A STUDY OF CLINICAL PROFILE IN MITRAL VALVE PROLAPSE SYNDROME – A SERIES OF 100 CASES

Dissertation Submitted to

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

M.D. BRANCH – I
GENERAL MEDICINE

GOVT. STANLEY MEDICAL COLLEGE AND HOSPITAL
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.
MARCH 2009

CERTIFICATE

This is to certify that the dissertation titled "**A STUDY OF CLINICAL PROFILE IN MITRAL VALVE PROLAPSE SYNDROME – A SERIES OF 100 CASES**" is the bonafide original work of DR**. S. SATHIS KUMAR** in the Department of General Medicine, Government Stanley Hospital, Stanley Medical College, Chennai – 600 001, in partial fulfillment of the University rules and regulation for the award of M.D. DEGREE BRANCH I GENERAL MEDICINE – under my guidance and supervision during the academic period from 2007 – 2008.

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I, **Dr. S. SATHIS KUMAR**, solemnly declare that the dissertation titled was done by me at Govt. Stanley Medical College and Hospital during 2007 – 2008 under the guidance and supervision of my unit chief, **Prof. S. SUNDAR, M.D**.

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ACKNOWLEDGEMENT

I owe my thanks to the Dean, Government Stanley Medical College and Hospital, **DR. J. MOHANASUNDARAM, M.D, Ph.D, DNB**, for allowing me to avail the facilities needed at his disposal for my dissertation work.

I am very grateful to **Prof. V. RUCKMANI, M.D.,** Professor and Head of the Department of Medicine, Government Stanley Medical College and Hospital for permitting me to do this study and for her encouragement.

I am very grateful to **Prof. S.RAMASAMY, M.D**., Professor of Therapeutics, Government Stanley Medical College and Hospital for his valuable assistance and guidance.

I am very grateful to unit chief, **Prof. S. SUNDAR, M.D**., Government Stanley Medical College and Hospital for his valuable assistance and guidance.

I am very grateful to **Prof. T.VENKATAKRISHNAN, M.D**., Government Stanley Medical College and Hospital for his valuable assistance and guidance.

I am very grateful to **Dr. G. VASUMATHI, M.D**., Registrar, Medicine Dept, Government Stanley Medical College and Hospital for her valuable

assistance and guidance.

I am extremely thankful to Assistant Professors **Dr. K. SUJIT M.D.** and **DR. K. SURESH KUMAR, M.D**., for their guidance and encouragement.

I am very thankful to **Prof. R. SUBRAMANIAN, M.D., D.M.,** Head of Department of Cardiology for the valuable guidance and co-operations and help on every stage of this study.

I am also thankful to my colleagues for their valuable help rendered to complete this study.

My great thanks to the patients who co operated for this study, without whom, this study could not have been undertaken.

CONTENTS

INTRODUCTION

The Mitral Valve Prolapse syndrome has been recognized as one of the most prevalent cardiac valvular abnormalities affecting 5 – 10% of the population. In majority of the patients with Mitral Valve Prolapse, the cause is unknown. The overwhelming majority of the patients are asymptomatic.

The clinical presentation of Mitral Valve Prolapse is also diverse. They present with a variety of symptoms such as fatigability, palpitation, postural giddiness and neuro psychiatric symptoms of autonomic dysfunction. Patients with Mitral Valve Prolapse may have a variety of cardiac and non cardiac abnormalities in addition to valvular lesion with its midsystolic click and murmur. This includes skeletal abnormalities like scoliosis, straight back syndrome, Pectus excavatum and asthenic build, abnormal cardiovascular and electrocardiographic responses to exercise, ST-T changes in resting ECG and a variety of Atrial and ventricular arrhythmias.

Wooley reported clinical similarities between Mitral Valve Prolapse and Da Costa syndrome, vasoregulatory asthenia described by Holmgren et

al and hyperkinetic heart syndrome reported by Gorlin.

The presence of chest pain, ST-T abnormalities and arrhythmias in the absence of hemodynamically significant valvular, myocardial or coronary arterial disease suggests the possibility of a disorder involving autonomic system. Greater attention and enthusiasm on this condition has been developed because of high prevalence of the condition and increased risk of sudden death. Since special therapeutic, prognostic and genetic factors must be considered in Mitral Valve Prolapse syndrome, precise identification of the condition is essential.

AIM OF THE STUDY

The Aim of this study is to study the clinical profile of Mitral Valve Prolapse Syndrome and investigating the existence of Autonomic Dysfunction in the subjects studied through bedside tests.

REVIEW OF LITERATURE

Mitral Valve Prolapse Syndrome, also variously termed the systolic click-murmur syndrome, Barlow's syndrome, floppy-valve syndrome, and billowing Mitral leaflet syndrome, myxomatous mitral valve syndrome and redundant cusp syndrome. [1] This is a relatively common, but highly variable clinical syndrome resulting from diverse pathogenic mechanisms of the mitral valve apparatus. The Mitral Valve Prolapse syndrome is one of the most prevalent cardiac valvular abnormalities. It results from diverse pathogenic mechanisms of one or more portions of the mitral valve apparatus, valve leaflets, chordae tendineae, papillary muscle, and valve annulus. Among these is excessive or redundant mitral leaflet tissue, which is commonly associated with myxomatous degeneration and greatly increased concentrations of acid mucopolysaccharide.

Using standardized echocardiographic diagnostic criteria, a community-based study showed that Mitral Valve Prolapse syndrome occurs in 2.4 percent of the population. [4] Mitral Valve Prolapse is a frequent finding in patients with heritable disorders of connective tissue, including the Marfan syndrome, Osteogenesis imperfecta, and the Ehler-Danlos syndrome. In most patients with Mitral Valve Prolapse, however, myxomatous degeneration is confined to the mitral (or less commonly the tricuspid or aortic) valves without other clinical or pathologic

manifestations of disease. The posterior leaflet is usually more affected than the anterior, and the mitral valve annulus is often greatly dilated. In many patients, elongated redundant chordae tendineae cause or contribute to the regurgitation.

Most frequently, Mitral Valve Prolapse occurs as a primary condition that is not associated with other diseases and can be familial or non familial. Familial Mitral Valve Prolapse is transmitted as an autosomal trait, and several chromosomal loci have been identified. The Mitral Valve Prolapse syndrome is more prevalent in young women, [12] who generally have a benign course, whereas severe myxomatous disease is more common in older men, who have a higher risk of complications, including the need for surgical Mitral Valve repair. Mitral Valve Prolapse has also been associated with many conditions, occurring quite commonly in heritable disorders of connective tissue that increase the size of the mitral leaflets and apparatus.

Echocardiographic evidence of Mitral Valve Prolapse is found in most patients with the Marfan syndrome and in many of their first-degree relatives. Mitral Valve Prolapse has also been associated with Ehlers-Danlos syndrome, Osteogenesis imperfecta, pseudoxanthoma elasticum, periarteritis nodosa, myotonic dystrophy, Von Willebrand disease, hyperthyroidism, and congenital malformations such as Ebstein anomaly of

the tricuspid valve, Atrial septal defect of the ostium secundum variety, the Holt-Oram syndrome, and Hypertrophic Cardiomyopathy. There may be a higher incidence of Mitral Valve Prolapse in patients with an asthenic habitus and various congenital thoracic deformities, including “straight back syndrome,” pectus excavatum, and a shallow chest. These associations have not been proved using rigorous echocardiographic criteria, and, with the exception of connective tissue disorders, it is not clear how many of these are chance associations. [33]

Mitral Valve Prolapse Syndrome
Younger age (20-50 yr)

Predominantly female

Click or click-murmur on physical examination

Thin leaflets with systolic displacement on echocardiography

Associated with low blood pressure, orthostatic

Hypotension, palpitations

Benign long-term course

Myxomatous Mitral Valve Disease
Older age (40-70 yr)

Predominantly male

Thickened, redundant valve leaflets

Mitral regurgitation on physical exam and echocardiography

High likelihood of progressive disease requiring mitral valve surgery

Secondary Mitral Valve Prolapse
Marfan syndrome

Hypertrophic cardiomyopathy

Ehlers-Danlos syndrome

Other connective tissue diseases.

In most patients with Mitral Valve Prolapse, the cause is unknown, but in some it appears to be a genetically determined collagen tissue disorder. A reduction in the production of type III collagen has been incriminated, and electron microscopy has revealed fragmentation of collagen fibrils. Mitral Valve Prolapse may be associated with thoracic skeletal deformities similar to but not as severe as those in the Marfan syndrome, including a high-arched palate and alterations of the chest and thoracic spine, including the so-called straight back syndrome. Mitral Valve Prolapse also may occur as a sequel of acute rheumatic fever, in ischemic heart disease, and in cardiomyopathies, as well as in 20% of patients with ostium secundum Atrial septal defect.

Mitral Valve Prolapse may lead to excessive stress on the papillary muscles, which in turn leads to dysfunction and ischemia of the papillary muscles and the subjacent ventricular myocardium. Rupture of chordae tendineae and progressive annular dilatation and calcification also contribute to valvular regurgitation, which then places more stress on the diseased mitral valve apparatus, thereby creating a vicious circle. The

electrocardiographic changes and ventricular arrhythmias appear to result from regional ventricular dysfunction related to increased stress placed on the papillary muscles.

Recent studies have found a direct role of rheumatic Mitral stenosis in the genesis of secondary Mitral valve prolapse.

GENETICS

New locus for autosomal dominant Mitral valve prolapse has been mapped to chromosome 13, in recent studies. [13]

PATHOLOGY

Findings include myxomatous proliferation of the Mitral valve leaflets, in which the spongiosa component of the valve (i.e., the middle layer of the leaflet between the atrialis and the ventricularis composed of loose, myxomatous material) is unusually prominent and the quantity of acid mucopolysaccharide is increased Electron microscopy shows a haphazard arrangement of cells with disruption and with fragmentation of collagen fibrils. Secondary effects include fibrosis of the surface of the Mitral Valve leaflets, thinning and/or elongation of the chordae tendineae, and ventricular friction lesions.

In mild cases, the valvular myxoid stroma is enlarged on histological examination, but the leaflets are grossly normal. However, with increasing quantities of myxoid stroma, the leaflets become grossly abnormal,

redundant, and prolapsed. There is interchordal hooding due to leaflet redundancy that includes both the rough and clear zones of the involved leaflets. Regions of endothelial disruption are common and are possible sites of endocarditis or thrombus formation. The severity of Mitral Regurgitation depends on the extent of the prolapse. The cusps of the mitral valve, the chordae tendineae, and the annulus may all be affected by myxomatous proliferation. Degeneration of collagen and myxomatous changes within the central core of the chordae tendineae, with associated decreases in tensile strength, are primarily responsible for chordal rupture, which often occurs and may intensify the severity of Mitral Regurgitation. Increased chordal tension resulting from the enlarged area of the valve cusps may play a contributory role. Myxomatous changes in the annulus may result in annular dilation and calcification, further contributing to the severity of Mitral Regurgitation.

Myxomatous proliferation, although most commonly affecting the mitral valve, has also been described in the tricuspid, aortic, and pulmonic valves, particularly in patients with the Marfan syndrome, and may lead to regurgitation of these valves as well as the mitral valve.

CLINICAL FEATURES

Mitral Valve Prolapse is more common in females. It affects individuals in a wide age range but most commonly those between the ages

of 14 and 30 years. However, serious Mitral Regurgitation occurs more frequently in older males (older than 50 years) with Mitral Valve Prolapse, than in young females with this disorder, and requires surgical treatment.

The clinical course is often benign. Mitral Valve Prolapse encompasses a broad spectrum of severities, ranging from only a systolic click and murmur and mild prolapse of the posterior leaflet of the mitral valve to severe Mitral Regurgitation due to chordal rupture and massive prolapse of both leaflets. In many patients, this condition progresses over years or decades.

Most patients are asymptomatic and remain so for their entire lives. However, Mitral Valve Prolapse is now the most common cause of isolated severe Mitral Regurgitation requiring surgical treatment in North America. Early studies called attention to a “Mitral Valve Prolapse syndrome” with a characteristic systolic non ejection click and various nonspecific symptoms, such as fatigability, palpitations, postural hypotension, and anxiety and other neuropsychiatric symptoms, as well as symptoms of autonomic dysfunction. Arrhythmias, most commonly ventricular premature contractions and paroxysmal supraventricular and ventricular tachycardia, have been reported and may cause palpitations, light-headedness, and syncope. Sudden death is a very rare complication. [6] Many patients have chest pain that is difficult to evaluate. It is often substernal, prolonged, poorly related to exertion, and rarely resembles angina pectoris. The discomfort may be secondary to abnormal tension on papillary muscles. In patients with Mitral Valve Prolapse and severe Mitral Regurgitation, the

symptoms of the latter (fatigue, dyspnea, and exercise limitation) may be present. Transient cerebral ischemic attacks secondary to emboli from the mitral valve due to endothelial disruption have been reported. Infective endocarditis may occur in patients with Mitral Regurgitation associated with Mitral Valve Prolapse.

The body weight is often low, and the habitus may be asthenic. Blood pressure is usually normal or low; orthostatic hypotension may be present. As already mentioned, patients with Mitral Valve Prolapse have a higher than expected prevalence of “straight back syndrome,” scoliosis, and pectus excavatum. Mitral Regurgitation ranges from absent to severe. The clinical and echocardiographic criteria for the diagnosis of Mitral Valve Prolapse have been well established.

Mitral Valve Prolapse during pregnancy is frequent, it accounts for 8.3%. Varies symptomatology was characteristic for all the groups with Mitral Valve Prolapse. The most frequent complaints were: dizziness, palpitation, and faintness. Women with Mitral Valve Prolapse are not protected by pregnancy.

The incidence of benign joint hyper mobility syndrome (BJHMS) in patients with Mitral Valve Prolapse was more frequent than the normal population and there was a significant correlation between the severity of Benign Joint Hyper Mobility Syndrome (according to BHS) and

echocardiographic features of the mitral leaflets and elastic properties of the aortic wall. [14]

AUSCULTATION

The characteristic systolic click and mid-to-late systolic murmur is a major diagnostic criterion. The auscultatory findings unique to the Mitral Valve Prolapse syndrome are best elicited with the diaphragm of the stethoscope. The patient should be examined in the supine, left decubitus, and sitting positions. The most important finding is a non ejection systolic click at least 0.14 second after S1. This can be differentiated from a systolic ejection click because it occurs after the beginning of the carotid pulse upstroke. Occasionally, multiple mid and late systolic clicks are audible, most readily along the lower left sternal border. The clicks are believed to be produced by sudden tensing of the elongated chordae tendineae and of the prolapsing leaflets. They are often, although not invariably, followed by a mid- to late crescendo systolic murmur that continues to A2. This murmur is similar to that produced by papillary muscle dysfunction, which is readily understandable because both result from mid- to late systolic Mitral Regurgitation. In general, the duration of the murmur is a function of the severity of the Mitral Regurgitation. When the murmur is confined to the latter portion of systole, Mitral Regurgitation usually is not severe. However, as Mitral Regurgitation becomes more

severe, the murmur commences earlier and ultimately becomes holosystolic.

There is considerable variability of the physical findings in the Mitral Valve Prolapse syndrome. Some patients exhibit both a midsystolic click and a mid-to-late systolic murmur; others present with only one of these two findings; still others have only a click on one occasion and only a murmur on another, both on a third examination, and no abnormality at all on a fourth. Conditions other than Mitral Valve Prolapse that may cause midsystolic clicks include tricuspid valve prolapse, Atrial septal aneurysms, and extra cardiac causes.

DYNAMIC AUSCULTATION

The auscultatory findings are exquisitely sensitive to physiological and pharmacological interventions, and recognition of the changes induced by these interventions is of great value in the diagnosis of the Mitral Valve Prolapse syndrome. The mitral valve begins to prolapse when the reduction of Left Ventricular volume during systole reaches a critical point at which the valve leaflets no longer coapt; at that instant, the click occurs and the murmur commences. Any maneuver that decreases Left Ventricular volume, such as a reduction of impedance to Left Ventricular outflow, a reduction in venous return, tachycardia, or an augmentation of myocardial contractility, results in an earlier occurrence of prolapse during systole. As a

consequence, the click and onset of the murmur move closer to S1. When prolapse is severe and/or Left Ventricular size is markedly reduced, prolapse may begin with the onset of systole. As a consequence, the click may not be audible, and the murmur may be holosystolic. On the other hand, when Left Ventricular volume is augmented by an increase in the impedance to Left Ventricular emptying, an increase in venous return, a reduction of myocardial contractility, or bradycardia, both the click and the onset of the murmur will be delayed.

During the straining phase of the Valsalva maneuver and upon sudden standing, cardiac size decreases, and both the click and the onset of the murmur occur earlier in systole. In contrast, a sudden change from the standing to the supine position, leg-raising, squatting, maximal isometric exercise, and, to a lesser extent, expiration will delay the click and the onset of the murmur. During the overshoot phase of the Valsalva maneuver (i.e., six to eight cycles following release) and with prolongation of the R-R interval, either following a premature contraction or in Atrial Fibrillation, the click and onset of the murmur are usually delayed, or the intensity of the murmur is reduced. Maneuvers that elevate arterial pressure, such as isometric exercise, increase the intensity of the click and murmur. In general, when the onset of the murmur is delayed, both its duration and intensity are diminished, reflecting a reduction in the severity

of Mitral Regurgitation.

The response to several interventions may be helpful in differentiating obstructive Hypertrophic Cardiomyopathy from Mitral Valve Prolapse. During the strain of the Valsalva maneuver, the murmur of Hypertrophic Cardiomyopathy increases in intensity, whereas the murmur of Mitral Valve Prolapse becomes longer but usually not louder. The murmur of Hypertrophic Cardiomyopathy becomes louder after amyl nitrite inhalation, whereas that of Mitral Valve Prolapse does not. Following a premature beat, the murmur of Hypertrophic Cardiomyopathy increases in intensity and duration, whereas that due to Mitral Valve Prolapse usually remains unchanged or decreases.

LABORATORY EXAMINATION

ELECTROCARDIOGRAM:

The Electrocardiogram most commonly is normal but may show biphasic or inverted T waves in leads II, III, and aVF, and occasionally supraventricular or ventricular premature contractions.

ECHOCARDIOGRAPHY:

Echocardiography plays an essential role in the diagnosis of Mitral Valve Prolapse and has been instrumental in the delineation of this syndrome. To establish the diagnosis, the two-dimensional echocardiogram must show that one or both mitral valve leaflets billow by at least 2 mm

into the left atrium during systole in the long-axis view. Thickening of the involved leaflet to greater than 5 mm supports the diagnosis. Findings of more severe myxomatous disease include increased leaflet area, leaflet redundancy, chordal elongation, and annular dilation. These findings are also helpful in identifying patients at significant risk for developing severe Mitral Regurgitation or infective endocarditis. The mitral annular diameter is often abnormally increased.

Systolic pulmonary venous flow reversal identified by pulsed Doppler echocardiography is useful for the diagnosis of severe mitral regurgitation. The direction of the mitral regurgitant jet in severe mitral regurgitation significantly influences the systolic pulmonary venous flow reversal, using transthoracic color Doppler echocardiography. [18]

In one Study, additional diagnostic criteria were searched. It was found that in patients with Mitral Valve Prolapse, the main pulmonary artery diameter was significantly larger (>23 mm) in patients with Marfan Syndrome at all ages when compared with controls. [11]

Transesophageal echocardiography provides additional details regarding integrity of the mitral valve apparatus, such as rupture of chordae tendineae. In Mitral Regurgitation secondary to Mitral Valve Prolapse, the echocardiogram also provides valuable information regarding Left Ventricular size and function.

The echocardiographic findings of Mitral Valve Prolapse may be observed in patients without a click or murmur. Others have both the typical echocardiographic and auscultatory features.

Buckling of the mitral valve, as seen from the short axis views, appears to provide a confirmatory role in diagnosing mitral valve prolapse, particularly in questionable cases; improving the overall accuracy.[16]

The echocardiographic findings of Mitral Valve Prolapse have been reported to occur in a large number of first-degree relatives of patients with established Mitral Valve Prolapse. Two-dimensional echocardiography has also revealed prolapse of the tricuspid and aortic valves in approximately 20 percent of patients with Mitral Valve Prolapse. [7] Conversely, however, prolapse of the tricuspid and aortic valves occurs uncommonly in patients without prolapse of the mitral valve.

Doppler echocardiography frequently reveals mild Mitral Regurgitation that is not always associated with an audible murmur. Moderate to severe Mitral Regurgitation is present in about two-thirds of patients with posterior leaflet prolapse and in about one-fourth of patients with anterior leaflet prolapse. Severity of Mitral Regurgitation should be assessed quantitatively as previously discussed. Studies in Department of Cardiovascular Hemodynamics, Osaka City University Medical School Hospital, Osaka, indicate that freehand 3D echocardiography is useful for

assessment of the involved lesion of the mitral valve in patients with mitral valve prolapse. [15]

ARRHYTHMIAS

Spectrums of arrhythmias have been observed in patients with Mitral Valve Prolapse. These include Atrial and ventricular premature contractions and supraventricular and ventricular tachyarrhythmias, as well as bradyarrhythmias due to sinus node dysfunction or varying degrees of atrioventricular block. The mechanism of the arrhythmias is not clear. [22] Diastolic depolarization of muscle fibres in the anterior mitral leaflet in response to stretch has been demonstrated experimentally, and the abnormal stretch of the prolapsed leaflet may be of pathogenetic significance.

Paroxysmal supraventricular tachycardia is the most common sustained tachyarrhythmia in patients with Mitral Valve Prolapse and may be related to an increased incidence of left atrioventricular bypass tracts. The incidence of Mitral Valve Prolapse among patients with the Wolff-Parkinson-White syndrome is increased. There is also an increased association between Mitral Valve Prolapse and prolongation of the QT interval, and this association may play a role in the pathogenesis of serious ventricular arrhythmias. Patients with Mitral Valve Prolapse have an increased incidence of abnormal late potentials on signal-averaged

Electrocardiographs, as well as reduced heart rate variability.

STRESS SCINTIGRAPHY.

The differential diagnosis between two common conditions— Mitral Valve Prolapse associated with chest pain and ECG abnormalities and primary coronary artery disease associated with Mitral Valve Prolapse — may be aided by exercise electrocardiography. However, myocardial perfusion scintigraphy using thallium-201 or sestamibi during pharmacological exercise stress is more specific for diagnosing associated coronary artery disease.

ANGIOGRAPHY

Angiography is not recommended for the diagnostic evaluation of Mitral Valve Prolapse. However, if angiography is performed for other indications, there are features of the left ventriculogram that are characteristic of Mitral Valve Prolapse. The right anterior oblique projection is most useful for defining the posterior leaflet of the mitral valve, and the left anterior oblique projection is most useful for studying the anterior leaflet. [20] The most helpful sign is extension of the mitral leaflet tissue inferiorly and posteriorly to the point of attachment of the mitral leaflets to the mitral annulus. Angiography may also reveal scalloped edges of the leaflets, reflecting redundancy of tissue. Other angiographic abnormalities in some patients with Mitral Valve Prolapse

include Left Ventricular dilation, decreased systolic contraction (especially of the basal portion of the ventricle), and calcification of the mitral annulus.

MAGNETIC RESONANCE IMAGING AND CARDIAC COMPUTED TOMOGRAPHY.

These advanced imaging techniques can help in determining the extent of Mitral Valve Prolapse and Left Ventricular function in patients with suboptimal echocardiographic examinations. CMR is also useful for evaluating presence and severity of Mitral Regurgitation.

DISEASE COURSE

The outlook for patients with Mitral Valve Prolapse in general is excellent; large majorities remain asymptomatic for many years without any change in clinical or laboratory findings. Serious complications (cardiac death, need for cardiac surgery, acute infective endocarditis, or cerebral embolic events) occur at a rate of only 1 per 100 patient years, and 4 percent of patients died during the 8 years. In contrast, one study reported a much more aggressive course in 833 patients with Mitral Valve Prolapse, with a 19 percent mortality rate at 10 years and a 20 percent rate of Mitral Valve Prolapse -related events, including heart failure, Atrial Fibrillation, Cerebrovascular events, arterial thromboembolism, and endocarditis. The apparent explanation for these latter observations is that

patients with Mitral Valve Prolapse could be risk stratified on the basis of several factors. The primary risk factors were moderate to severe Mitral Regurgitation and/or Left Ventricular ejection fraction less than 50 percent, and secondary risk factors included mild Mitral Regurgitation, left Atrial dimension 40 mm or greater, flail leaflet, and age 50 years or older. Patients with a primary risk factor had excessive mortality and morbidity, as did those with two or more secondary risk factors. Other series support these observations, demonstrating greater risk of cardiac death or Mitral Valve Prolapse -related complications in men, those older than 45 years old, those with holosystolic murmurs, those with severe Mitral Regurgitation, and those with left Atrial dimension greater than 40 mm. Other series that have reported a lower prevalence of adverse sequelae of Mitral Valve Prolapse have included relatively fewer patients with these risk factors. Progressive Mitral Regurgitation with gradual increase in left Atrial and Left Ventricular size, Atrial Fibrillation, pulmonary hypertension, and the development of congestive heart failure is the most frequent serious complication, occurring in about 15 percent of patients over a 10- to 15-year period. Patients with the Mitral Valve Prolapse syndrome are also at risk of developing infective endocarditis. Both severe Mitral Regurgitation and endocarditis develop more frequently in patients with both murmurs and clicks than in those with an isolated click, in

patients with thickened (greater than 5 mm) and redundant mitral valve leaflets, and in men older than 50 years . In many patients, rupture of chordae tendineae is responsible for the precipitation and/or intensification of the Mitral Regurgitation. Infective endocarditis often aggravates the severity of Mitral Regurgitation and therefore the need for surgical treatment.

The prevalence of mitral valve prolapse in Stickler syndrome has been reported to be much higher than in the general population. [17]

Acute hemiplegia, transient ischemic attacks, cerebellar infarcts, amaurosis fugax, and retinal arteriolar occlusions have been reported to occur more frequently in patients with the Mitral Valve Prolapse syndrome, suggesting that cerebral emboli are unusually common in this condition. It has been proposed that these neurological complications are associated with loss of endothelial continuity and tearing of the endocardium overlying the myxomatous valve, which initiates platelet aggregation and the formation of mural platelet-fibrin complexes. Although it has been proposed that embolization secondary to Mitral Valve Prolapse may be a significant cause for unexplained strokes in young people without cerebrovascular disease, a large case-controlled study showed no association between Mitral Valve Prolapse and ischemic neurological events in persons less than 45 years of age.

MITRAL VALVE PROLAPSE AND SUDDEN DEATH

The relation between the Mitral Valve Prolapse syndrome and sudden death is not clear. However, the best evidence suggests that Mitral Valve Prolapse increases the risk of sudden death slightly, especially in patients with severe Mitral Regurgitation [10] or severe valvular deformity, and those with complex ventricular arrhythmias, QT interval prolongation, and a history of syncope and palpitations. [34]

AUTONOMOUS NERVOUS SYSTEM:

It consists of Sympathetic and Parasympathetic Systems.

ANATOMY:

The autonomic outflow is regulated by the centres in Hypothalamus, Midbrain, Pons and Medulla.

Sympathetic outflow is from T1 to L2. Preganglionic fibres are small myelinated fibres that synapse in Para vertebral ganglia. Small unmyelinated post ganglionic fibres innervate the body organs.

Parasympathetic outflow is Cranio Sacral outflow. Cranial nerves are 3, 7, 9 and 10 and from S2 to S4. Preganglionic fibres are long myelinated fibres that synapse with post ganglionic fibres nearby the viscera.

AUTONOMOUS FUNCTION TESTS:

I. Cardiovascular

1. Resting Heart Rate:

2. Beat to beat variation of Heart Rate:

There is variation in heart beat from beat to beat by various influences including the depth of respiration. Change in Vasomotor tone also matters.

3. Heart Rate variation to deep breathing:

Subject breaths deeply and heavily at a arte of 6 breaths per minute. ECG is recorded. Maximum and minimum Heart Rate during 10 seconds is recorded. Mean of 3 cycles is taken. Normally the difference is >15.

4. Valsalva Manuoevere:

This test is performed by asking the subject to sit quietly and then blow with mouth closed. There are 4 phases. The ratio of longest RR interval shortly after Manuoevere to shortest RR interval during the Manuoevere is measured and expressed as Valsalva ratio. The mean of 3 successive Valsalva Manuoeveres is taken. Low Valsalva ratio implies parasympathetic abnormality.

5. Postural Hypotension:

Subject lies quietly in a couch for 15 minutes. Blood Pressure is recorded in supine position. Then Blood Pressure is again recorded 5 minutes after standing. Fall of systolic Blood Pressure > 30 mmHg or Diastolic Blood Pressure > 15 mmHg is abnormal. This is test for

Cardiovascular sympathetic efferent and Baroreflex pathway.

6. Postural tachycardiac Index:

During postural change from lying to standing a characteristic immediate rapid rise in heart rate occurs which is maximal at about the 15^{th} beat after standing, followed by relative overshoot bradycardia at 30^{th} beat, Normal ratio is > 1.04 in young adults.

7. Sustained Handgrip test:

Maximum sustained voluntary contraction of hand muscles is steadily maintained, upto 5 minutes. Blood Pressure is measured on the non-exercising arm 3 times at rest and 1 minute interval during handgrip. The difference in Diastolic Blood Pressure is taken. Normally there is increase in 16 mmHg.

8. Atropine Test:

On injecting atropine intravenously there is increase in heart rate; normally an increase of 20 beats per minute.

9. Cold pressor test:

Hand is immersed in cold water at 4^0 C for 5 minutes. Blood Pressure, Pulse Rate is recorded and compared with rest. Normally there is increase in systolic Blood Pressure by 15 – 20 mm and diastolic Blood Pressure

increase by 10 – 15 mm.

10. Trinitroglycerine test:

The Heart Rate, Blood Pressure of the subject is taken before and after 0.6mg sublingual Trinitroglycerine. Blood Pressure is taken supine and standing position. Fall in Blood Pressure is noted.

II. Sudomotor Function Tests:

1. Quantitative Sudomotor Axon Reflex Test (QSART) measures sweat output from skin.
2. Galvanic Skin response.
3. Thermal Sweat Test.

III. Pilomotor Response:

Skin of the subject at the nape of neck is gently stroked with a pin. Time taken for development of cutis anserine is noted.

IV. Tests of Lacrimation:

1. Schrimer's test.
2. Pupil Cycle time.
3. Pupil response to drugs.

V. Gastrointestinal Function tests:

1. Barium Studies.
2. Video cineradiography.
3. Gastric emptying studies.

4. Intraluminal pressure studies.

VI. Tests of Genitourinary Functions.

1. Penile Plethysmography.

2. Intracaval Papavarine.

3. Urodynamic studies.

MITRAL VALVE PROLAPSE AND AUTONOMIC DYSFUNCTIONS:

Many of the clinical features of Mitral Valve Prolapse are attributed to abnormal neural function. Such a dysfunction has long been suspected because of stress related arrhythmias and hyperkinetic ventricular contractions and because of abnormal response to various maneuvers.

Barlow et al noted high prevalence of anxiety and cognitive disorders in patients with Mitral Valve Prolapse. Similar observations made by Hancock et al and Cohn, who found symptoms of seemingly neuropsychiatric origin.

INNERVATION OF MITRAL VALVES IN NORMAL AND PROLAPSED VALVES:

Immunochemical tests were conducted both in normal and prolapsed mitral valves. Immunochemical location of S – 100 proteins, Glial Fibrillary Acid Protein (GFAP), Neurofilament Protein (NFP) were examined to detect the distribution of all nerve endings, choline acetyl transferase [ChAT] to detect the distribution of cholinergic nerve fibres and

Neuropeptide Y and Calcitonin Gene Related Peptide (CGRP) to detect the distribution of nerve fibres by and in brush peroxidase complex method. The distribution of adrenergic nerve fibres was examined.

In normal valve S – 100 proteins was demonstrated in base and body of the cusps. The distribution of GFAP, ChAT, NPY, CGRP were found to be as that of S – 100 protein in both normal and prolapsed valves.

PATHOPHYSIOLOGY:

Various studies have shown strong evidence of Autonomic disturbance in patients with Mitral Valve Prolapse Syndrome, probably involving both sympathetic and parasympathetic systems. Metabolic and neuroendocrine abnormalities in patients with Mitral Valve Prolapse Syndrome include catecholomines, hyper response to adrenergic stimulus, due to altered β adrenergic receptor coupling to adenyl cyclase, parasympathetic abnormalities, abnormalities of baroreceptor reflex modulation, Renin Angiotensin System, Atrial Natriuretic Factor secretion, decreased intravascular volume and decreased Left Ventricular volume.

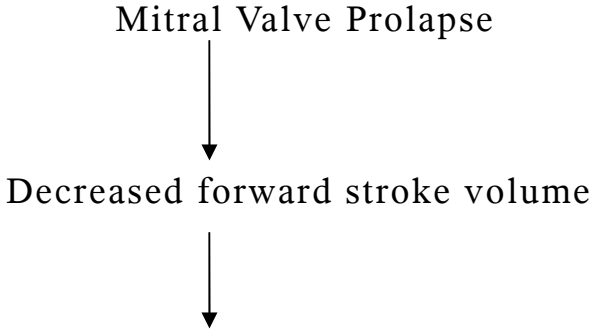
Gaffney et al studied Mitral Valve Prolapse and found that when they were exposed to lower body negative pressures, they showed greater decrease in forearm blood flow and a lesser increase in calf blood volume suggesting excessive α adrenergic responses. He also performed ice water immersion to trigger the diving response and demonstrated that the patients

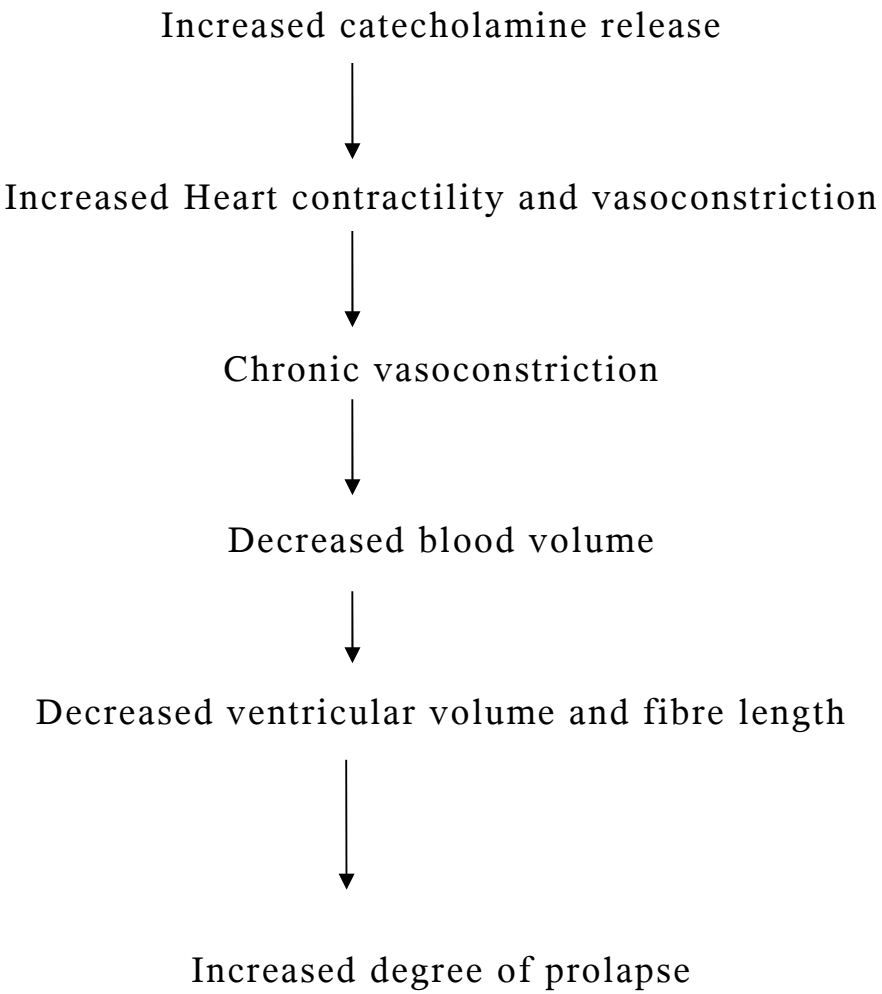
with Mitral Valve Prolapse had less Bradycardia than Normal persons.

Bo doulas and co workers demonstrated that the mean 24 hour urinary excretion of Catecholomines was significantly greater in Patients with Mitral Valve Prolapse.

Pasternak demonstrated significantly elevated total plasma Catecholomines and plasma nor epinephrine levels in all fifteen symptomatic patients. They observed that Heart Rate was lower than in normal subjects in supine position but returned to normal in upright position. This observation suggested that increase in both resting Sympathetic and vagal tone. [5] This observation of relative sinus Bradycardia had variance with data reported by Decavallo et al, Coghan et al. Heart Rate And Blood Pressure response to Standardized Valsalva maneuver and postural tests in 41 treated patients with Mitral Valve Prolapse and observed that Bradycardia became greater in more prolonged after returning to recumbency position.

A proposed pathway for orthostatic tolerance in symptoms in patients with Mitral Valve Prolapse is as follows





- FA Gaffney et al, AMJ Cardiology, 1983.

The common occurrence of ST-T changes at rest and during stress in Mitral Valve Prolapse Syndrome patients also in consistent with concepts of Autonomic dysfunction. Several investigators have attempted to look for the presence of ST-T abnormalities with high incidence of arrhythmias in Mitral Valve Prolapse Syndrome. Support for a relationship between autonomic dysfunction and arrhythmias in Mitral Valve Prolapse Syndrome may be derived from data of Combs et al.

CLINICAL AND THERAPEUTIC APPLICATIONS:

The existence of hyper adrenergic state associated with vagotonic state may provide the pathophysiological basis for the spectrum of arrhythmias observed in these patients.

Adrenergic blockade may be indicated in symptomatic patients with Mitral Valve Prolapse Syndrome. It may provide a protection against life threatening arrhythmias and even against the risk of sudden death which may occur in as many as 1.4% of all patients with arrhythmias. However before any Adrenergic blockade, the exact nature of autonomic defect in individual patients must be determined to assess whether α or β or both are required.

For e.g. Propanolol may cause increased α adrenergic activity and depending on whether patients with Mitral Valve Prolapse have increased α or β activity, the drug may alleviate or increase the symptoms.

Management:

Patients with the physical findings of Mitral Valve Prolapse (and those without such findings who have been given the diagnosis) should undergo transthoracic echocardiography. This procedure also should be performed in first-degree relatives of patients with Mitral Valve Prolapse. The diagnosis of Mitral Valve Prolapse requires definitive echocardiographic findings, and over diagnosis and incorrect “labeling” have been a major problem with this condition. Asymptomatic patients (or

those whose principal complaint is anxiety), with no arrhythmias evident on a routine extended ECG tracing and without evidence of Mitral Regurgitation, have an excellent prognosis. They should be reassured about the favorable prognosis and be encouraged to engage in normal lifestyles, but should have follow-up examinations every 3 to 5 years. This should include a two-dimensional echocardiogram and a color flow Doppler study.

Patients with a long systolic murmur may show progression of Mitral Regurgitation and should be evaluated more frequently, at intervals of approximately 12 months. Endocarditis prophylaxis is no longer recommended routinely for patients with Mitral Valve Prolapse, including those with a systolic murmur and typical echocardiographic findings.

Patients with a history of palpitations, lightheadedness, dizziness, or syncope or those who have ventricular arrhythmias or QT prolongation on a routine ECG should undergo ambulatory (24-hour) ECG monitoring and/or exercise ECG to detect arrhythmias. Because of the risk, albeit very low, of sudden death, further electrophysiologic studies may be carried out to characterize arrhythmias if they exist. Beta-adrenergic blockers are useful in the treatment of palpitations secondary to frequent premature ventricular contractions and for self-terminating episodes of supraventricular tachycardia. These drugs may also be useful in the treatment of chest discomfort, both in patients with associated coronary artery disease and in

those with normal coronary vessels in whom the symptoms may be due to regional ischemia secondary to Mitral Valve Prolapse. Radiofrequency ablation of atrioventricular bypass tracts is useful for frequent or prolonged episodes of supraventricular tachycardia.

Aspirin should be given to patients with Mitral Valve Prolapse who have had a documented focal neurological event and in whom no other cause, such as a left Atrial thrombus or Atrial Fibrillation, is apparent.

Patients with Mitral Valve Prolapse and severe Mitral Regurgitation should be treated similarly to other patients with severe Mitral Regurgitation and may require MV surgery. MV repair without replacement is usually possible. Therefore the threshold for surgical treatment in these patients is lower than in patients with Mitral Regurgitation in whom MV replacement may be necessary, providing that patients are referred to a surgical team with established success in MV repair, as noted previously. The majority of all MV repairs for Mitral Regurgitation are now carried out in patients with Mitral Valve Prolapse. Resection of the most deformed leaflet segment, usually the middle scallop of the posterior leaflet, and insertion of an annuloplasty ring to reduce the dilated annulus is the most commonly employed procedure.[2] Repair of anterior leaflet prolapse is more challenging. Chordal transfer can sometimes treat rupture of the chordae tendineae to the anterior leaflet from the posterior leaflet. In other

patients, shortening of the chordae tendineae and/or papillary muscle is necessary. The average operative mortality is 2 to 3 percent, and long-term studies demonstrate excellent durability of MV repair in the majority of patients. However, Mitral Regurgitation recurs in a subset of patients, at which point it may be necessary to perform MV replacement.

Coronary arteriography is reasonable in patients with angina pectoris on effort and/or ischemic ECG changes, and especially in those with abnormalities on a stress myocardial perfusion scans.

In one study, the 10-year survival in patients after mitral valve replacement with biologic or mechanical valve prostheses was compared. It was found that, choice of biologic or mechanical prosthesis does not significantly affect long-term patient survival after mitral valve replacement. [19]

Treatment should take into account both the responsiveness of symptoms to medical management and the coronary anatomy.

Although this discussion has focused attention on complications of the Mitral Valve Prolapse syndrome, it should not be forgotten that, on the whole, this is a benign condition and that the vast majority of patients with this syndrome remain asymptomatic for their entire lives and require, at most, observation every few years and reassurance.

MATERIALS AND METHODS

INCLUSION CRITERIA

All patients with

- Age 14 - 43
- Mid systolic click
- Late systolic murmur
- Or both

EXCLUSION CRITERIA

- Hypertension
- Diabetes Mellitus
- Coronary Artery Disease
- Congestive Cardiac Failure
- Those on cardio active or neuro active drugs
- Systemic illness

PLACE AND PERIOD:

This study was done in Govt. Stanley Hospital. Study was done for a period of 1 year, from September 2007 to august 2008. 100 cases were taken into the study.

HISTORY AND EXAMINATION

The patients who were referred for cardiac symptoms, to cardiology Outpatient Department, from Medical departments, are included in the study. Patients from 14– 43 yrs, both males and females were included. People belonging to various socioeconomic classes were included.

All patients were questioned for detailed history. In addition to general symptoms, cardiac symptoms like chest pain, palpitation, dyspnoea, syncope, focal neurological deficit were carefully evaluated. Past history was taken regarding hypertension, other congenital heart diseases (Atrial Septal Defect, etc), Rheumatic heart disease, syphilis, congestive cardiac failure. Treatment history like, surgery, previous admissions and drugs taken for cardiac illness (e.g. arrhythmias), neuro active drugs were taken. Family history mainly focused to assess the first degree relatives, with symptoms. If the relatives were available, they were also examined.

Next, careful general examination was done to find pectus excavatum, carinatum, scoliosis, reduced antero-posterior diameter, straight thoracic spine and features of Marfan's syndrome. Blood pressure was taken in both arms, lying and standing positions and with sustained handgrip maneuver. All cases were carefully examined for evidence of congestive cardiac failure, associated anomalies of heart, focal neurological deficit, infective endocarditis and arrhythmias.

Auscultation of the heart was performed in lying supine, standing and left lateral positions. Other maneuvers like leg rising, Valsalva, after isometric exercise also performed. Efforts were taken to find out the presence of pulmonary hypertension, Atrial Septal Defect, Aortic Regurgitation, Tricuspid Regurgitation, Dissection, Aneurysm of Aorta and Hypertrophic Cardiomyopathy.

LABORATORY:

Blood tests and urine tests were done to check for Diabetes mellitus and Renal diseases. Hemogram to rule out Anemia was done. Chest X-ray PA view was taken in all of the patients to assess the cardiac size, pulmonary vasculature, aortic morphology, thoracic anomalies and mitral annular calcification. A 12 lead ECG was taken to look for ST-T changes, T wave inversions, VPD, if any, that can occur in Mitral Valve Prolapse Syndrome. Also ECG was taken after deep breathing at 6 breaths per minute and during Valsalva maneuver to look for autonomic dysfunction, if any, that is common in Mitral Valve Prolapse Syndrome. Echocardiography was done in all cases to confirm the diagnosis and look which cusp are involved and associated lesions. Both M Mode and 2D echo were done. 2D echo was done in all 4 views mainly parasternal long axis view. Redundancy of valve leaflets, Left ventricular and Left Atrial measurements, Main Pulmonary Artery measurements were taken. Other

valves like Tricuspid and Aortic were also screened for any anomalies like prolapsed, etc. 100 cases were selected for the study.

BEDSIDE TESTS:

The following tests for autonomic function was also done namely,

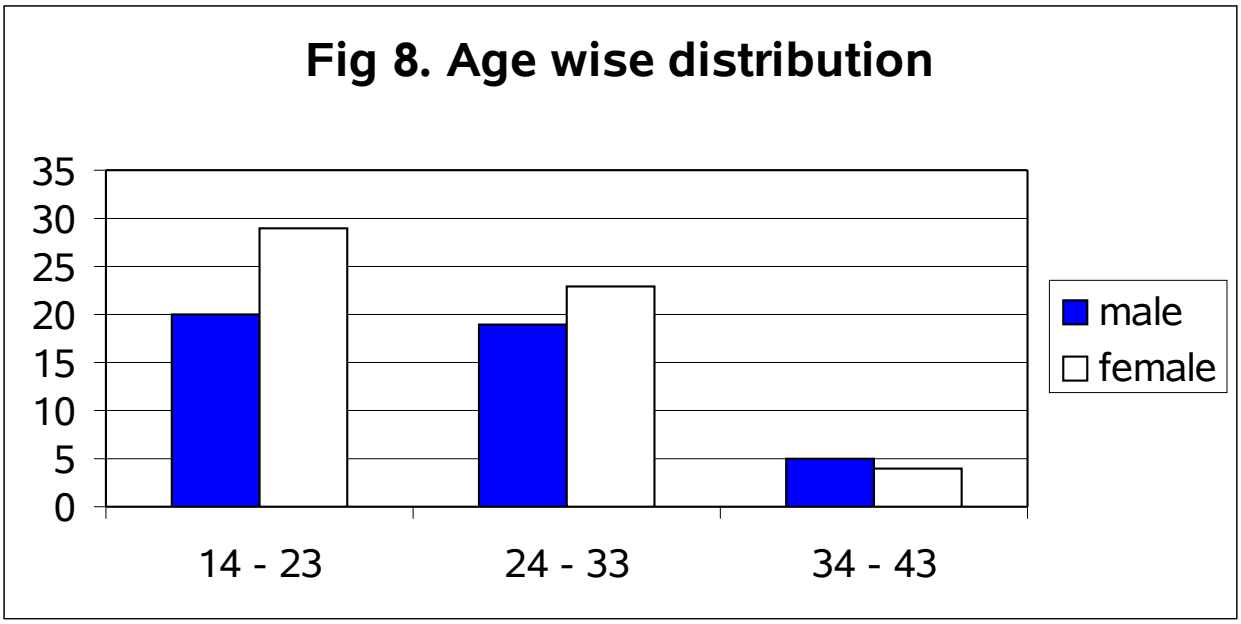
1. Postural hypotension: Blood Pressure in lying and standing position
2. Sustained Hand grip: Blood Pressure during rest and during sustained Hand grip.
3. Postural tachycardia index: Heart rate measured at 15 and 30 seconds after standing through an ECG
4. Valsalva ratio: ECG during various phases of Valsalva manuere.
5. Heart rate variation during deep breathing: through ECG recording during deep breathing.

All the data were recorded in the master chart and the reports were then taken for analysis.

OBSERVATION AND RESULTS

I. Age wise distribution

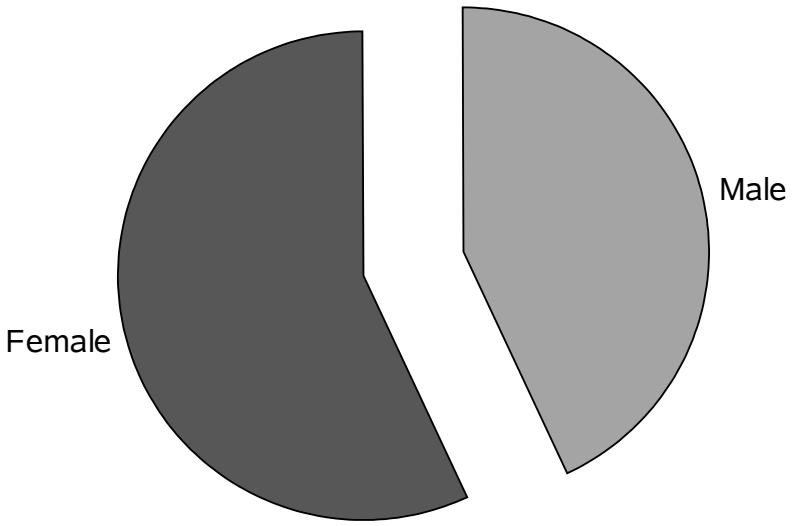
Table No: 1



II. Sex distribution

Table No: 2

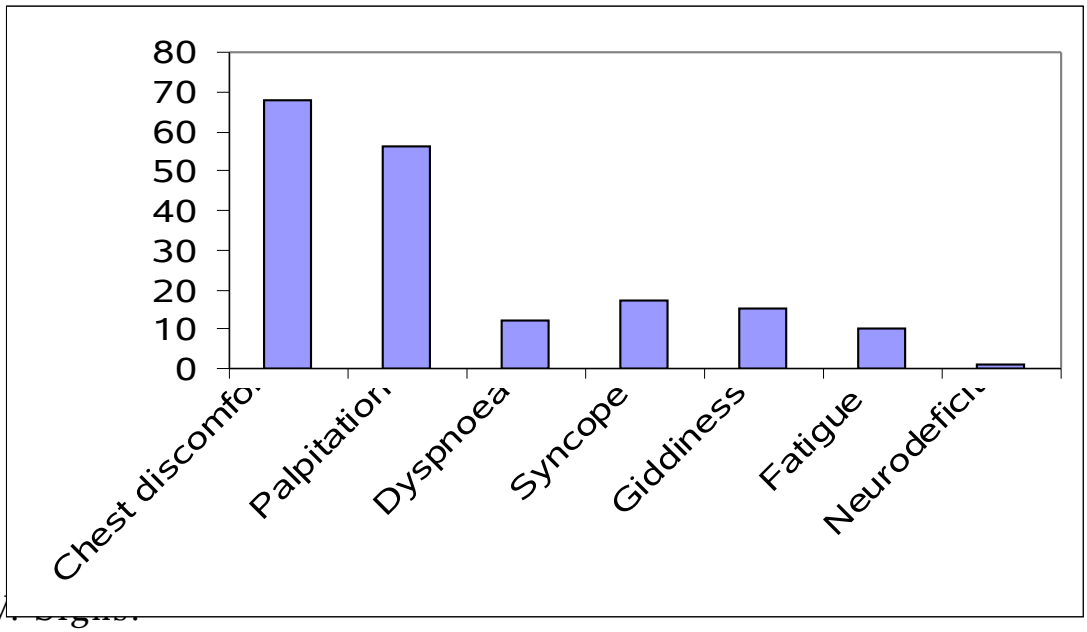
Fig 9. Sex Distribution



III. Symptoms

Table No: 3

Fig 10. Symptoms.



IV. Signs:

Table no: 4

V. BONY ABNORMALITIES:

Table no: 5

Scoliosis	15
Pectus excavatum	1
Straight Back Syndrome	2

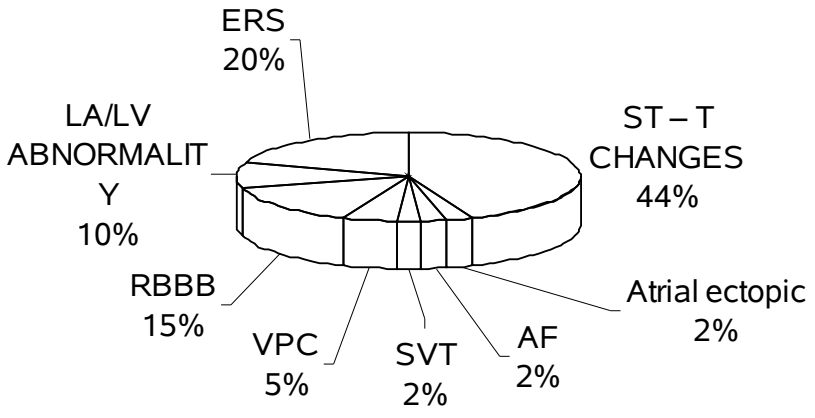
Marfanoid Habitus: 56

VI. ECG CHANGES

Table No: 6

ST – T CHANGES	18
Atrial ectopic	1
Atrial Fibrillation	1
SVT	1
VPC	2
RBBB	6
LA/LV ABNORMALITY	4
ERS	8

Fig 11. ECG Changes



VII. ECHOCARDIOGRAPHY

All cases had Mitral Valve Prolapse

Thickness of Mitral valve >5mm: 43

Table No: 7

Anterior leaflet	31
Posterior leaflet	76
Both	07

VIII. ASSOCIATED CONDITIONS:

Table No: 8

TVP	1
ASD	4
Takayasu Arteritis	1

IX. COMPLICATIONS

Table No: 9

CCF	10%
IE	1%
STROKE	3%

X. AUTONOMIC FUNCTION STUDIES:

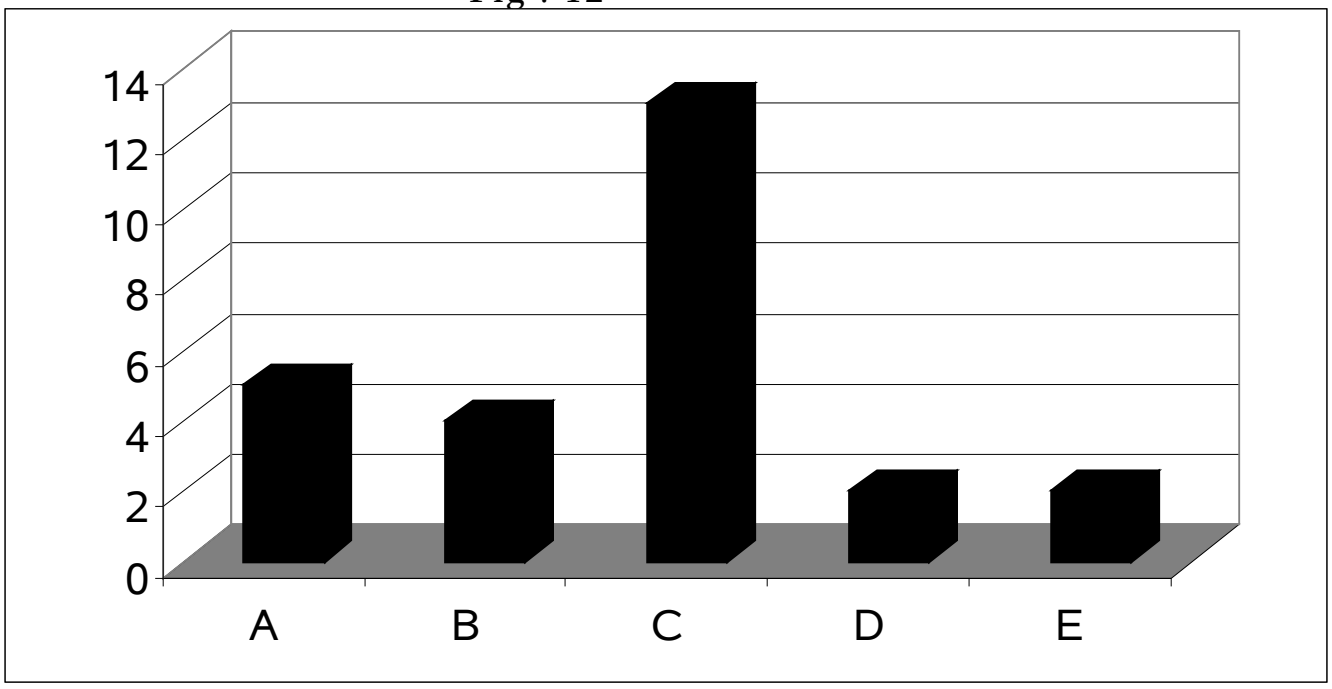
Table No: 10

Postural hypotension (S B P > 30 mm) (A)	5
BP changes to sustained hand grip (DBP< 10mm) (B)	4
Imm HR response to Standing 30:15 ratio (<1.00) (C)	13
Valsalva ratio (<1.20) (D)	2
H R variation to deep breathing (<10 beats) (E)	2

No of patients studied: 100

No of patients with positive studies: 16

Fig : 12



DISCUSSION

Although the auscultatory findings of Mitral Valve Prolapse has been known for a century, only three decade have elapsed since wide spread recognition of association of mid systolic clicks or late systolic murmurs or both with clinical features including atypical chest pain, palpitation, stroke and sudden death. The present study was designed to evaluate the clinical profile and association of co-existent autonomic nervous system dysfunction which is present in a subset of patients.

Out of 100 cases, 56 cases were females and 44 cases were males. So the disease is common in females. It was most common in the young females. 29 females were found in the age group of 14 - 23 years. 59.18% were females and 40.81% were males. In older age groups, it was common in males. 55.55% of males and 44.44% of females in 34 - 43 age groups. Deveseux et al also observed the same occurrences in men.

Age group analysis in our study revealed that maximum occurrence of Mitral Valve Prolapse was in the 14 - 23 year age groups, with 49 patients (49%), followed by 24 – 33 year age group 42 patients (42%).

According to one study done by Rokicki et al, in which, all 67 cases were included below the age of 20 years, 40 were girls, which comes to 59.7% and 27 boys which comes to 40.3%. In our study, in age 14 – 23, 29 were females and 20 were males. This comes to 59.18% in females and

40.80% in males.

The incidence of Mitral Valve Prolapse above 24 is 52.9% in females and 47.05% in males. Familial occurrence of Mitral Valve Prolapse is very uncommon. But according to Rokicki et al, it was 20%. The same author noticed the associated bony abnormalities in 20% cases. But in our study, it was found to be 13.5% of cases. 6.5% less.

Detailed analysis of symptoms in our study found that chest discomfort was found in 68% of cases, followed by palpitation in 56% of cases, dyspnea in 12% of cases, syncope in 17% of cases, Giddiness in 15% of cases, Fatigue in 10% of cases and neurological deficit in 1% of cases.

Detailed analysis of signs revealed that, 66% of cases had clicks and murmur in 54% of cases. Murmurs were typed into Late systolic murmur (33), Midsystolic (17) and Holosystolic (4). Clicks only were present in 46% of cases, murmur only in 34% of cases and both murmur and click in 20% of cases.

ECG analysis revealed that 18% of cases had ST-T changes, 1% of cases had atrial ectopics, 1% of cases had atrial fibrillation, 1% had Supraventricular Tachycardia, 2% of cases had Ventricular Premature Complexes, 6% of cases had Right Bundle Branch Block, 8% of cases had Early Repolarisation changes, and 4% of cases had Left Atrial / Left Ventricular Abnormality.

Echocardiography showed that all cases had Mitral Valve Prolapse. Involvement of Posterior leaflet was common. But 7 had involvement of both leaflets. Associated TVP was present in 1 case.

Associated conditions were also found. ASD was found in 4 cases and Takayasu's Arteritis (which was proved by Aortogram) was present in 1 case.

Marfanoid habitus was found in 56 %patients. Scoliosis was present in 15 Patients, Pectus excavatum in 1 patient and Straight Back Syndrome in 2 patients.

Analysis of the complications showed that, 10% of cases had Congestive Cardiac Failure, 1 % of cases had Infective Endocarditis, 3 % of cases had stroke.

Analysis of Autonomic Dysfunction by bed side tests showed that 16% of patients were found to be affected. The Heart Rate response to standing from sitting (30:15 ratio) was the most common abnormality, found in 13 patients, Postural Hypotension in 5 patients, Blood Pressure response to sustained Hand Grip in 4 patients, Valsalva ratio in 2 patients, Heart rate response to deep breathing in 2 patients.

This was similar to observation made by Taylor et al, who found that Postural Tachycardia is the most common Autonomic abnormality in Patients with Mitral Valve Prolapse. Similar observation was also made by

Coghlan et al, who found that patients differed from controls by widely oscillating heart rate during upright posture. Vagal Innervations of heart was essential efferent pathway in maintaining variation of heart rate which decreases as age advances due to lowered vagal tone. As most of these patients were young, the abnormality is unlikely to be age related. Postural hypotension was found in 4 % of patients. This is a well known feature of Autonomic neuropathy. This is due to the decrease in plasma volume during change of posture from lying to standing. Gaffeney et al demonstrated that the plasma volume tends to be low in patients with Mitral Valve Prolapse and that is the reason for the exaggerated response.

The role of Autonomic scoring as pointed out by Ewing in 1986 is to be established. This finding is presented as an observation and has to be proved by a case control study with more number of subjects in future.

CONCLUSION

THE PRESENT STUDY INDICATES

1. Out of 100 cases, 56 cases were females and 44 cases were males. So the disease is common in females.
2. The most common symptom is Chest discomfort followed by Palpitation
3. The most common sign is click followed by Murmur
4. The most common involved valve is Posterior Mitral Leaflet.
5. Isolated Mitral Valve Prolapse is the most common presentation and only rarely associated with others like Atrial Septal Defect.
6. The most common ECG abnormality was ST – T changes.
7. Marfanoid Habitus was present in 56 patients.
8. Autonomic Dysfunction revealed by bedside tests was found in 16 patients. Of which Immediate Heart Rate response to Standing 30:15 ratio was the most common abnormality.

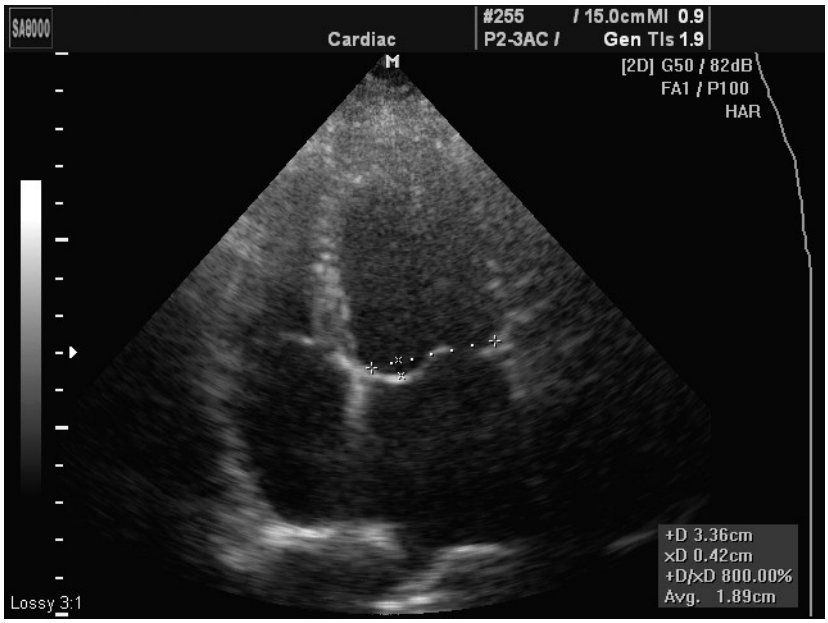


Fig 2. Mitral Valve Prolapse

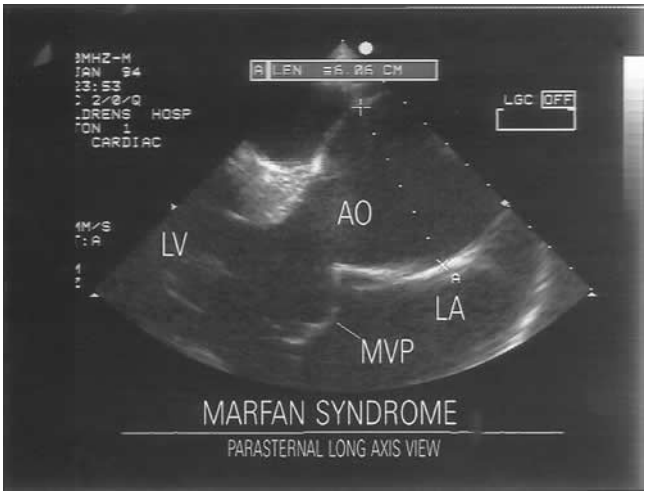


Fig 3. Parasternal long axis view

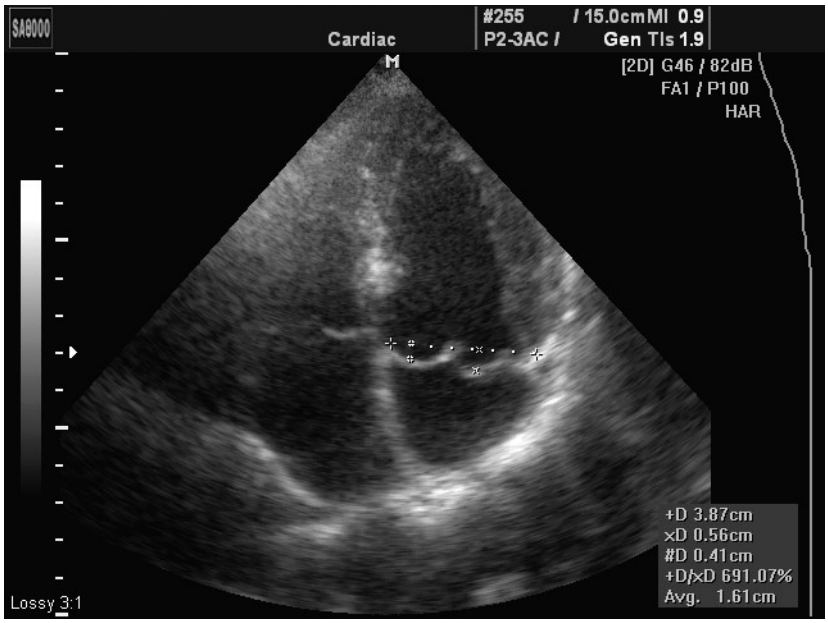


Fig 4. Myxomatous degeneration of cuspis mitral valve

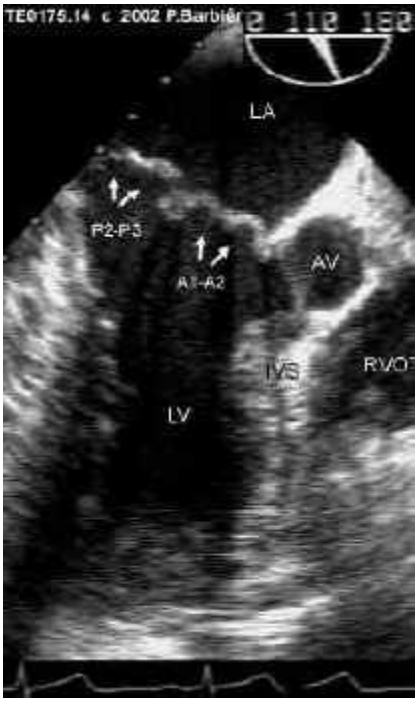


Fig 5. Floppy Mitral Valve, Severe Bi-leaflet Prolapse

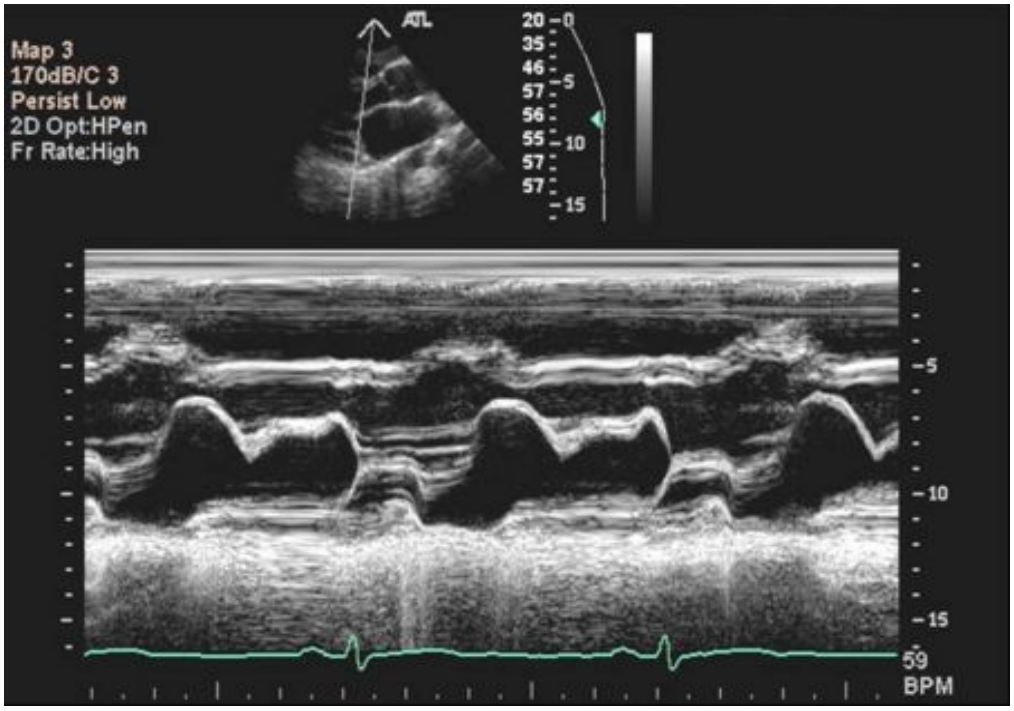


Fig 6. M- mode Mitral Valve Prolapse

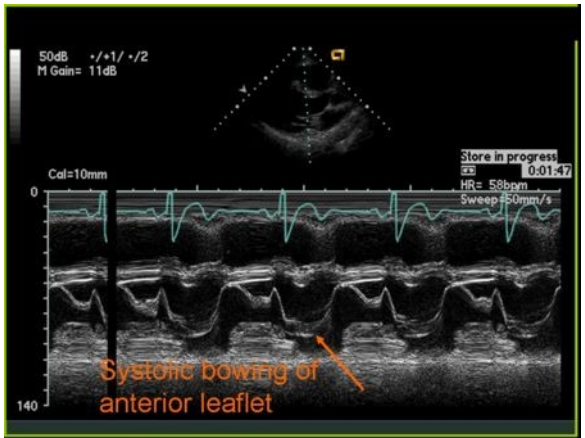


Fig 7. Systolic billowing of valve

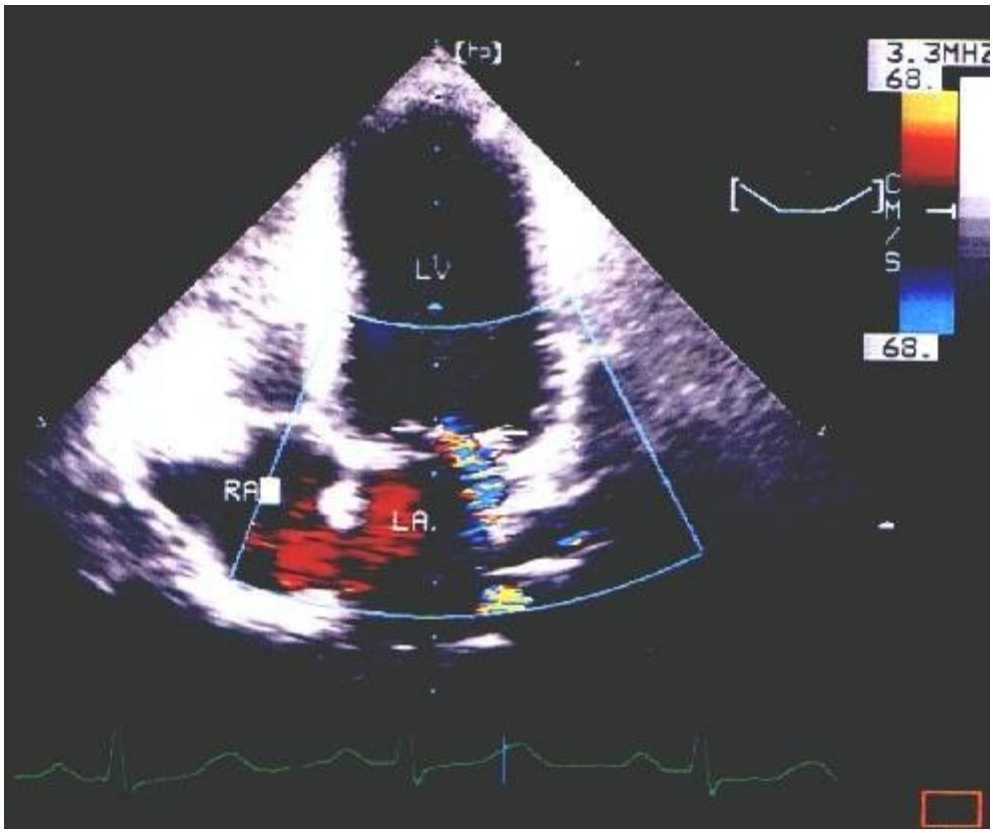


Fig 8. Transthoracic echocardiographic image mitral valve with mitral insufficiency secondary to prolapse

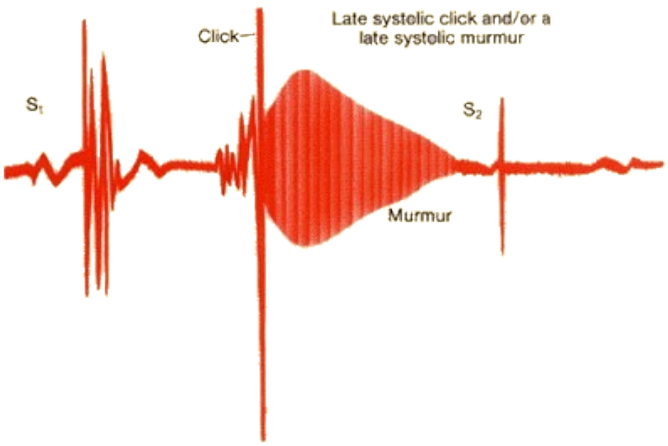


Fig 1. Murmur and click of MVPS

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PROFORMA

Name:	Age:	Case No:
Occupation:	Sex:	CD No:
Address:	MRD No:	Echo No:

Chief Complaints:

Chest Pain – Type
Location
Radiation
Relation To exertion

Palpitation - Regular / Irregular

Breathlessness – Exertional / rest

Fatigue / Syncope/ headache / dizziness

Weakness of limbs

Pas H/o

IE / CVA / TIA / Rheumatic Fever /

RHD / HT / CAD / Anxiety

Family H/o

Sudden Death / MVP

Treatment H/o

Previous admissions / drugs / surgery

General Examination:

Height: Weight: BMI:

Pulse: BP: Standing: Supine:

JVP: Kyphosis / Scoliosis / Both

Marfanoid Features:

Iridodonesis: Wrist Sign:

High Arched Palate: Thumb Sign:

Arm Span / Height Ratio: US/LS Ratio:

CARDIOVASCULAR SYSTEM:

S 1: Soft / Normal / loud

Click: Single / multiple

Murmur: mid / late / holosystolic

Radiation: Y/N

CNS: - ANS: - Bedside Tests:

Heart Rate Response: (ECG)

Postural tachycardia index:

Valsalva ratio:

Heart rate variation during deep breathing:

BP Response:

Postural hypotension:

Sustained Hand grip:

RS: ABD:

INVESTIGATIONS:

ECG: T Inversion

ST – T changes

QT Prolongation

APD / VPD

Others

Chest X – Ray: CT Ratio

Lung Fields:

Echo Cardiography:

Prolapse AML / PML

Redundancy of leaflets:

MR – No / Trivial / Mild / Mod / Severe

LVD Measurements:

LA Dimensions:

MPA Dimensions:

Other Associted Lesions: