CLINICAL AND ECHOCARDIOGRAPHIC PATTERNS OF MITRAL VALVE PROLAPSE AMONG MEDICAL STUDENTS AT MUHAS, DAR ES SALAAM. TANZANIA

By

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree Master of Science (Cardiology) of the Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for the examination a dissertation ***titled: Clinical and Echocardiographic patterns of Mitral Valve Prolapse among medical students at MUHAS; Dar es Salaam Tanzania*** in fulfillment of the requirements for the degree of Master of Science (Cardiology) of the Muhimbili University of Health and Allied Sciences

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DECLARATION AND COPYRIGHT

I Sulende D. M. Kubhoja, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

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DEDICATION

This work is dedicated to my wife, Jamilla Mwanga, for her kindness, tolerance and everlasting support throughout my studies and to my children; Susana, Grace and Bwire for missing me most of the time.

ABSTRACT

MVP is a valvular heart disease characterized by the displacement of an abnormally thickened mitral valve leaflet into the Left Atrium (LA) during systole. Its aetiology is yet to be elucidated.

Clinically, MVP has been associated with a wide variety of non-specific clinical features.

Its complications include; infective endocarditis, cerebralvascular accidents (CVA), frail leaflets, mitral regurgitation, heart failure, etc.

The prevalence of MVP and it's characteristics in Sub-Saharan Africa and particularly in black Africans, including Tanzania has not been well studied.

There is lack of awareness on the magnitude of MVP in Tanzania based on clinical and echocardiographic criteria specific for diagnosing MVP, thus, the rationale for conducting the study.

Objective: To determine the prevalence, clinical and echocardiographic patterns of MVP among medical students at MUHAS, Dar es Salaam. Tanzania.

Study design and site; A cross- sectional descriptive study was done, involving MD4 and MD5 students at MUHAS, Dar es Salaam. Tanzania.

Method: Classic MVP was defined as an upward displacement of the leaflet(s) exceeding 2mm and maximal thickness of ≥ 5mm on a 2-dimensional Echocardiography. Non classic mitral valve prolapse diagnosis was accepted when the displacement exceeded 2mm but maximal thickness was less than 5mm.

Study procedure: A designed structured questionnaire for the purpose of the study was administered to all consenting MD4 and MD5 medical students. Social demographic data, history, clinical cardiac findings and echocardiographic results were recorded.

Results: A total of 202 students were recruited, 101 from each class. Among them, 136 (67.3%) were males and 66 (32.7%) were females, with a male to female ratio of 3:1. Majority of the study group were in the age group 24-26 years, with a mean age of 25.71 ± 1.58 (Range 22-29 yrs).

The prevalence of classic MVP was 0.99% with equal gender distribution.

None of those with MVP had a past history of heart diseases e.g. heart failure, atria fibrillation, cerebral vascular accident, or syncope attack. Chest pain and heart palpitations were the only two common presenting symptoms, while systolic click was the only significant clinical sign detected in students with classical MVP.

Five (2.5%) students had mitral valve prolapse. Three (1.5%) had non-classic MVP, while two (0.99%) had classic MVP. The two (0.99%) who had classic MVP, all had symmetric type of prolapse with no cardiac abnormalities or co-morbidities.

Conclusion and recommendations

From a sample size of 202 presumably healthy medical students, the prevalence of classic MVP was 0.99% supporting some previous studies. A bigger sample sized community based study is recommended so as to determine the actual prevalence of MVP, the associated symptoms and signs, and echocardiographic patterns in our community.

LIST OF ABBREVIATIONS

ACC.....American College of Cardiology

AF.....Atrial Fibrillation

AHA.....American Heart Association

AMVL.....Anterior Mitral Valve Leaflet

ASD.....Atrial Septal Defect

BMI..... Body Mass Index

CAD.....Coronary Arterial Diseases

CFM.....Color Flow Mapping

EF..... Ejection Fraction

HCM.....Hypertrophic Cardiomyopathy

LA.....Left Atrium

LV.....Left Ventricle

LVEF.....Left Ventricular Ejection Fraction

MD.....Doctor of Medicine

MMC.....Muhimbili Medical Centre

MNH.....Muhimbili National Hospital

MR.....Mitral Regurgitation

MUHAS.....Muhimbili University of Health and Allied Sciences

MVP.....Mitral Valve Prolapse

OPD.....Outpatient Departments

PMVL.....Posterior Mitral Valve Leaflet

PWD.....Pulsed Wave Doppler

RHD.....Rheumatic Heart Disease

SCD.....Sudden Cardiac Death

USA.....United States of America

LIST OF TABLES

Table 1.....31
Table 2.....32

LIST OF FIGURES

Figure 1 14
Figure 2 33
Picture A 57
Picture B 57
Picture C 58
Picture D.....58

TABLE OF CONTENTS

Certification.....ii
Declaration.....iii
Acknowledgement.....iv
Dedication.....v
Abstract.....vi
Abbreviations.....viii
List of tables.....ix
Table of contents.....x
1.1 Background.....1
1.2 Anatomy and Histology.....1
1.3 Physiology.....2
1.4 Etiology and pathology.....3
1.5 Prevalence.....4
1.6 Natural history and complications.....7
1.7 Mitral regurgitation.....8
1.8 Definition.....9
1.9 Classification.....10
1.9.1 Primary MVP.....10
1.9.1.1 Familial MVP.....10
1.9.1.2 Non-familial.....11
1.9.2 Secondary MVP.....11
1.9.3 Functional MVP.....12
1.9.4. Current classification.....12
1.9.4.1 Classic versus non-classic.....12
1.9.4.2 Symmetric versus asymmetric.....13
1.9.4.3 Flail versus non-flail.....13
1.10 Clinical features.....14

1.10.1 Chest pain 15
1.10.2 Anxiety.....16
1.10.3 Palpitations.....16
1.10.4 Hyperventilation.....16
1.10.5 Associated skeletal abnormalities.....17
1.11 Diagnosis.....18
1.11.1 Symtomatology.....18
1.11.2 Auscultatory features.....18
1.11.3 Echocardiography.....19
1.11.4 M-mode criteria.....20
1.11.5 2-D echocardiographic criteria.....20
1.12 Monitoring 22
2. Problem Statement and Rationale 23
2.1 Problem Statement 23
2.2 Rationale of the study 24
3. Study Objectives.....25
3.1 Broad Objectives 25
3.2 Specific Objectives.....25
4. Methodology.....25
4.1 Study design.....25
4.2 Study setting..... 25
4.3 Study population 26
4.4 Duration of the study.....26
4.5 Sample size estimation.....26
4.6 Recruitment and selection of study subjects.....27
4.7 Sampling procedure.....27
4.8 Exclusion criteria.....27
4.9 Definition of terms.....28
4.10 Data collection procedure.....28

4.10.1 Physical examination.....28
4.10.2 Echocardiography.....28
4.11 Ethical clearance and patients benefit 29
4.12 Data analysis.....30
5. Results.....31
6. Discussion.....34
7. Study limitations.....43
8. Conclusion.....43
9. Recommendations.....43
10. References.....44
11. Appendix I (Questionnaire).....50
12. Appendix II (Consent form to participate in the study).....54

1.0 INTRODUCTION AND LITERATURE REVIEW:

1.1 Background

The mitral valve forms a complex apparatus whose closing and opening with the heartbeat co-ordinates the flow of blood from the left atrium (LA) to the left ventricle (LV). On average in human life span, it does a command performance to the tune of about three billion heartbeats.

The mitral valve (also known as the bicuspid valve or left atrioventricular valve), is a dual flap valve that lies between the left atrium (LA) and the left ventricle (LV). In Latin, the term mitral means shaped like a miter, or bishop's cap. The orientation of the two leaflets resembles a bishop's miter, which is where the valve receives its name. The mitral valve and the tricuspid valve are also known collectively as the atrioventricular valves because they lie between the atria and the ventricles. [1, 2]

1.2 Anatomy and Histology

The mitral valve has two cusps/leaflets. The anteromedial /Anterior Mitral Valve Leaflet (AMVL), the largest leaflet and the posterolateral/ Posterior Mitral Valve Leaflet (PMVL) which guards the MV opening. The anterior cusp/ AMVL protect approximately two-thirds of the valve. The PMVL usually has two minor indentations or clefts. The valves are collagenous structures covered by the continuous layer of endothelium that lines the cardiovascular system. Histologically each leaflet is composed of three layers of tissue; the atrialis, fibrosa, and spongiosa. [1,2,3]

The MV opening is surrounded by a fibrous ring known as the mitral valve annulus. The valve leaflets are prevented from prolapsing into the left atrium by the action of tendons attached to the posterior surface of the valve, chordae tendineae which are

white, fibrous, collagenous cords that connect the MV leaflets to two left ventricular papillary muscles.

The inelastic chordae tendineae are attached at one end to the papillary muscles and the other to the valve cusps. Papillary muscles are finger like projections from the wall of the LV. Chordae tendineae from each muscle are attached to both leaflets of the mitral valve. Thus when the left ventricle contracts, the intraventricular pressure forces the valve to close, while the tendons keep the leaflets coapting together and prevent the valve from opening in the wrong direction. This prevents blood to flow back into the left atrium. The chords have different thicknesses. The thinnest ones are attached to the free leaflet margin while thickest ones (strut chords) are attached quite away from the free margin. This disposition has important effects on systolic stress distribution physiologically. [1,2,3]

The MV apparatus therefore consists of the Valve leaflets, chordae tendinae, and papillary muscles as well as a valvular annulus. By size, the MV orifice is less than the Tricuspid Valve orifice (mean circumference = 9cm in males and 7cm in females).
The normal average adult mitral valve area is 4.0 to 5.0 cm^2. [2,3]

1.3 Physiology

During left ventricular diastole, the mitral valve opens, and blood travels from the LA to the LV. About 70% to 80% of the blood that travels across the MV occurs during the early filling phase of the LV. This early filling phase is due to active relaxation of the ventricular myocardium, causing a pressure gradient that allows a rapid flow of blood from the LA across the MV. This early filling across the MV is seen on Doppler echocardiography of the MV as the E wave. After the E wave, there is a period of slow filling of the ventricle.

Left atrial contraction (LA systole) causes added blood to flow across the MV immediately before left ventricular systole. This late flow across the open MV is seen on

doppler echocardiography of the MV as the A wave. The late filling of the LV contributes about 20% to the volume in the LV prior to ventricular systole, and is known as the atrial kick. [2,3]

1.4 Etiology and pathology

The etiology of MVP has yet to be elucidated. The observation that the leaflets are histologically identical in primary and secondary MVP, suggests that primary MVP may be a form of the Marfan or other connective tissue syndrome. A connective tissue abnormality is believed to predispose and weaken the mitral valve leaflet(s) to be damaged from daily hemodynamic stresses, leading to a continual process of damage and repair and finally to myxomatous change of the valve(s). [2,3,4]

The leaflets and chordae tendineae may both be involved in the myxomatous process. The interstitial cells of the valve itself can contribute by regulating matrix degradation and remodeling. Rabkin E. et al [5] studied immunohistologic staining characteristics of valves from patients with MVP and mitral regurgitation. The interstitial cells revealed features of activated myofibroblasts and expressed increase levels of catabolic enzymes, including matrix metalloproteinases, endoproteinases, and interleukin-1 beta. Macroscopic changes in these structures included the following:-

- Thickening and redundancy of the leaflets
- Thinning, stretching, and sometimes rupture of the chordae tendineae
- Dilatation of the mitral annulus

Both the anterior and posterior leaflets may be involved, although the middle scallop of the posterior leaflet is most frequently affected. Histologic examination of involved areas reveals disruption of collagen bundles and accumulation of acid mucopolysaccharides within the spongiosa layer of the valve leaflets. [2,3,4,5]

1.5 Prevalence

The prevalence of MVP in the USA previously (1970's) was estimated to be at 4% to 5%, with variations in age and gender. However, the findings differed from study to study. [6,7]

Freed et al, [8] in 1999 using two-dimensional (2-D) echocardiographic criteria to examine 1845 women and 1646 men found an overall prevalence of 2.4%, Classic MVP was detected in 1.3% and nonclassic MVP in 1.1%. The prevalence was similar in both gender and was evenly distributed among age groups. Severe mitral regurgitation (MR) was present in 7% of patients with classic MVP compared to none with nonclassic MVP. These findings suggested that nonclassic MVP is part of the normal range of mitral valve anatomy and not a disease condition.

Flack et al, [9] in a community-based echocardiographic study of 4136 young adults, aged 23 to 35 years, found a prevalence of 0.6% that was similar in both gender and ethnicity. Among the 2.7% of subjects who had a prior diagnosis of MVP, only 0.45% had definite echocardiographic evidence of a prolapse.

In view of the above findings, if the results are to be generalized in the community today, it will be obvious that the estimated prevalence of MVP using modern echocardiographic techniques will be around 0.6% to 2.4%. [8,9]

In the last decade, improved technology and community based rather than hospital-based studies in developed countries have ascertained a prevalence of MVP to be 2.4%.

This reduced prevalence is in part explained by better understanding of the 3-dimensional architecture of the mitral valve annulus provided by 3-dimensional echocardiography. This led to standardized echocardiographic criteria for the diagnosis of MVP. With 2.4% prevalence, MVP is expected to be present in 7.2 million individuals in the United States and 144 million people worldwide. [10,11,12]

Two large studies from Italy in 1990's by Zuppiroli A et al, [13,14] after reviewing a total of 8252 consecutive subjects echocardiographycally, MVP was diagnosed in 288 subjects (3.5%). In another community based study, the prevalence of MVP in a population of 420 university students was, functional MVP in 27/420 (6.4%) and anatomical prolapse in 2 cases (0.5%).

From Sweden, Bryhn M and Persson S [15] in early 1980's did an epidemiological survey on asymptomatic Swedish population of 100 women and 101 men echocardiographycally to determine the prevalence of MVP. Similar approach was done by Hickey AJ et al, [16] from Australia in 1980s in 200 volunteers (100 men and 100 women), MVP was found in 7% and 4% of the studied populations respectively.

Bochkov et al, [17] from Russia studied 1934 people aged 11years to 70 years who were screened clinically and phonocardiographically for MVP. Based on old criteria standards, 2.5% of the study subjects had MVP. The incidence of MVP was concluded not to be significantly dependent on gender and age.

From Asian countries; Leong et al, [18] did a review on MVP. The prevalence was difficult to ascertain due to differences in diagnostic criteria and population selection. But the prevalence in the studied community was estimated to range from 5% to 15%.

The prevalence of MVP and its characteristics in Africa and Africans in general has not been well studied.

Hassadi MF et al, [19] from Arab Medical University, Benghazi Libya, observed 200 patients echocardiographically using old criteria. MVP was the commonest single abnormality (16%). Although this does not indicate the prevalence of MVP in the general population in Libya, the study however, indicated that MVP could be the commonest valvular abnormality seen in a hospital setting in Libya.

Oke DA et al, [20] from Nigeria assessed 62 patients in a three year follow up, (clinically and echocardiographycally) at the Lagos University Teaching Hospital. Eighty percent (80%) had mitral valve leaflet prolapse (MVLP) affecting mainly the AMVLs.

Oladapo OO et al, [21] from University of Ibadan Nigeria in the year 2000, reported the prevalence of MVP from fifty presumably healthy adult Nigerians to be 10% based on 2-Dimensional echocardiography. However, this was a small sample size and did not use the current criteria for diagnosing MVP.

From Addis Ababa Ethiopia, Hodes RM [22] reviewed 385 patients who were seen in the cardiology clinic of Tikur Anbessa Hospital over 20 months. MVP was most common (25%). However, the measurements and criteria used to diagnose MVP which included the non-classic type probably made the disease to be high up in the list of anomalies.

Joubert J et al, [23] from Pretoria South Africa in their review article about cardiac status of 102 consecutive black stroke patients, MVP was found in 5.8%.

In early 1980's Wann L S et al, [24] studied 100 presumably healthy young women for MVP and reported a prevalence of 3% while Mody GM et al, [25] in 1987 from South Africa reported a similar prevalence of MVP to be 3% (by old criteria) from a randomly selected group of 101 patients with rheumatoid arthritis in order to determine the prevalence of cardiac co-abnormalities.

Maro Eden and Ramaiya K [26] in Dar-es-Salaam Tanzania reviewed patients who were referred to a private cardiac clinic with a provisional diagnosis of MVP. They reported that 65.9% of patients had a correct diagnosis of MVP echocardiographycally. It did reflect the magnitude of the problem in Dar-es-Salaam.

Freers J et al, [27] from Makerere University Medical School, Kampala, Uganda did almost a similar study to what Maro Eden and Ramaiya K did in Dar-es-salaam. Among

the five hundred consecutive cardiac patients reviewed echocardiographically, 90% had MVP.

1.6 Natural history and complications of MVP

The natural history of MVP is generally believed to be benign, but serious complications have been reported. The most common serious documented complications are infective endocarditis, cerebrovascular accidents, thromboembolism, flail leaflet, mitral regurgitation, heart failure (the need for mitral valve surgery), arrhymias such as atrial fibrillation and even death. Fortunately, the complications of MVP although some are serious, are reported to be uncommon and probably affecting not more than 3% of those with MVP. [2,3,8,28,29]

In the 1970s, clinicians relied on physical examination and phonocardiogram for the diagnosis of MVP and its complications. Reports from that time indicate that serious complications occurred at the rate of approximately 1% per year. In the 1980s, with increasing use of echocardiography, clinical investigators described higher complication rates of approximately 2% to 4% per year. [30,31,32]

Avierinos JF et al, [33] did a community-based retrospective review of 833 people who were first diagnosed to have asymptomatic MVP between 1989 and 1998 in USA. At a median follow-up of 5.4 years, an estimated 10 year overall and cardiovascular mortality were 19% and 9%, respectively. Cardiovascular morbidity occurred in 30%. MVP-related events (death or heart failure related to MVP, endocarditis, or mitral valve surgery) occurred in 20%. Valve surgery was performed in 65 patients (7.8%). From these figures, it is perhaps not surprising that MVP is the single most common cause for surgical repair or replacement of the mitral valve in the US today.

From Avierinos study, [33] the major risk factor for cardiovascular mortality was moderate to severe MR, which was present in 16%. Almost similar findings were noted in other

reports, in which the likelihood of developing MVP-related complications was directly related to the severity of the MR. [34,35]

Left Ventricular Ejection Fraction (LVEF) is reported to be a less common primary risk factor for cardiovascular mortality in patients with MVP. In the same study, it occurred in 3.7% of patients. Secondary risk factors that were independently predictive of cardiovascular morbidity were slight MR, left atrial dimension ≥40 mm, flail leaflet, atrial fibrillation (AF), and age ≥50 years. [33]

Atrial Fibrillation has been documented also as a risk factor for mortality in patients with MVP. The same studies, reported the rate of developing AF to be about 5% per year. The major independent risk factors for developing AF were age ≥65 years and baseline left atrial dimension ≥50 mm. [33,34]

In an attempt to evaluate the prevalence of AF in 246 patients with MVP who were about to undergo mitral valve repair or replacement, 37 (15%) were in AF and another 32 (13%) had a history of AF that reverted to sinus rhythm either spontaneously or with antiarrhythmic drug therapy. [33]

1.7 Mitral regurgitation (MR)

Acute rheumatic fever and chronic rheumatic valvular heart diseases with MR, ranks among the major causes of MR and other cardiovascular conditions in Africa. MVP with MR, functional MR and endocarditis constitute the remaining frequent causes of valvular heart diseases in this region [36]

Because of its relatively high prevalence (0.6% to 2.4%) in the USA general population, MVP is said to be the most common cause of chronic MR in the US and other developed countries. Moderate to severe MR is reported to be present in 16% to 23% of patients with MVP. [33,34,35]

Valvular lesion in MVP is characterized by thickening and degeneration of the leaflets and chordae. These changes reflect repeated damage to the valve leaflets, which deforms the valve, thereby preventing proper coaptation of the leaflets. The mitral annulus dilates and increasingly leaks as regurgitation worsens. An increase in prolapse may further stretch and damage the chordae tendineae. A weakened chorda can rupture suddenly producing a flail mitral leaflet and wide-open severe mitral regurgitation. [2,3,4]

It has been reported that mitral regurgitation in mitral valve prolapse tends to progress, leading to worsening of hemodynamic status and ultimately to clinical symptoms. Progression is usually gradual but can be abrupt if chordal rupture occurs. The degree of MR is an essential determinant of the hemodynamic alterations, left ventricular remodeling, and outcome. [35]

It has been also estimated that as many as 10% of patients with MVP may require mitral valve surgery at one stage in their lifetime. Corrective surgery is indicated in selected patients with severe chronic MR as usually determined by Doppler echocardiography. The criteria for surgery and monitoring of patients are according to the 2006 ACC/AHA guidelines. [10]

1.8 Definition

Prolapse is defined as "the slipping of a body part from its usual position in relation to other parts". Prolapse of the mitral valve refers to systolic billowing of one or both mitral valve leaflets across the plane of the mitral valve annulus into the left atrium. The extent of prolapse may be insignificant or grossly abnormal with a significant degree of mitral regurgitation. [3]

Mitral valve prolapse is a valvular heart disease characterized by the displacement of an abnormally thickened mitral valve leaflet into the LA during systole. In its nonclassic form, it carries a low risk of complications. In severe cases of classic MVP, it may

complicate to mitral regurgitation, infective endocarditis, and in rare circumstances even cardiac arrest, resulting in sudden death. [3]

Patients with classic mitral valve prolapse have been described to have an excess connective tissue that thickens the spongiosa and separates collagen bundles in the fibrosa. This has been also described as due to an excess of dermatan sulfate, a glycosaminoglycan. This weakens the leaflets and adjacent tissue, resulting in increased leaflet area and elongation of the chordae tendineae. Elongation of the chordae often causes rupture or tear, and is commonly found in the chordae tendineae attached to the posterior leaflet. Advanced lesions also commonly involving the posterior leaflet lead to leaflet folding, inversion, and displacement towards the left atrium. [2,3,4,5]

1.9 Classification

Mitral valve prolapse is classified as primary, secondary, or functional, based upon the anatomic or physiologic defects responsible for the abnormal leaflet motion. [2,3]

1.9.1 Primary MVP:

Primary or classic MVP is an idiopathic valvular abnormality characterized by myxomatous degeneration of the mitral valve leaflets and subvalvular apparatus in the absence of any recognizable systemic connective tissue disorder. As a result, primary MVP often is called myxomatous mitral valve disease. [2,3]

The tricuspid valve is involved in up to 40% or 50% of patients and the aortic valve in 10% to 20%. Pulmonic valve involvement is less common. [2,3] Primary MVP can either be familial or non-familial. [3]

1.9.1.1 Familial MVP

Familial MVP has been described by Devereux et al [37] as a condition that can be inherited as an autosomal dominant with incomplete penetrance. There are a number of

studies which report that the prevalence of familial MVP in first degree relatives ranges from 30% to 50%. [37,38,39,40]

Three different loci have also been identified, although the genes have not been identified: The three different loci are:- MMVP1 on chromosome 16p, [38] MMVP2 on chromosome 11p15 [39] and MMVP3 on chromosome 13q31. [40]

1.9.1.2 Non-Familial

Another rare type of myxomatous valvular dystrophy affecting males, the sex-linked valvular dysplasia, is transmitted as an X-linked recessive trait. The gene has been mapped to Xq28 as documented by Trochu et al [41]. This disease is characterized by nonsyndromic mitral valve myxomatous degeneration. It is frequently associated with aortic valve degeneration. The valve lesion has been seen in female carriers and is said to be usually less severe.

1.9.2 Secondary MVP

MVP can be secondary to:- Marfan's syndrome, other connective tissue diseases or Rheumatic heart disease (RHD), Reduced LV dimensions, Hypertrophic cardiomyopathy (HCM), Atrial septal defect (ASD),

Secondary MVP is characterized by myxomatous degeneration of the mitral valve leaflets in the context of a recognizable connective tissue disorder. Associated conditions include the Marfan's and Ehlers-Danlos syndromes, adult polycystic kidney disease, osteogenesis imperfect a, and pseudoxanthoma elasticium. Histologically the valve leaflets have been described to be identical with that in primary MVP. [3,20] The MVP of particular importance in our set up is the one secondary to Rheumatic heart disease which should not be confused with the primary MVP. [3,36]

MVP has also been found in as many as 15% of patients with Ebstein's anomaly. Ali SK et al [42] from Sudan also has documented the association of Ebstein's malformation with MVP in 12 African children with the anomaly echocardiographycally. [3,42]

1.9.3 Functional MVP: Is a prolapse of an anatomically normal mitral valve leaflet(s) which can occur in either of the following conditions:

- Papillary muscle dysfunction due to myocardial ischemia or coronary arterial diseases
- Dilated mitral annulus secondary to dilated cardiomyopathy.
- A left ventricular cavity that is too small to accommodate the mitral valve or due to reduced LV-dimensions. This condition is frequently observed in patients with hypertrophic cardiomyopathy or in some patients with hypovolaemia due to anorexia nervosa, dehydration or in patients with a secundum atrial septal defect, pulmonary hypertension, straight-back syndrome/ pectus excavatum, flail MV leaflet(s) or normal variant. [3,20,23]

1.9.4 Current classification (Figure 1)

Based on 2-D Echocardiographic criteria, MVP has now been classified into a number of subtypes. The classification is based on the leaflet thickness, concavity, and type of connection to the mitral annulus. The subtypes are, classic, nonclassic, symmetric, asymmetric, flail, or non-flail. [12]

1.9.4.1 Classic versus non classic

Prolapse occurs when the mitral valve leaflets are displaced more than 2 mm above the mitral annulus high points. The condition can be further divided into classic and nonclassic subtypes based on the thickness of the mitral valve leaflets: up to 5 mm is considered nonclassic, while anything beyond 5 mm is considered classic MVP.

1.9.4.2 Symmetric versus asymmetric

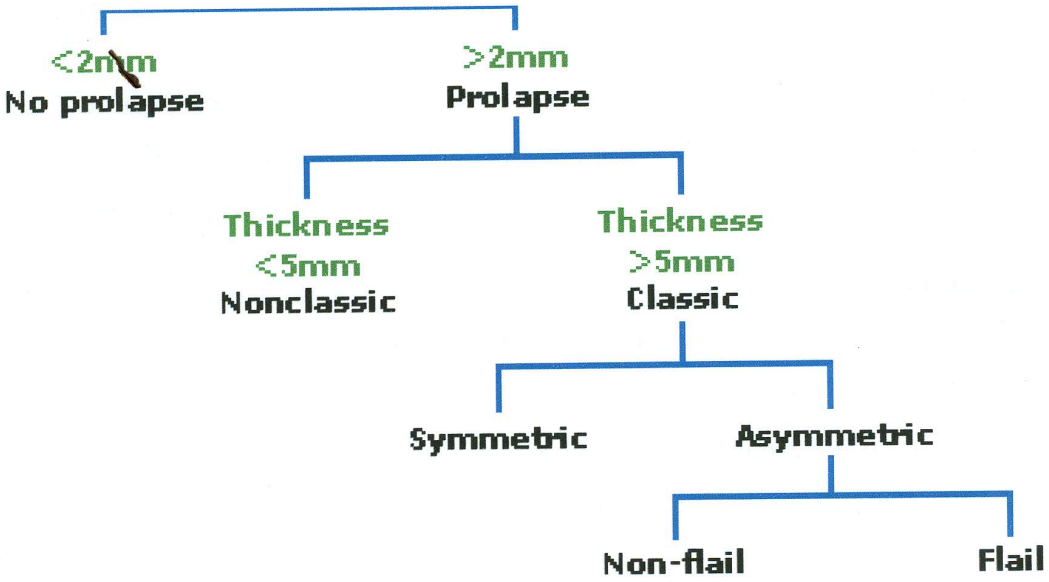
Classical prolapse may be subdivided into symmetric and asymmetric, referring to the point at which leaflet tips join the mitral annulus. In symmetric coaptation, leaflet tips meet at a common point on the annulus. Asymmetric coaptation is marked by one leaflet displaced towards the atrium with respect to the other. Patients with asymmetric prolapse are susceptible to severe deterioration of the mitral valve, with the possible rupture of the chordae tendineae and the development of a flail leaflet with MR.

1.9.4.3 Flail versus non-flail

Asymmetric prolapse is further subdivided into flail and non-flail. Flail prolapse occurs when a leaflet tip turns outward, becoming concave towards the left atrium, causing the deterioration of the mitral valve. The severity of flail leaflet varies, ranging from tip eversion to chordal rupture. Dissociation of leaflet and chordae tendineae provides for unrestricted motion of the leaflet (hence "flail leaflet"). Thus patients with flail leaflets have a higher prevalence of mitral regurgitation than those with the non-flail subtype.[3,12,38]

Figure 1

Mitral leaflet displacement based on 2-D Echocardiography



All the measurements described before and in the above diagram refer to adult patients, applying them to children may be misleading.

1.10 Clinical features

MVP has been characterized and studied for more than thirty years. It has been given a variety of names including the floppy valve syndrome, Barlow's syndrome, the click-murmur syndrome and Myxomatous mitral valve disease. The abnormal Mitral Valve Leaflets have also been described as myomatous, voluminous, floppy, hooding or billowing among others. The term MVP was coined by J. Michael Criley in 1966 and gained acceptance over the other descriptor of "billowing" of the mitral valve, as described by JB Barlow. [3,4,43]

MVP has been associated with a wide variety of clinical features. In addition, a variety of more non-specific complaints have also been associated with MVP. Atypical or non-anginal chest pain is the most common symptom attributed to MVP. Other features may include: -

Palpitations, dyspnea, exercise intolerance, dizziness or syncope, panic and anxiety disorders, numbness or tingling, skeletal abnormalities, abnormal resting and exercise electrocardiograms. [2,3,44,45,46,47,48]

Any combination of these symptoms and signs plus the typical auscultatory features of MVP as described below, have been defined as the mitral valve prolapse syndrome. [3] Current literature suggests that autonomic dysfunction, a hyper adrenergic state, metabolic disturbances or combinations, are a potential explanation for the constellation of symptoms, often associated with MVP [3]. Common clinical features of MVP are as follows:-

1.10.1 Chest pain

The chest pain attributed to MVP has been described to be of atypical in nature and easily distinguishable from angina pain. The pain is generally mild in character but can be disabling and recurrent in some patients.

In view of these, it is therefore recommended that, patients with chest pain and suspected MVP be evaluated in the same manner as any other patient with chest discomfort. If no cause is found, it is also recommended that no need of drugs like beta blockers; because currently there is no evidence that they are effective. However, a modest change in lifestyle including an aerobic exercise program has been documented that it can be beneficial. [3,45]

1.10.2 Anxiety

Anxiety has also been described or associated with MVP. Some patients with MVP have or can have an anxiety disorder. Patients with MVP presenting also with symptoms diagnostic of anxiety disorder, panic disorder, or depression, it is recommended that they should be managed for these illnesses with the same indications as those without MVP. [8,47]

1.10.3 Palpitations

Awareness of heart beats (Palpitations) are common presenting complaint in people with MVP. Similarly, patients with symptomatic palpitations with MVP should be evaluated in the same manner to those without MVP. Palpitations in MVP have been associated with ventricular premature beats, but supraventricular arrhythmias have also been documented. [3,8]

In addition, palpitations may be reported by patients at a time when an arrhythmia is absent on ECG including continuous ambulatory recordings. Thus, it is recommended that the presence of an arrhythmia should be confirmed before beginning any antiarrhythmic therapy. It is suggested that giving beta blockers may be helpful in patients who present with hyperadrenergic symptoms such as tachycardia, palpitations, nervousness, and an exaggerated heart rate response to exercise. [3,10]

1.10.4 Hyperventilation

Symptoms of hyperventilation, including dyspnea, dizziness, numbness and tingling, are also common in MVP patients. Objective exercise testing in these symptomatic patients is said to be usually normal and the symptoms frequently have been reported to respond well to lifestyle modifications. In this respect, it is generally agreed that symptomatic relief of patients with MVP may require both general and pharmacologic measures. [3,10,12]

1.10.5 Associated skeletal abnormalities

For many years, MVP was a poorly understood anomaly often associated with a wide variety of both related and seemingly unrelated symptoms and signs as mentioned above including skeletal abnormalities. To link between skeletal abnormalities and MVP, several authors tried to look into this association. In one study Russo L et al [48] developed an epidemiologic screening among 299 secondary school girls (average 16.5 years)] to verify the incidence of idiopathic MVP and associated thoracic-skeletal abnormalities in young female population. The incidence of MVP among scoliotic subjects was 19.5%. However, the inclusion and assessment protocol was not clearly elaborated.

It has been observed that people with MVP tend to have a low body mass index (BMI) and are typically leaner than individuals without MVP, the reason behind is not well established.[3] Secondary MVP is frequently recognized in individuals with Marfan's syndrome and other musculoskeletal anomalies. [2,3,4,48]

While managing all these associated or related conditions mentioned above, it is recommended that reassurance about the benign nature of the disorder is often adequate to reduce the severity of symptoms in many patients with MVP. Many patients also appear to benefit from a change in lifestyle, including aerobic exercise training, the avoidance of stimulants such as caffeine, avoidance of alcohol, undue fatigue, and a reduction in stress. Scordo et al [45] evaluated the efficacy of aerobic exercise in 32 symptomatic women with MVP. Compared to control subjects, the exercise group showed a decrease in anxiety scores, an increase in general well-being and a decline in the frequency of chest pain, fatigue, dizziness, and mood swings.

1.11 Diagnosis

The diagnosis of MVP includes use of symptoms, auscultatory findings and 2-D echocardiographic criteria.

1.11.1 Symptomatology

Symptoms are not a reliable indicator of MVP. A study done by Devereux et al [49] showed that 26% of patients referred with a diagnosis of MVP based on symptoms only, did not have auscultatory or echocardiographic evidence for MVP. Since symptoms for MVP are non-specific, the diagnosis of MVP should be based on physical examination and confirmed by echocardiography. This has been clearly shown in a number of studies including Framingham.[49,50]

The diagnosis of MVP can be made or suspected in some patients by a careful cardiac physical examination but auscultatory findings can be subtle. The patient should be examined in different positions; supine, sitting, and standing positions. This is because changes in left ventricular volume can affect the degree of prolapse, resulting in inconsistent and occasionally absent auscultatory findings. In most patients, echocardiography is used to confirm the diagnosis. [3,49,50]

1.11.2 Auscultatory features

The classic auscultatory features of MVP are mid-systolic click or multiple clicks followed by a mid-systolic to late systolic murmur (when present) at the apex. These findings may be transient depending in part upon LV volume.

Non-ejection mid-systolic clicks or the mid-systolic clicks of MVP are heard earlier in systole when left ventricular volume is decreased. Sitting or standing will therefore move the clicks closer to the first heart sound. Tricuspid valve prolapse may accompany MVP and produce similar clicks along the left sternal border over the tricuspid area.

These non-ejection clicks (i.e., not associated with the aortic valve) probably do represent the sudden snapping of the chordae tendineae as the mitral and tricuspid leaflets bow back into the left or right atrium. This is analogous to the snapping of ropes on a sailboat when the sail is suddenly filled by a gust of wind.

Careful examination must therefore be taken to differentiate the non-ejection clicks of MVP from other systolic clicks and sounds. The differential diagnosis in this case will include ejection clicks of the aortic and pulmonic valves, a split first or second heart sound, pericardial sounds, and sounds originating from nonvalvular structures such as an aneurysm of the interatrial septum. [3,49]

Normally Non-ejection clicks have different auscultatory findings from other heart sounds. In comparison to clicks of MVP, other ejection clicks are usually of higher intensity, heard nearer to the first heart sound, and do not vary in timing with changes in position. Ejection clicks occur before the upstroke of the carotid impulse (with aortic valve opening), while non-ejection clicks occur after the carotid upstroke. [3]

Clicks from an interatrial aneurysm can be difficult to distinguish from MVP non-ejection clicks. However, one distinguishing feature is that, clicks associated with an interatrial aneurysm are not associated with a late systolic murmur if present. The late systolic murmur of MVP represents turbulent mitral regurgitant flow. It behaves similarly in response to maneuvers and pharmacological vasoactive agents as a mitral regurgitant murmur not caused by MVP. As the prolapse worsens, the murmur of MR may become holosystolic and indistinguishable from other causes of mitral regurgitation. [3]

1.11.3 Echocardiography

Currently echocardiography is the most useful noninvasive investigation for the diagnosis and assessment of MVP. Patients with auscultatory findings suggestive of MVP should be subjected to echocardiographic examination in order to determine the

degree of prolapse, severity of thickening of the mitral valve leaflets, amount of mitral regurgitation, involvement of the subvalvular apparatus, LA measurements and left ventricular functions. [3,10,49]

The 2006 American College of Cardiology and American Heart Association (ACC/AHA) guidelines on the management of valvular heart disease recommended performing echocardiography in MVP. Routine echocardiography to diagnose MVP is not indicated in the absence of physical findings unless there is supportive clinical evidence of structural heart disease or a family history of myxomatous valve disease. [10]

1.11.4 M-mode criteria

The M-mode echocardiography is now rarely used for the diagnosis of MVP. M-mode criteria for the diagnosis of MVP include at least a 3mm holosystolic displacement or at least 2 mm late systolic displacement of the mitral leaflet echo behind the CD line. This finding, however, is not very sensitive because it relates leaflet motion to a fixed transducer location rather than to surrounding heart structures. The normal motion of the base of the heart in this case can therefore either mask or mimic true prolapse; as a result, two-dimensional echocardiography is the preferable method today.

M-mode echocardiography is useful for measuring the thickness of the valve leaflets. Leaflets that are at least 5 mm at the midpoint of the EF slope are considered thickened and thought to be at an increased risk for developing endocarditis and progression to severe mitral regurgitation. [3,11,12]

1.11.5 2-D echocardiographic criteria.

This method can reveal both displacement and leaflet thickness criteria for MVP. The normal mitral valve leaflets coapt on the ventricular side of a line connecting the annular hinge points on the long axis of a two-dimensional view. Leaflet displacement $\geq$2 mm above the plane of the mitral annulus is highly suggestive of MVP. However, this

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finding is not true of the four-chamber view. The mitral valve annulus is saddle-shaped and not planar; as a result, what appears to be a prolapse in the four-chamber view can actually be within the normal range of leaflet excursion. [11,12]

Thus, care is needed in using the apical four-chamber view alone in making a diagnosis of MVP. Echocardiographic evaluation of MVP is therefore more reliable if parasternal and apical long-axis views are done. Transesophageal echocardiography can be done if the transthoracic views are non-diagnostic.

The long-axis view can also be used to measure leaflet thickening. Leaflets measuring at least 5 mm in the midportion of the anterior mitral leaflet are considered thickened. Leaflet thickness is typically measured in diastole from a parasternal long axis view. [11,12]

Patients with ≥2 mm leaflet displacement and maximum leaflet thickness ≥5 mm are considered to have classic MVP, while those with leaflet thickness less than 5 mm have nonclassic MVP. All measurements above refer to adult patients, applying them to children may be misleading. Nonclassic MVP probably represents the normal variation in mitral valve anatomy. These patients should not be considered to have mitral valve disease unless there is evidence of significant mitral regurgitation.

Diffuse thickening of the mitral leaflets and redundancy have been associated with an increased prevalence of infective endocarditis, moderate to severe MR, and the need for mitral valve replacement. Redundancy of the mitral valve leaflets has not been rigorously defined, but has been diagnosed on the parasternal short axis view when the circumference of the leaflets appears to be disproportionate to the chamber size. [3,11,12,51,52]

Other abnormalities associated with MVP on 2-D echocardiographic criteria are increase in leaflet length, annular diameter, and chordal length. Malkowski et al [52], revealed that over 80% of patients with MVP have at least one of these findings, and over 50% have at least two.

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The severity of MR can also be established by 2-D and color flow Doppler echocardiography. MR is an important predictor of complications and cardiac events. Moderate to severe MR is a known risk factor for mortality and for complications such as atrial fibrillation, heart failure, chordal rupture, infective endocarditis, and the eventual requirement for valve replacement. [49,50,51]

1.12 Monitoring of patients with MVP

The 2006 ACC/AHA guidelines recommend the following approach in monitoring of patients with MVP. [10]

- Asymptomatic patients with no MR should receive follow-up clinical examinations at three to five year intervals to evaluate the likelihood of associated complications.
- Routine repeated echocardiography is not indicated in asymptomatic patients with no MR or in patients with mild MR and no change in symptoms or signs.
- Clinical evaluation and repeat echocardiography at yearly intervals in patients with high-risk findings on the initial echocardiogram (e.g., diffuse thickening of the mitral leaflets and redundancy), or moderate MR.
- Clinical evaluation and repeat echocardiography every six to twelve months in patients with severe MR
- Clinical evaluation and echocardiography at any time when there is a change in symptoms or signs.

2.0 PROBLEM STATEMENT AND RATIONALE

2.1 PROBLEM STATEMENT

A large proportion of patients attending cardiac OPD clinics or who have undergone echocardiograhic Examination at MNH or peripheral hospitals in Dar es Salaam have the diagnosis of MVP. The criteria for diagnosing people with MVP at this hospital(s) lack proper guidelines. It has been observed that people with mitral displacement less than 2mm even without MR which do not qualify for MVP diagnosis are commonly included in this category. Furthermore, there is no differentiation between primary versus secondary or classical versus non classical or even functional type of MVP.

The advent of ultrasonography provide new imaging modalities for the definition of MVP diagnosis criteria. Problems of diagnostic sensitivity and specificity as well as non strict criteria for the early imaging modalities resulted in diagnostic confusion about the prevalence of MVP. In the current situation where there is an increased ability to diagnose, monitor and prevent disease progression it is important that clinicians are able to properly diagnose and manage patients.

A consistent yet controversial finding in many clinical studies of patients with MVP syndrome has been the prevalence of anxiety, panic attacks, and other complaints that are considered to be neuropsychiatric symptoms.

The problems seen in this set up include:

- The limited information/agreement regarding the diagnostic criteria for MVP.
- The prevalence of MVP at our set up has not been looked into in detail.

- Few attempts have been made to relate this disease either to the total hospital admissions or to the total cardiac patients.

- The relationship between MVP and anxiety disorders remains something of an enigma at our set up.

2.2 RATIONALE OF THE STUDY

MVP could be a problem of public health importance in Dar es Salaam and Tanzania in general. This is evidenced by the number of patients referred to or attending at MNH OPD cardiac clinics with a clinical diagnosis of MVP and registered in the Echocardiogram register. There are few published studies in Tanzania on the prevalence and clinical patterns of MVP. One hospital based study done in Dar-es-Salaam by Eden Maro and Ramaiya K [26] reported the prevalence of MVP among patients referred to a private cardiac clinic with a provisional diagnosis of MVP based on clinical and Echocardiographic profile to be 65.9%. No community based study has been done.

It is well known that patients with MVP, are prone to develop mitral regurgitation, endocarditis, thromboembolism, atrial fibrillation or even heart failure. Majority of these complications can be avoided if proper classical MVP and its magnitude is recognized early, followed by subsequent primordial prevention and proper management. There is lack of awareness on the magnitude of MVP; based on clinical features and classical echocardiographic criteria specific for diagnosing MVP. Common clinical features and complications of MVP are also not well known and documented in Tanzania. Due to the above reasons, this study was conducted with the aim of determining the prevalence, clinical and echocardiographic patterns of MVP among medical students (MD4 and MD5) at Muhimbili University of Health and Allied Sciences (MUHAS), Dar-es-Salaam. It is hopped that it will form a basis to improve the diagnosis, characterize the clinical patterns, and hence subsequent proper management of patients with MVP.

3.0 OBJECTIVES

3.1 Broad Objective:

To determine the prevalence, clinical and echocardiographic patterns of MVP among MD4 and MD5 medical students at MUHAS, Dar-es-Salaam. Tanzania

3.2 Specific Objectives:

3.2.1 To determine the prevalence of MVP by age and sex.

3.2.2 To describe the common presenting symptoms of MVP.

3.2.3. To describe the clinical signs of MVP.

3.2.4 To describe the Echocardiographic patterns of MVP.

4.0 METHODOLOGY

4.1 Study design:

A Cross –sectional descriptive study was conducted.

4.2 Study setting:

The study was done at Muhimbili National Hospital adjacent to the Muhimbili University of Health and Allied Sciences (MUHAS) in Dar-es-Salaam. Muhimbili National Hospital has an Echocardiography machine which is operating daily for both inpatients and outpatients. This is a university teaching hospital and a tertiary level referral hospital in Tanzania. It is situated in Dar es Salaam city with an estimated population of over three million.

4.3 Study Population:

All Doctor of Medicine (MD) Degree programme students in their last four semesters i.e. semesters 7& 8 (MD4) and semesters 9 & 10 (MD5) were recruited for the study.

4.4 Duration of the study

The study was done from March to April 2008 and again in October to November 2008.

4.5 Sample size estimation:

The sample size was determined using the Epi-Info version 6 with the following assumptions:

- The MVP occurs in approximate 2.4% of the general population
- The significance level = 95%

Sample size was calculated using the following formula:

$$n = \frac{Nz^2 P(1-P)}{d^2 (N-1) + z^2 P(1-P)}$$

Where:

N= total population (400)

Z= value (corresponding to the confidence level) 1.96

P= Expected proportion in the population (prevalence) 2.4%

d= absolute precision 2%

$$\text{Sample size (n)} = \frac{400 \times 1.96^2 \times 2.4 \times (1-2.4)}{2^2 (400-1) + 1.96^2 \times 2.4 (1-2.4)}$$

$$= 145.$$

The minimum sample size required was 145 students. The sample size was increased by 10% to allow for non-responses, incomplete investigations and other factors that could have decreased the yield of responses. The sample size was again increased to 202 students due to low yield. Total sample size was 202 students.

4.6 Recruitment and selection of study subjects

All Doctor of Medicine (MD) Degree programme students for the academic year 2007/2008 in their last four semesters i.e. semester 7 & 8 for MD4 and semester 9 & 10 for MD5 were eligible for the study. In MD4 there were 183 students (134 males and 49 females). In MD5 there were 205 students (161 males and 44 females), making a grand total of 388 students with an M/F ratio of 3:1. Out of 388 students, 202 were recruited into the study.

4.7 Sampling procedure

Using the 2007/2008 Students' University register book for MD4 and MD5, two hundred and two (202) students were randomly selected using a simple random sampling technique. Students were serially recruited. For every three male students, one female student was enrolled alternatively from both MD4 and MD5 until the sample size was reached.

4.8 Exclusion criteria

Students were excluded from the study if they did not consent.

4.9 Definition of terms

- Mitral valve prolapse (Classic diagnosis) was diagnosed if an upward displacement of the leaflet(s) exceeded 2mm and maximal thickness was ≥ 5mm on a 2-dimensional Echocardiography.
- Non classic mitral valve prolapse diagnosis was accepted when the displacement exceeded 2mm but maximal thickness was less than 5mm.

4.10 Data collection

All recruited students were evaluated by the investigator. For each student, a detailed past and recent cardiac history aimed at identifying symptoms and signs of MVP (including fatigue, dizziness, syncope, dyspnoea, chest pain, palpitations) etc were determined (looked for). A structured questionnaire designed for the purpose of the study was used to collect social demographic data (i.e. name, age, sex etc,) history, clinical findings and echocardiographic results. (Appendix I)

4.10.1 Physical examination

A thorough general and cardiovascular examination was done to all participants in the study by the investigator. Pulse rate, blood pressure, precordial abnormalities, heart sounds and cardiac murmurs were assessed and filled in the questionnaire. (Appendix I). All physical findings commonly associated with MVP were recorded in the questionnaire. These included skeletal abnormalities such as pectus excavatum, kyphoscoliosis etc. (Appendix I).

4.10.2 Echocardiography

Standard echocardiographic views were done to all the study students. The aim was to assess anatomical orientation of the MV, cardiac chambers and function, as well as measuring ejection fraction and fractional shortening. A detailed MV assessment/ measurement using the standard protocol for MVP assessment were done.

Assessment to identify those with congenital heart diseases, rheumatic heart disease and other anomalies was also done.

Echocardiographic Cardiac assessment was done using Phillips SONOS 7500 Ultrasound Machine (Model 2004) a 2-Dimension unit with a 3.8MH transducer. Trans-thoracic echocardiography; parasternal long axis, short axis, apical four chambers and sub xiphoid views were done.

Two-dimensional (2D) Pulsed Wave Doppler (PWD), Continuous Doppler and Color Flow Mapping (CFM) was documented and recorded on VHS Video cassettes. Studies were performed and reviewed in real time and stop-framemodes. M-Mode recordings were recorded and standard measurements taken according to the recommendations of The American Society of Echocardiography. [10]

Interpretations were done by the investigator, counter checked and or confirmed by an experienced cardiologist before being filled in the questionnaire for analysis. (Appendix I).

4. 11 Ethical clearance and participants benefit

Study participants were managed according to the usual protocols of any disease condition that was detected.

The aim of the study and all the procedures involved were clearly explained to students. A pre and post echocardiographic examination results were well explained to the study participants. Counseling of students on the benign nature of the disorder for those who had MVP was done by the investigator. Students were requested to give an informed written consent before participating in the study. Confidentiality during physical cardiac evaluation and Echocardiographic examination were maintained. All the information obtained was kept secret for the purpose of the study only.

Ethical clearance was obtained from the MUHAS high degree ethical committee of the research and publication committee. At the end of the study, all students with cardiac

abnormalities were informed and referred to MNH cardiac clinic for long-term follow-ups. Detected cardiac abnormalities were made available to the doctors attending them.

4.12 Data analysis

Data was first cleared and entered in a computer using Epi-Info data entry program. Epi-info version 6 Statistical package was used for data analysis. Data was summarized using frequency distributions. Two way tables were used to compare group measures.

5.0 RESULTS

A total of 202 students were recruited, 101 from each class. Among them 136 (67.3%) were males and 66 (32.7%) were females, with a male to female ratio of 3:1. Majority of students were in the age group 24-26 years. The mean age of the students was 25.71 ± 1.58 (Range 22-29 yrs), (Table 1).

Table 1

Age and sex distribution of the study group

	Male	**Female**	**Total**
	N (%)	**N (%)**	**N (%)**
MD4	68 (67.3)	33 (32.7)	101
MD5	68 (67.3)	33 (32.7)	101
Age (years)			
21-23	8 (5.9)	9 (13.6)	17 (8.4)
24-26	61 (44.9)	50 (75.8)	111 (55.0)
27-29	67 (49.2)	7 (10.6)	74 (36.6)
Total	**136 (67.3)**	**66 (32.7)**	**202 (100)**

The prevalence of classic MVP was 0.99% (2/202), one student from each sex. The prevalence of non-classic MVP was 1.5% (3/202), one student from each age group, two were females and one male.

Chest pain and palpitations were the two presenting symptoms in all the two students with classical MVP, while systolic click was the only clinical sign detected in both two students with classical MVP.

Among students with MVP, 5 had MV displacement of ≥ 2mm. Two had MV thickness of ≥ 5mm, 3 with MV thickness of < 5mm. Out of those with MVP; 2 had classic MVP and 3 non-classic MVP. One student had both trivial mitral and tricuspid regurgitation. Among students without MVP, 3 had mitral valve displacement of < 2mm. One had MV thickness ≥ 5mm, 4 had MV thickness of < 5mm and 5 had features of RHD. Small pericardial effusion, trivial mitral, tricuspid and aortic regurgitations were found separately in 4 students, (Table 2).

Table 2

Distribution of echocardiographic findings in students with and without MVP

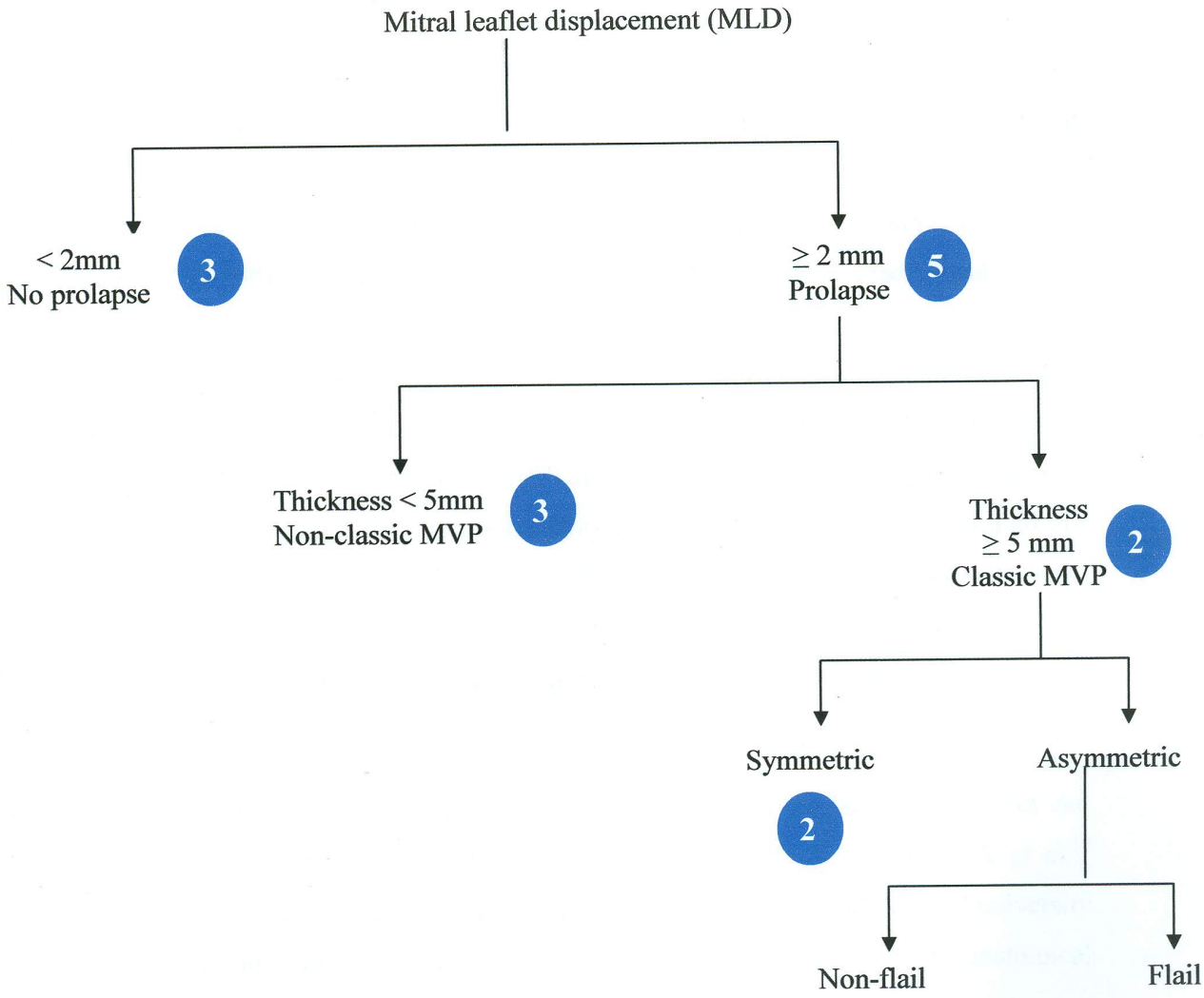
With MVP		Without MVP	
Parameter	**N**	**Parameter**	**N**
MV displacement ≥ 2mm	5	MV displacement <2mm	3
MV thickness ≥ 5mm	2	MV thickness ≥ 5mm	1
MV thickness < 5mm	3	MV thickness < 5mm	4
MVP (Classic)	2	RHD	5
MVP (Non-classic)	3	Small pericardial effusion	1
Trivial MR	1	Trivial MR	1
Trivial TR	1	Trivial TR	1
–	–	Trivial AR	1

NB: Students may have various combinations of these findings.

Five students had mitral leaflet displacement of ≥ 2mm (prolapse). Out of these, three had mitral valve thickness < 5mm (Non-classic MVP) and two had thickness of ≥ 5mm (Classic MVP). All had symmetric prolapse. (Figure 2)

Figure 2

Distribution of mitral leaflet displacement and thickness based on 2D-Echocardiography findings. (NB: Number in blue circles indicates the number of students)



prolapse classical (MVP) in 2 cases (0.5%). This is almost similar to the current study results possibly because they were university students with almost similar demographic characteristics. [14]

Before the Framingham study, the prevalence of MVP was thought to be much higher in women, however, with new criteria and modern echocardiographic detailed findings, it is now believed that MVP affects both gender and age groups equally. [8,9]

In Flacks' study [9] findings, the prevalence was similar in both gender groups, as well as in black and white people. Among the 2.7% of people who had a prior diagnosis of MVP, only 0.45% had classical MVP. Studies by Zupiroli, Freed, and Flacks were all large community based. [8,9,13,14]

The current study shows that the inclusion of non-classic MVP in this disease condition which was found in 3 (1.5%) students as well as inclusion of 3 students with mitral leaflet displacement < 2mm if were to be included in the diagnosis, this could contribute to a much higher prevalence rate of 8/202 (3.96%). It is probable that this was the case in some previous study findings.

In the United States, previously the prevalence of MVP has been estimated at 4% to 5% with great variations in age, gender and from different studies. This was attributed to lack of strict criteria for diagnosis, differences in study designs and selection bias. [3,6,7]

Because of its relatively high prevalence (0.6% to 2.4%) in the USA general population, and MVP being the most common cause of chronic MR (moderate to severe) present in 16% to 23% of patients with MVP, it is not surprising that this is the most common indication for MV surgical repair or replacement in developed countries.[34,35,36]

However in Africa and other developing countries and worldwide today where rheumatic heart conditions still accounts for the majority of mitral valve disease as it was found in 5/202 students (2.47%), when this is combined with the MVP burden, it is

not surprising again that in the surgical series of patients undergoing MV repair or replacement, MVP and Rheumatic heart diseases ranks the top.[36]

In this study, none of the students with MVP had MR or other cardiac abnormalities. Five (2.47%) students were found with non prolapsing thickened both MV leaflets involving the sub-valvular apparatus. The thickness was < 5mm in four students and ≥ 5mm in one, all had no regurgitations or vegetations, and they could not fit in the MVP criteria. Although none had previous history of rheumatic fever, in view of the findings and high rate of RHD, they were categorized as rheumatic heart condition.

Hospital based studies emanating from Africa, [19,20,21,22,23,26,27] show differences in MVP prevalences. The prevalence ranges between 3% and 16%. Almost all available study findings from Africa were hospital based, and none had used the current criteria for diagnosing MVP. Few studies tried to separate between functional and anatomical conditions resulting in MVP. This indicates that, although clinicians in this region could be aware of the problem, they probably do lack a standardized reference criteria for diagnosing this common valvular heart disease, hence its proper prevalence remain yet unknown.

These studies have tried to relate MVP either to the total hospital admissions or to the cardiac conditions prevailing in our hospitals but with much prevalence variations. It is therefore suggested that further studies using current echocardiographic criteria be done to ascertain the proper prevalence of MVP in Africa.

In the current study, the presenting symptoms in the two students who had classical MVP were a non-specific; occasional chest pain and on and off awareness of heart beats. These symptoms were not found in the other three students who had non classic MVP as well as in the large group of students who had normal echocardiographic findings. The symptoms were present occasionally without any precipitating or aggravating factors and no one was incapacitated or could seek medical attention for the

particular symptoms. This is similar to other findings where majority of people with MVP have been found to present with non specific symptoms. [6,7,8,9]

MVP has been associated with a number of signs and symptoms. The symptoms include: chest pain, breathlessness, fatigue, dizziness, anxiety, palpitations, vertigo, paresthesia, sweating, presyncope or syncope. These may occur without a satisfactory explanation.[3,8,9,14] In previous studies, as many as 50% of patients with MVP were symptomatic of palpitations, chest pain or dyspnea. The mean age of the population in those studies was 41 years than in the current study with a mean age of 26 years. This suggests that asymptomatic patients with MVP in young age may become symptomatic as they grow older. In the current study non classic MVP subjects and the rest of the study described as normal, had no symptoms suggestive of MVP. This supports the hypothesis that non classic variant of MVP is probably the normal version of mitral valve.

MVP syndrome refers to the occurence of symptoms resulting from neuroendocrine or autonomic dysfunction in patients with MVP in whom the symptoms cannot be explained on the basis of the valvular abnormality alone. This classification is clinically useful because it separates patients with MVP and symptoms related to MV dysfunction like MR, arrythmias, thromboembolism, vegetations or even heart failure from those whose symptoms may be secondary to autonomic dysfunction or other underlying conditions. In the current study, the two students with MVP could not fit in the category of "MVP syndrome" neither their sypmtoms could not be explained as due to valvular dysfunction as this was absent, and the symptoms were present only very occasional with no clear pattern.

Although the correlation between these nonspecific symptoms and MVP remains unclear, many patients are said to present with palpitations as was the case in the current study. [8,13,14] Some studies suggest that these patients are also at increased risk of sudden

cardiac death (SCD) compared to the general population, but the exact reason behind and incidence remains unknown. [3,13,14,33,]

In view of the fact that only two candidates (0.99%) had Classic MVP, it is difficult to make a firm conclusion regarding the symptomatology specific for MVP. However, this was not the case in the nonclassic group (1.5%) or the rest of the students. Given the nonspecific nature of these symptoms, despite that they were found only in the two students with classic MVP, taking into consideration of its mode of presentation, it is again unlikely that, these symptoms are related to MVP. The association of symptoms and MVP in the current study cannot be rejected outright. Even though early studies suggested that MVP is associated with a variety of symptoms as explained above, these associations have not been substantiated by carefully performed, controlled studies. [3,8,9,13,14,33,34]

The diagnosis of MVP is usually suspected from cardiac auscultatory findings and then confirmed by echocardiography. In this study, the cardiac auscultatory finding in students who had classic MVP was non-ejection systolic click without cardiac murmurs. Characteristically the systolic clicks changed with posture from squatting to standing (valsava maneuver). This has been a key to the clinical diagnosis of MVP. The presence of non-ejection systolic click(s) with or without late mitral systolic murmur constitutes the auscultatory criterion for the diagnosis of MVP.[3,8,26,46,49,50]

The most specific physical diagnostic criteria for the diagnosis of MVP are the characteristic changes of the systolic click(s) or the MV regurgitation murmur that occur with postural changes. The systolic clicks normally move close to the first heart sound with upright posture often merging with the first heart sound. Prompt squatting from the standing position results in the systolic click(s) to move to late systolic positions. This sequence has been well documented and was clearly appreciated in the current study. Continuous auscultation was done in several positions in the two students with classical MVP. This should be performed when examining people suspected of MVP. Although a

midsystolic non ejection click and late systolic murmur are widely accepted as specific evidence of MVP, prolapse may exist with a normal physical examination which has been observed in the non classic MVP in this study.

Adrenergic state, intravascular volume status and pharmacological agents that affect the heart rate, the LV volume, and myocardial contractility may change the auscultatory findings especially in the upright position. Thus, β- blocking agents may markedly attenuate or abolish the ascultatory findings. It follows therefore that, lack of diagnostic auscultatory findings for MVP in patients receiving these agents does not exclude the diagnosis. [3,49,50]

Skeletal abnormalities have been reported in up to two thirds of patients with MVP.[3,31,48,49] Skeletal abnormalities of the chest and spine include scoliosis, narrow anteroposterior diameter, straight back, pectus excavatum, and pectus carinatum. In this study, none of the two students who had classic MVP or the other three with nonclassic MVP had skeletal abnormality. However, one student with classical MVP had an asthenic habitus with no skeletal abnormality that did not fit for any specific criterion of a recognizable connective tissue disorder. This is important in order to distinguish the primary (classic MVP) from the secondary causes which can be identified due to its association with skeletal abnormalities and or body habitus.

Many people with MVP are reported to be thinner than normal, with the height: weight ratio greater than normal and arm span greater than height. This was not found in this study; however, this is what is normally seen in syndromes like Malfans (secondary causes) or in people with functional MVP secondary to other connective disorders. Therefore, care should be taken to exclude them or other associated anomalies when found with MVP. The abnormality of the mitral apparatus in these conditions is a feature of the underlying disease process rather than a primary abnormality of the MV.

It is not possible to make a sound conclusion from this study regarding the association of MVP with skeletal anormalies. However, a great suspicion of secondary MVP should

be made in the presence of athenic habitus and skeletal anomalies hence, a careful examination of the musculoskeletal system is mandatory.

Secondary MVP may be associated with heritable disorders of the connective tissue. This has been documented in several studies. [3,4,9] The connective tissue disorders and musculoskeletal abnormalities can be part of the presenting complaints and can give the clue of the underlying MV anomaly. In this regard, the extremities should be checked for arachnodactyly, characteristics of the Marfan syndrome, and conditions like joint hypermobility present in diseases like Ehlers-Danlos syndrome. The fingers, wrists, elbows, knees, hips, and ankles should be evaluated.

Echocardiography is the most useful non-invasive technique for the diagnostic evaluation of patients with suspected MVP. The echocardiogram also identifies the presence and the magnitude of MVP, the thickness of the mitral valve leaflet(s), the mitral annulus size, the chordae tendineae length, and the LV as well as the LA size and functions. Furthermore, associated cardiac abnormalities like regurgitation(s), emboli, vegetations and other acquired or congenital anomalies can be defined.

The most important and reliable view for mitral valve prolapse is by a parasternal long axis view from a two-dimensional echocardiogram which can clearly identify a definite displacement of the mitral leaflet into the left atrium. This position is determined by extending a line from the base of the aortic valve to the atrioventricular junction roughly parallel to the plane of the atrioventricular ring: A normal valve does not reach this plane.

Most studies in the past did not use the current 2-D echocardiographic criteria to exclude non-classic type, functional, or secondary MVP. This contributed to a much higher prevalence rate of MVP based on echocardiographic findings.

The echocardiographic criteria for MVP must be adhered to and should be based on firm structural changes, such as leaflet thickening, redundancy, increased surface area,

annular dilatation, and chordal elongation. This is important in the diagnosis of MVP and has significant impact on patients care by avoiding unnecessary over diagnosing MVP. It also avoids unneccessary patients concerns with minor valvular abnormalities.

The classic prolapse is defined as systolic displacement of the mitral leaflet(s) of greater than 2mm into the LA across the annulus plane in a 2D long-axis view and a maximal leaflet thickness of 5mm or more. The three-dimensional shape of the mitral annulus is nonplanar (often described as saddle-shaped). It led to the realization that the mitral leaflets can appear to be on the LA side of the annulus in the apical four-chamber view when, in fact, leaflet closure is normal and other signs of MVP are absent. This also applies for thickness and valve redundancy [3]. In this current study, echocardiography was performed from multiple acoustic windows and no single numerical value was used to classify patients.

In this study, 5 students (2.5%) had mitral valve thickness with no prolapse, 4 had <5 mm thickness and only 1 had >5 mm thickness. Although, they had no history of rheumatic fever but were considered to have previous rheumatic fever attack hence rheumatic heart disease. If they had prolapse they would have been in the category of functional MVP.

In this study one student with classic MVP had an affected contralateral atrioventricular (Tricupid Valve). This has been also documented by Ali SK[42]. He reported Ebstein's malformation in Sudanese patients associated with MVP. It has been documented that MVP pathologic process may involve more than one valve. [2,3,4,5]

Mitral regurgitation (MR) is the common complication in patients with MVP. In this study one student with symmetric classical MVP had trivial mitral regurgitation. This has been consistently found in most previous studies.[6,7,8,9,34,35,49] The degree of MR in patients with MVP is reported to correspond approximately to the extent of leaflet thickening and redundacy. Moderate to severe MR is reported to occur in 66% of patients with posterior leaflet prolapse and to about 25% of those with anterior leaflet

prolapse.[34,35] In this study, no student had asymmetric prolapse which is commonly associated with MR. Also no student had thrombi, endocarditis, LV dysfunction or other complications associated with MVP.

The most important principle in the management of patients with suspected MVP is to avoid overdiagnosis. There is no known medical therapy to prevent progression of the underlying disease process in patients with MVP. The basic principle of medical therapy is to prevent complications, identify and treat co-morbid diseases, provide education, reassurance, and periodic evaluation. Use of β blockers have been documented to provide relief to symptomatic patients with arrhythmias and should only be considered in selected cases. Most patients with MVP are amenable to surgical repair rather than valve replacement. [3,10]

7.0 STUDY LIMITATIONS

- All the subjects in the study were in their final years of medical school. They could have sufficient knowledge of heart diseases and could have undergone previous diagnostic procedures well ahead before the current study. Those who were previously diagnosed as heart disease patients may have volunteered to participate in the study so as to confirm their previous diagnoses.

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- The time for the study was very short thus limiting for a bigger sample size study.

8.0 CONCLUSIONS

From a sample size of 202 presumably healthy medical students aged between 21 to 28 years, the prevalence of classic MVP was 0.99%. This shows a low prevalence of MVP among the studied population.

9.0 RECOMMENDATIONS

A bigger sample sized community based study is recommended so as to determine the actual prevalence of MVP and its associated symptoms and signs as well as its echocardiographic patterns in our community.

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