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ORIGINAL ARTICLE

Clinical Profile and Pattern of Valvular Involvement in Rheumatic Heart Disease in Children: Local Regional Experience from Pakistan

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ABSTRACT

Objective: The aim of study is to look for clinical spectrum and echocardiographic features of particularly valvular involvement in children with rheumatic heart disease.

Study Design: Observational study.

Place and Duration of Study: For this observational study, 451 subjects were recruited over 3.5 years from 1st January 2018 till 30th June 2021 presenting for the first time in Children Hospital/DHQ hospital Faisalabad.

Material and methods: Demographical profile, clinical spectrum and pattern, and severity of valvular involvement were recorded in pediatric population and analyzed by SPSS version 20.0

Results: Among the 451 enrolled children, male to female ratio was 1:1.3 with age range between 60 to 194 months (median 125 months). 71.4% patients belonged to rural areas. In this cohort, 143 (31.7%) were hospitalized due to congestive heart failure, 102 (22.8%) with recurrence of acute rheumatic fever, 78 (17.3%) with LRTI and 6.3% with arrhythmia. 83.4% had mitral valve involvement. Mitral regurgitation was present in 51.9%, isolated mitral stenosis (MS) was in 2.0% and mixed mitral valve disease (Combination of MR and MS) was in 5.9%. Aortic regurgitation (AR) in isolation was present in 3.8%.

Conclusion: In conclusion, mitral valve is the most commonly involved valve in RHD in our study and mitral regurgitation followed by multi-valvular (dual-valve) involvement are the most common lesions. Majority of the cases had already progressed to severe valvular lesion at their first presentation to an equipped hospital. Congestive heart failure is the most common presentation followed by recurrence of acute rheumatic fever.

Key Words: Rheumatic heart disease, Valvular lesion, Children

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INTRODUCTION

Pediatric cardiac diseases are either congenital or acquired and they exhibit diverse spectrum. Like congenital heart defects, acquired heart diseases constitute a major cause of cardiovascular

morbidity and mortality worldwide and being a global phenomenon, it poses a major public health problem in many parts of the world.¹ Rheumatic heart disease (RHD) continues to be the dominant form of acquired valvular heart disease in most low- and middle-income countries. Recent

echocardiography-based surveys in some developing countries have estimated the prevalence of RHD to be 3–10 times compared to previous estimates based on clinical examination which shows the tendency to be more subclinical. In Pakistan, the prevalence of RHD is 21.9/1000 children.² The prevalence of RHD has been profoundly lowered down in developed nations but the “hot spots” of RHD have been documented in middle-income countries across the globe specially in developing world due to multiple factors.³

RHD is a problem of adolescents and teens thus affecting predominantly the young population but pediatric population also have a large impact of this disease. The impact of RHD on the society particularly socio-economically under privileged population is amplified. Limited studies are available on the prevalence of valvular heart disease in pediatric population as studied by echocardiography, although large series are available in literature based on autopsy and surgical pathology on the patterns of valvular heart lesions. Multi-valvular involvement is documented in more than one third of all cases. Although recent school surveys in region continue to demonstrate a declining trend in the prevalence of RHD, rheumatic involvement is still the most prevalent form of acquired valvular heart disease as socioeconomic status is the key determinant that influences multiple potential risk factors for RHD.^{3,4} In Pediatric population, isolated mitral regurgitation (MR) or the combination of mitral and aortic regurgitation (MR, AR) are more frequently present in rheumatic heart disease. The severity of rheumatic mitral and aortic valve disease in the low-and middle-income countries differs in many ways from the industrialized countries.^{5,6} Studies from developed countries show that stenosis was considered a delayed manifestation and less common especially in the first decade of life, suggesting that it takes several decades to evolve. But the condition is quite opposite in the developing countries where the pediatric population present early with the stenotic valvular heart disease. The reasons for this early valvular damage in developing countries are likely due to recurrent attacks of rheumatic fever, limitation and challenges in availability of prophylactic penicillin and lack of early detection of disease progression.^{7,8}

We aimed to analyses age distribution, pattern and severity of valvular heart lesion and clinical presentation of RHD in pediatric population in our local setup and complications associated with it. This will help to identify the gender predisposition and type of valvular involvement and their clinical presentation and the age distribution so that we can report our local data. The identification of this would help in planning focused screening program and awareness campaign for early detection of rheumatic heart disease and complications associated with it. This will not only decrease chances of life threatening complications but also minimize cost used to treat them. It will also help to reduce psychosocial trauma to family.

MATERIAL AND METHODS

This observational study (prospective and retrospective surveillance of patients with RHD) was conducted at the Pediatric Cardiology Department, The Children Hospital Faisalabad, and Pediatric Medicine Department DHQ/Allied Hospital Faisalabad, Pakistan over a period of 3.5 years from 1st January 2018 till 30th June 2021. The cardiology department has the facilities for echocardiography and computerized database. These are tertiary care centers in the Punjab province having a population of over 120 million^{9,10} where we get referrals from other tertiary care hospitals in the region for diagnostic and management issues. Institutional Ethical committee approved the study protocol. All children presenting to the hospital for the first time and diagnosed as rheumatic heart disease were evaluated for inclusion in the study. Detailed clinical and physical examinations were carried out to determine patient symptoms and condition at presentation. All newly diagnosed RHD patients with age less than 16 year who have not undergone cardiac surgery or intervention fulfilling the inclusion (Patients fulfill WHO criteria¹¹ for echocardiographic diagnosis of RHD at time of admission to our center) and exclusion criteria (functional or unspecified mechanisms of mitral regurgitation (MR), bicuspid aortic valve with trivial to mild aortic regurgitation (AR) or due to sclerotic aortic valve or unspecified causes and trivial or functional tricuspid regurgitation (TR)) were enrolled. The diagnosis was based on Trans-thoracic echocardiography performed by consultant pediatric cardiologist. Data was

collected on specially designed proforma fulfilling the inclusion and exclusion criteria.

Data analysis: Data was entered in SPSS version 20.0 and analysed. Frequency was calculated for qualitative variables including gender and type of valvular involvement of rheumatic heart disease. Mean and SD were calculated for quantitative variables like age. Data was presented as frequency and percentages. P value of <0.05 was taken as significant.

RESULTS

In this study, 451 subjects were recruited over a period of 3.5 years from 1st January 2018 till 30th June 2021. During this period, 7452 echocardiographies were performed and 451 patients had a diagnosis of rheumatic heart disease confirmed by echocardiography. There were 257 (57.0%) girls with girls to boys ratio of 1.3:1. Median age at the time of presentation was 125 months (range 60-194 months). Nearly 71.4% patients belonged to rural areas. In this cohort of 451 children, 143 (31.7%) were hospitalized due

to congestive cardiac failure, 102 (22.8%) with recurrence of acute rheumatic fever and 78 (17.3%) presented with lower respiratory tract infection. Atrial fibrillation was the common arrhythmia and 6.3% children had this presentation and they were predominantly male (table 1).

TABLE 1: Clinical manifestation at presentation in rheumatic heart disease

Clinical presentation	Numbers (n)	Percentage
CCF	143	31.7
PH	7	1.6
Arrhythmia	30	6.7
SBE	21	4.7
Recurrence	103	22.8
Pneumonia	78	17.3
Chorea	8	1.8
Palpitation	48	10.6
Stroke	13	2.8
Total	451	100.0

CCF=Congestive cardiac Failure, PH= Pulmonary hypertension, SBE= Sub acute bacterial endocarditis,

TABLE 2: Pattern of valve involvement and severity of lesion

Valvular lesion	Total (n=451) n (%)	Grade of lesion n (%)	Male n (%)	Female n (%)	
Isolated MR	234 (51.9)	Mild	81 (34.6)	101(43.1)	133(56.9)
		Moderate	102(43.6)		
		Severe	51 (21.8)		
Isolated AR	17 (3.8)	Mild	8 (47.1)	8(47.1)	9 (52.9)
		Moderate	5 (29.4)		
		Severe	4 (23.5)		
Isolated MS	9 (2.0)	Mild	3 (33.3)	4(44.4)	5 (55.6)
		Moderate	5 (55.5)		
		Severe	1 (11.2)		
Isolated TR	5 (1.1)	Mild	3 (60.0)	2(40.0)	3 (60.0)
		Moderate	2 (40.0)		
		Severe	0 (0)		
Mixed mitral valve disease	27 (5.9)	-----	-----	13(48.1)	14 (51.9)
Multi valvular heart disease	159 (35.3)	-----	-----	66(41.5)	93 (58.5)

Mitral valve (MV) was the most common valve involved in rheumatic heart disease followed by aortic, Tricuspid and pulmonary valve. Out of 451 children, 376 (83.4%) had either isolated mitral valve involvement or in combination with other valves. Mitral regurgitation (MR) was the most common lesion in children and it involved almost 51.9% (n=234) patients. Out of these patients with mitral regurgitation, 34.6% (n=81) children had mild MR, 43.6% (n=102) children had moderate

MR and 21.8% (n=51) children had severe MR. Isolated mitral stenosis (MS) was in 9 (2.0%) children and mixed mitral valve disease (Combination of MR and MS) was in 27 (5.9%) children and mitral regurgitation was the dominant lesion in most of these children. Considering single valve lesion, aortic valve was the second most common valve involved in RHD. Aortic regurgitation (AR) in isolation was present in 17 (3.8%) children and no patient had aortic stenosis.

Mild aortic regurgitation was in 47.1% and moderate in 29.4% children. Isolated tricuspid regurgitation (TR) was present in 5 (1.1%) children and isolated pulmonary valve either regurgitation or stenosis was not reported in any patient (table 2).

In our study, there was difference in age and gender distribution according to the valvular involvement in rheumatic heart disease. The valvular involvement was observed in much early age group and there was a case of moderate

mitral regurgitation even at 5 years of age which was rheumatic in etiology. There were 22 cases of ≤ 6 years of age with predominant female involvement (72.7%) and combined mitral and aortic regurgitation was the dominant lesion. The peak incidence of valvular involvement was among the children of 10-12 years age group that comprised almost 36.8% of the valvular involvement. In almost all cohorts of age and gender, the majority of children belonged to rural area as compared to urban population (table 3).

TABLE 3: Distribution of valvular heart disease according to age, gender and area

AGE (Years)	MR	AR	TR	MS	Mixed MV	Multi-valvular	Total	Male (%)	Female (%)	Rural vs Urban (%)
3-6	10	00	00	00	00	12	22	6 (27.3)	16 (72.7)	14(63.6) vs 8 (36.4)
7-9	54	03	01	02	04	67	131	54 (41.2)	77 (58.8)	94(71.8) vs 37(28.2)
10-12	103	09	03	03	11	37	166	73 (43.9)	93 (56.1)	129(77.7)vs 37(22.3)
13-16	67	05	01	04	12	43	132	54 (40.9)	78 (59.1)	86(65.1) vs 46 (34.9)

Combined mitral and aortic regurgitation was the commonest mixed lesion. Combination of mitral, aortic and tricuspid regurgitation comprises of almost 35.3% (n=159) of total valvular involvement and among these the combination of mitral and aortic involvement was 29.0% (n=131). Majority of these patients had mixed moderate mitral and mild aortic regurgitation.

Several complications of these valvular lesions were observed in our study. Pulmonary hypertension was present in 18.2% (n=82) and majority of these kids were having severe MR or

severe Mitral stenosis. In our study, there was higher incidence of pulmonary hypertension with severity of MS (6.3% in mild MS vs 51.9% in severe MS, p<0.005). Arrhythmias in the form of atrial fibrillation was present in 6.7% (n=30) and it was associated with dilatation of left atrium (P=0.0001). Two patients with severe mitral stenosis had a thrombus in the left atrial (LA) appendage. Four patients with severe mitral stenosis had swirling of blood (spontaneous echo contrast) in the LA. Thrombo-embolic events with embolic strokes occurred in 2.8% (n=13) patients, leading to presumed hemiparesis (table 4).

TABLE 4: Complications of Rheumatic heart disease and predominant lesions

Complications	Numbers	Percentage	Dominant lesion	p –value
Pulmonary hypertension	82	18.2	MR	p<0.005
Stroke	13	2.8	MS	p=0.002
Infective endocarditis	21	4.7	MR	p=0.210
Atrial fibrillation	30	6.7	MR	p=0.003
Valvular cardiomyopathy	26	5.8	MR+AR	p<0.005
LA thrombus	02	0.45	MS	p<0.005

DISCUSSION

Rheumatic heart disease (RHD) is sequelae of immune-mediated, non-suppurative infection of group A beta hemolytic streptococci that causes long-term, irreversible damage to heart valves. It is a major public health dilemma in developing countries like Pakistan even in the pediatric population. This preventable cardiac lesion is related to socio-developmental indices, and its prevention lies in the understanding of host

demographic and genetic factors, oral hygiene, better living standards and clinical manifestations for timely diagnosis and prompt management in children. The current study was conducted in a tertiary care high-volume pediatric cardiac unit in Punjab with the objective of systematically analyzing the large volume of echocardiographic data on valvular heart disease.

There was female predominance in our study which is comparable to the literature.^{2,5,12,13} Median age of presentation was 125 months

(range 60-194 months) which is similar from other reported literature, Lubega et al,¹² Rothenbühler et al,¹⁴ Shrestha et al,¹⁵ which had a median age of 8-11 years. As the disease is associated with poverty and low socioeconomic status, so majority of the literature was from the developing countries which has shown early development of disease even at 5 or <5 years of age as compared to developed world.^{16,17}

Usually the patients of rheumatic heart disease present in hospital with worsening of symptoms or complications. In our study, majority of children 31.7% (n=143) presented with heart failure followed by recurrence of acute rheumatic fever 22.8% (n=103). The data is comparable with the literature in other studies in different regions of the world.^{17,18} Arrhythmia was usually common in patients with LA dilatation and mitral regurgitation or in patients with combined mitral valve disease. Recurrence in the form of new attack of acute rheumatic fever was not only common in the patients with first presentation but also in patients on follow up and who were poor compliant of medication and benzathine prophylaxis. It was 22.8% as compared to 17.2% by Lilyasari et al¹⁸ and also comparable in literature¹⁹. The complications associated with the RHD were also common in our data. The most common complication was pulmonary hypertension that comprised 18.2% (n=82) patients. Pulmonary hypertension is usually associated with severe mitral valve disease either regurgitation or stenosis of the valve. In some studies in Africa by Bigna, et al²⁰, the incidence was 36.9% and a study in Ethiopia by Yirga²¹, the incidence was 60.3% and although in both these studies, incidence was much high as compared to our data but the most common lesion in all these was mitral regurgitation. Valvular cardiomyopathy in our data was 5.8% (n=26) and by Zühlke et al²² it was 5.3%. Infective endocarditis in our data was 4.7% (n=21) and it was 2.3% in low income and 5.7% in upper middle income countries²².

Regarding valvular involvement, mitral valve (MV) is the most commonly involved valve in our study. 51.9% (n=234) children had an isolated mitral regurgitation. In literature review, previous studies have shown more or less similar results. The study conducted by Sani et al⁵, it was 38.0%, Alkhalifa, et al⁶, it was 84.0%, Lilyasari et al¹⁸, it

was 39.1%, Animasahun et al²³, it was 42.5% and Koirala et al²⁴, it was 46.1%. So, mitral valve involvement in the form of regurgitation was the major valve affected in literature and it is because the MV is under shear stress throughout the circulation but still the reason for the overwhelming predisposition of mitral valve is yet to be unraveled. In some studies,⁶ multi-valvular heart disease involving mitral, aortic and tricuspid valve was most common (84.0%), but in our data the combination of these valves was the 2nd most common lesion comprising of 35.3% (n=159) patients. Mitral stenosis (MS) is usually a disease of adolescents and young adults but pediatric population in the developing countries do have a fair percentage of this lesion. It is discussed in literature that it usually takes a decade to develop mitral stenosis²⁵, but our data and studies from other developing world has shown development of MS in early age as well. Isolated MS was present in 2.0% (n=9) patients of rheumatic heart disease and mixed mitral valve disease with MS as predominant lesion was in 5.9% (n=27) patients. Unlike in adults, MS is the 2nd commonest lesion and even in some studies,²⁵ it comprised of 52.6% of the valvular defects. Aortic valve involvement is fairly common in combination with mitral valve but isolated aortic regurgitation is usually a rare entity in pediatric population. In our data, isolated aortic regurgitation was 3.8% (n=17) and literature^{5,12} also showed somewhat similar burden of the disease in pediatric population. Similar to our study, literature has shown involvement of isolated pulmonary regurgitation and isolated tricuspid regurgitation a rare entity. In literature, Shafi et al also concluded that the tricuspid valve is rarely affected by rheumatic carditis, but functional regurgitation of tricuspid valve had an association with mitral valve disease.²⁵

Age dependent variability always differs in industrialized world and the developing world. There is tendency of early development of RHD in developing countries. Almost 5.0% patients in our study developed RHD in the cohort of age group of 3-6 years. The reason of early age involvement in developing countries is poor adherence to treatment and secondary prophylaxis and even the shortage of benzathine penicillin that may lead to recurrence of the disease and development of early degenerative changes in the valves. The

major portion of the valvular involvement was in the cohort of age group of 10-12 years which comprised of almost 36.8% (n=166) of the total valve involvement. This observation is common in other studies^{18,23} in which the school age group is the most frequently involved of the pediatric population. Although the anti-inflammatory treatment in active carditis is mostly done aggressively but non-adherence to well sustained secondary prophylaxis and lack of bed rest in this age group leads to significant ongoing carditis and ultimately early and permanent development of valvular heart disease. Compared to urban areas, the prevalence of rheumatic heart disease was higher in rural areas and in our study, around 71.4% children belonged to rural areas. Although reasons are not well understood but individual risk is partly influenced by genetic factors along with consistent distal risk factors present in rural areas like poverty, social deprivation, poor-quality housing, household crowding, poor nutritional status and lesser access to good medical facilities in these areas play a significant role.

Limitations: There was an inherent limitation of collection of data from one or two tertiary care hospital settings in the study and it only included the patients who did reach to such facilities and may have missed some patients who presented to GP clinics. Our patients are not likely to be representative of the full extent of the disease burden at the community level.

CONCLUSION

In conclusion, the mitral valve is the most commonly involved valve in RHD in our study and mitral regurgitation followed by multi-valvular (dual-valve) involvement are the most common lesions. Majority of the cases had already progressed to severe valvular lesion at their first presentation to an equipped hospital. Congestive heart failure is the most common presentation followed by recurrence of acute rheumatic fever. Preventive strategies aimed at screening programs at community level with echocardiographic confirmation of diagnosis and secondary prophylaxis of RHD can contribute in reduction of disease burden and its sequelae.

Conflict of interest: None

Financial Disclosure: Nil

Ethical approval: Institutional review board approved the ethical aspect of study.

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