Original Article

SUB AORTIC MEMBRANE "A RARE BUT REAL THREAT" 5 YEARS EXPERIENCE AT A TERTIARY CARE CENTER

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ABSTRACT:
Background: Sub aortic membrane is an unusual cause of sub aortic stenosis. Disease has male preponderance. Associated congenital cardiac defects are found in 25-50% of the cases.
OBJECTIVES: To see pattern, determine associated congenital cardiac defects and establish clinical course among our local population with subaortic membrane.
MATERIAL and METHODS: This prospective, observational study was conducted at Cardiology Department, Mayo Hospital, and Lahore. The purpose of the study was explained and informed consent was obtained from each patient. After a thorough history, clinical examination and twelve lead ECG, TTE was performed on all patients. TOE, CT angiography and cardiac catheterization were done in 4 patients due to inadequate information on TTE. Surgery was performed on 8 patients. Follow up was done for 5 years by TTE.
RESULTS: We studied consecutive 14 patients (10 females & 4 males). Overall mean age in years was 26.71±13.57. Breathlessness (n=10), palpitation (n=8), angina (n=6), syncope (n=3) and pre-syncope (n=3) were the chief symptoms. LV function and dimensions were preserved in all except 2 patients. Mean LVIDD and LVIDS were 49.92±13.55 and 32.57±15.00mm respectively. Mean EF was 64.71%. Mean diastolic IVS and LVPW were14.4±2.8mm and 13.35±2.4mm. Type 1 & 2 (n= 10 and 4) were present among our patients. Mean gradient across LVOT was 74.04±42.78. Most common cardiac defects were PDA(4n) , Co-arctation (4n) and AS (3n). VSD (2n), ASD (1n), Parachute mitral valve (1n) and MVP (1n) were other associated defects. A total of 3 patients died, one during early perioperative period due to acute renal failure (ARF) and 2 late due to infective endocarditis (IE) (n=1) and redo surgery (n=1) at five years.
CONCLUSION:Our study showed that disease has different gender distribution with female preponderance in Asian population. Associated congenital cardiac defects are responsible for early symptoms in young patients.
KEY WORDS:Sub aortic stenosis, subaortic membrane, congenital cardiac defects.
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INTRODUCTION

Sub aortic membrane is an infrequent disease that produces variable degree of obstruction to the egress of blood across LVOT[1]. Its prevalence is 1-2% of all congenital cardiac defects and causes 15-20% of all fixed LVOT obstructions. Disease has overall male preponderance with gender ratio of 2:1 to 3:1[2]. The prevalance of discrete sub aortic stenosis (DSS) is increasing in adults due to greater number of repaired CHDs[3]. It has four basic anatomical variants[4]. Type I & type II accounts for 70-80% of all the cases[5] It is located 0.5-1.5cm below the aortic valve with variable degree of attachment to IVS, AML and LVOT. It may encroach the AV and can cause progressive damage to the valve itself and results in AR of varying severity[6].

VSD, ASD, PDA, co-arctation of aorta, bicuspid aortic valve, parachute mitral valve, and persistent LSVC are among the associated congenital cardiac defects in 25-50% of the cases. Disease etiology is not completely understood. Various anatomical characteristics that promote chronic flow disturbances in LVOT include a steep aorto septal angle of more than 1300, increased mitral and aortic annular separation, exaggerated override of aorta with misalignment of IVS, sub aortic shelf and surgical intervention for obstructive lesions during early childhood [2, 7,8].

Diagnosis is often late as disease progresses

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over a period of years and symptoms that urge investigations are infrequent during infancy and early childhood. Children usually become symptomatic at the age of 10-20 years. Exertional dyspnea, effort angina and syncope are most common symptoms. Angina is caused by increased oxygen demand and diminished supply and results from combined effect of pressure and volume overload. Syncope in adults is due to exercised induced vasodilatation and hypotension where as in children it is caused by arrhythmia. Cardiac systolic function is preserved until very late. Sudden cardiac death and cardiac failure may be the first symptom in 2-10% of the patients with moderate to severe stenosis. On cardiovascular examination, a low pitched 2-4/6 ejection systolic murmur in second and third left intercostal space with radiation to suprasternal notch and absent ejection click is the most important clue for the diagnosis of SAM. No specific lab test is helpful in the diagnosis. ECG may show LVH (50-85%) and strain pattern in 25% of the patients. Echocardiography is the main imaging study. 2D echo allows definition of exact type, location, extent of LVOT and aortic valve involvement. CW Doppler records peak and mean pressure gradient across LVOT. TOE allows per operative evaluation of lesion, guides surgical resection and provides immediate surgical results[9].

Color flow imaging helps detecting MR, AR or shunt. Cardiac catheterization and CT Angiography is reserved for those who have multi-level obstruction and other associate congenital cardiac defects. Treatment options are medical follow up in patients with mild obstruction. Surgery is recommended in patients with symptoms, LVH and LVOT gradient of 50mmHg. Surgical resection with or without myomectomy is the treatment of choice. For recurrent and tunnel like AS modified kono procedure may be performed[10]. Patients with significant AR and MR needs valve replacement along with infective endocarditis prophylaxis[11, 12]. Early surgical mortality is less than 3%[8, 13-15]. Follow up echo is mandatory every three months in infants and children and every six month in adults even after its complete resection[12].

MATERIAL AND METHODS:

Our study population comprised of consecutive 14 symptomatic patients, who were presented in Cardiology Department Lahore from 2007 to 2012. After a quick but thorough history and clinical examination, a 12 lead ECG, Transthoracic Echocardiography (TTE) and routine lab tests were done. TOE, CT angiography and Cardiac catherization were done in those 4 patients who had inadequate information on Transthoracic Echocardiography, and had multilevel obstruction and other associated congenital cardiac defects. Combined M-mode, 2D echo and Doppler study was used to measure LV dimensions; function; record peak gradient across LVOT; aortic valve and detect shunts or regurgitation across valves. After complete diagnosis, patients were discussed in Cath Conference and referred for surgical resection of membrane and other mandatory procedure. These patients were followed up by Echocardiography in the immediate post-operation period and up till 5yrs. Data was entered and analyzed by using computer software SPSS version 20. Quantitative data such as age and Echocardiographic parameter was presented in the form of mean± SD. Qualitative data like gender was presented in the form of frequency and percentage.

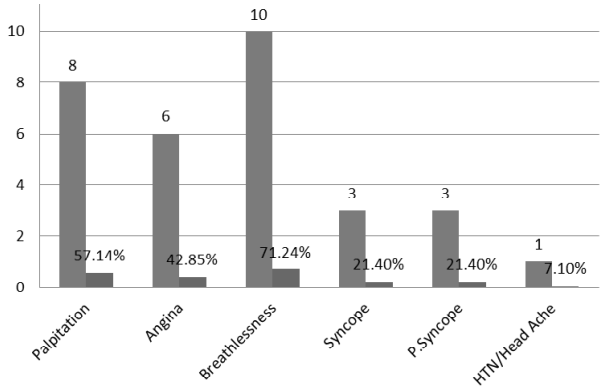
RESULT:

Our study population comprised of 14 patients (10 female, 4 male), overall mean age in years was 26.71±13.57 (30.75±9.32 for males and 25.1±15.06 for females, range 6-48 years) (Table-1). Main presenting symptoms were exertional breathlessness (n=10, 71.24%), effort angina (n=6, 42.85%), palpitation (n=8,57.14%), syncope (n=3, 21.4%) and pre-syncope (n=3, 21.4%) over a mean duration of 2.13±1.92 years (4 months to 8 years). One patient presented with headache (7.14%) and two patients (14.28%) had significant orthopnea and PND (Fig-1). Cardiovascular examination revealed normal pulse (n=9), slow rising (n=2) and collapsing (n=3). Normally placed, forceful apex beat was found in 10 patients while it was hyper dynamic and displaced in 4 patients (mild=2, marked=2). A low pitched, 3-4/6 ejection systolic murmur was present along left upper sternal border with radiation to suprasternal notch and associated with palpable thrill in 10 patients. A high pitched EDM was heard in 3rd and 4th left intercostal space in 6 patients. A 3-4/6 pan systolic murmur was heard at apex and along left lower parasternal border with radiation to axilla and base respectively. ECG showed LVH (n=8), Strain (n=5), and RBBB (n=1) while it was normal in two patients. Echocardiography revealed LVH in 12 patients; [mild (n=5), moderate (n=5) and severe (n=2)] while it was borderline in two patients. The mean IVS and LVPW thickness was 14.4±2.8 and 13.35±2.4mm (range 10-20mm and 9-16mm). Mean LVIDD and LVISD were 49.92±13.55mm (range 35-90mm) and 32.57±15.00mm (range 16-79mm). Mean global ejection fraction was 64.71±14.47% (range 25%-86%). An isolated discrete, circular membrane encircling the entire LVOT was found in three patients (21.4%). While seven patients in addition to discrete

Table-1: Gender, Age, ECG, Echocardiography and Clinical Outcomes.

SEX	**Male (n=4)**	**Female (n=10)**	**Overall (n=14)**	
Age (years) Mean ± S.D	30.75±9.32	25.1±15.06	26.71±13.57	
Range	21-32	4-48	6-48	
ECG Findings	LVH	8		
	LV Strain	5		
	RBBB	1		
	NORMAL	2		
Echocardiography	Circular Discrete Membrane	10		
	Fibrous Fold	4		
Duration of Symptoms (Years)		2.13±1.92yrs		
		Mean	Range	
Distance of SAS from AV (cm)		1.02±0.41	0.5-1.5	
		Mean	Range	
M-Mode Dimension	LVIDDmm	49.92±13.55	35-90	
	LVIDSmm	32.57±15.00	16-79	
	EF%	64.71±14.47	25-86	
	IVSmm	14.4±2.8	10-20	
	LVPWmm	13.35±2.4	9-16	
Operated Patient Gradients mmHg	Pre Operative (n=14)		Post Operative (n-8)	
	Mean	Range	Mean	Range
	74.04±42.78	13-150	29.17±12.01	14-39
Pressure Gradient Across Coarctation	38.74±7.97	30-46		
Pressure Gradient Across Aortic Valve mmHg	82.23±25.14	61-110		
CFM(AR)	No:10, Mild:4, Mod:4, Severe:2			
CFM(MR)	No:4, Mild:2, Mod:1, Severe:1			
Other Associated Cardiac Anomalies	Yes:11, No:3			
	PDA:4,MVP:1,Mild Coarctation: 3, VSD:2, ASD:1, RVOTO:1, Parachut MV:1			
Operative Procedure	Membrane Resection:8,AVR:1, MVR:1, VSD Closure: 3			
Intervention/Outcome	In Follow Up		12	
	Lost Follow Up		2	
	Operated		8	
	Overall Mortality		3	
	Cause of Mortality	Redo-Operation	IE	ARF
		1	1	1
	Operation not required		2	

Fig-1: Clinical Symptoms of Patients



circular membrane attached to IVS and AML had associated congenital cardiac defects like PDA (n=4), parachute MV (n=1), coarctation of aorta (n=3), AS (n=3) and ASD (n=1). (Table-1)

Discrete, small fibrous fold, attached to basal IVS (Type II) was found in 4 patients. These four patients had moderate sized VSD and RVOT obstruction& overriding of aorta (n=1), small VSD, coarctation of aorta& bicuspid aortic valve with AS (n=1) and mild MVP (n=1). (Table-1)

Overall mean distance of membrane from AV was 1.02cm±0.41cm. Membrane encroaching and causing damage to AV with significant AR was observed in three patients. Overall mean PG across LVOT was 74.04±42.78mmHg (range= 13-150mmHg). CFM showed at least some degree of AR in 10patients, [mild (n=4), moderate (n=4) and severe (n=2)]. MR was observed in 4 patients [mild (n=2) moderate (n=1), severe (n=1) due to MVP (n=1) and flail parachute mitral valve MV (n=1)].Overall mean PG across coarctation was 38.75±7.97mmHg (range= 30-46mmHg). Pulmonary hypertension was present in three patients [(severe (n=2) & mild (n=1)]. Significant AS was present in 3 patients with overall mean pressure gradient of 82.23±25.14 (range= 61-110mmHg) only one patient had bicuspid aortic valve. Surgery was recommended in 10 patients due to significant LVOT gradient and associated other cardiac defects. Only seven patients with membrane resection through aortotomy were operated at Mayo Hospital, Lahore. Out of these seven, one patient had AVR while another had aortic valve repair and mitral valve replacement. (Table-1)

DISCUSSION:

Sub-aortic membrane is an uncommon form of a fixed type of LVOT obstruction in most cases although flail and cystic types have been reported as case, report[16, 17].Previously SAS was considered exclusively to be disease of early childhood [6, 10, 13, 18, 19] now, is being increasingly reported in adults too[18,20]. This anomaly is dangerous not only because of impediment to the flow of blood across LVOT and associated hemodynamic impairment but also because of its complications like AR, cardiac failure or death. Our study population comprised of 14 patients(10 female and 4 male) with male to female gender ratio of 1:2.5, which was controversial to many international references that reported male preponderance with a gender ratio of 2:1 to 3:1[2] and 67% in males as observed by Oliver[4]. However, only one Chinese study comprising 19 patients has reported an overall high ratio(13:6) of female patients, analogous to our observation thus depicting the probability that disease may differ racially and geographically in gender distribution mandating further research to validate it. Mean age (in years) of our symptomatic patients was 26.71±13.57 which too was compatible with

Oliver's[3] study, who reported symptoms at mean age of 31.0±17 years while age range given by Butany[4] was 26-75 years, possibly explaining the fact that disease has progressive nature and may develop significant LVOT obstruction with symptoms later on in adult life [20]. Mean duration of symptoms among our study population was 2.13±1.9 years while Butany[4] reported it to be three months to two years.

Most frequent symptoms were breathlessness (n=10) and palpitation (n=8) followed by effort angina (n=6), syncope (n=3.) and pre-syncope (n=3). Once again our results conformed to Oliver's i.e. breathlessness 40% and angina 25% however; Butany[4] reported dyspnea, fatigue and palpitation as most typical symptoms. Before these patients presented in our outpatient department, they were being followed up in another tertiary care center and in spite of significant symptoms; they were misinterpreted as aortic stenosis. The only clinical findings that prompted us further workup were 3-4/6 ejection systolic murmurs along the left upper sternal border in 10 patients. Moreover, 3 patients had additional 3-4/6 pan systolic murmur at left lower sternal border and at apex while 6 patients had early diastolic murmur in left third intercostal space. 12 lead ECG identified LVH in 8 patients whereas echocardiography showed LVH in 12 patients [mild(n=5), moderate(n=5), severe(n=2)]. LV strain was observed only in 5 patients. One patient had right bundle branch block. In literature, the prevalence of LVH and strain has been reported in 50-80% and 25% of the patients, respectively. Type-I SAS was found in 71.24% of the patients. 9 patients had central opening while one patient had posterior aperture. A total of 4 patients had type-II sub aortic membrane with no significant gradient. The reported prevalence of type-I & II by other was 79%[4]. Mean pressure gradient across LVOT was 74.04± 42.78 mmHg. SAS was isolated in only 3 patients while 71.24% (n=11) had other associated congenital cardiac defects. Large size PDA and significant coarctation were found in 4 patients (28.5%), 2 patients had VSD (14.25%) and mitral valve abnormalities (MVP & Parachute mitral valve). RVOT obstruction, ASD and bicuspid valve were found, each in one patient.[9] 3 patients had significant AS. In a study of 35 patients, the prevalence of associated other congenital cardiac defects was 65% [PDA (34%), VSD(20%), Coarctation (23%), PS (9%) and miscellaneous defects (9%)[21]. An intensive search should be carried out to detect these congenital cardiac defects at an early age to avoid complication and ensure complete corrective surgery. LV function and dimensions were preserved in all patients, except two who had LV dilation and impairment of function due to associated MR, AR, large size PDA and VSD. Almost similar observations were made by others indicating the facts that LV function and dimensions are preserved even in patients with significant obstruction due to isolated SAS until very late. Two patients who had a long follow up of 20-29 years had early childhood surgical closure of PDA (n=1) and balloon aortoplasty for significant coarctation of aorta (n=1) were not diagnosed to have sub aortic membrane at that time, probably due to insignificant gradient across LVOT, or the membrane developed later on. One patient who had membrane resection at the age of 14 developed aortic stenosis but no membrane recurrence after 29 years of follow up. In our study one young girl who had large size VSD, RVOT obstruction and type-II sub aortic membrane, also did not have significant gradient across LVOT. Such a case was reported by David Fischer too, showing the fact that patient may have silent sub aortic membrane producing absolutely no gradient and failure to recognize such may result in further growth of membrane and gradient later on if left during surgery for other congenital cardiac defect e.g. surgical closure of VSD & MVR [22, 23]. Surgical interventions were recommended in all patients except two who had insignificant gradient across sub aortic membrane. In addition to surgical resection of membrane, MVR (n=2), AVR (n=2), PDA closure (n=2), VSD closure (n=2), ASD closure (n=1) and aortoplasty (n=3) were required. Seven patients underwent surgical intervention at Mayo Hospital, Lahore while one was operated at Chaudhry Pervaiz Elahi Institute of Cardiology, Multan. All patients at Mayo Hospital were monitored in the immediate postoperative period and every six months for up to 5 years. One patient, whose surgical ligation of PDA was missed, died during second postoperative week due to an acute renal failure and septicemia. Two patients developed significant restenosis after five years. One patient died due to infective endocarditis on aortic valve prosthesis as she was on no infective endocarditis prophylaxes and another died during redo surgery. These both patients had post resection residual gradient of 39-42 mmHg. Our statistics showed early and late mortality to be 14.28% and 28.56% respectively. Reported early surgical mortality by others is 3% [8, 13-15] and postoperative survival is > 85-95%. Late mortality related with redo operation is 18%[18]. Three patients opted to other centers for surgery. Three patients did not need immediate surgical resection due to gradient < 50 mmHg as medical follow up is recommended in these patients because of high incidence of recurrence and late

reoperation with high mortality[8,13,14].Due to its high rate of postoperative recurrence regular follow up Echocardiography is recommended every 4-6 months in children and three to twelve months in adults who have high postoperative residual gradient as the abnormal flow pattern that initiates the development of sub aortic membrane may cause regrowth of membrane, even after complete resection. The other risk factors for recurrence rate of 10-50% at 10 years follow ups are type-III SAS, incomplete removal of discrete membrane and age younger than 10 years at surgery[10,14]. The children and adolescent should avoid strenuous exercise and weight lifting if LVOT gradient is more than 50 mmHg, AR more than mild, significant LVH and history of significant SVT or VT. Sub aortic membrane though is a rare condition but can be fatal. Therefore it should be timely diagnosed and closely monitored. A through search should be made to detect other associated congenial cardiac defects to avoid missing them during surgical resection.

CONCLUSION:

Our study showed that disease has different gender distribution with female preponderance in Asian population. Associated congenital cardiac defects are responsible for early symptoms in young patients.

Author's Contribution

BA: Principal investigator, designing study, literature search and data management
AH: Data management and statistical analysis
WA: Literature search and management
KS: Data management, data screening and literature search
SE,SE: Write-up and literature search

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