1994.

In 1994, he joined National Institute of Cardiovascular Diseases, Dhaka as the Professor of Cardiology, became its Director and Professor after some time and served till 2001 when he retired from the government service. During his tenure the institute was shifted to its present building. There was remarkable development work of the institute at that time.

He remained active after the retirement from government services. He joined Red Crescent Holy Family Medical College initially and later Bangladesh Medical College as the Principal. In both the institutions he was the Head of the Department of Cardiology. After leaving services at medical colleges, he remained associated with Metropolitan Medical Centre, Dhaka where he served as Managing Director till his death.

He served as the editor, Journal of Dhaka Medical College; editor, Bangladesh Heart Journal and Chairman, editorial board, Bangladesh Heart Journal. He was the founding member of Bangladesh Cardiac Society.

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