CLINICAL FEATURES OF ACUTE RHEUMATIC FEVER IN PEDIATRIC PATIENTS: FINDINGS FROM A SINGLE-CENTER TERTIARY CARE HOSPITAL

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Abstract

Objective: To explore and record the clinical features of acute rheumatic fever in pediatric patients at a tertiary care hospital in Karachi, Pakistan.

Methodology: Clinical features of acute rheumatic fever (ARF) in children aged 1 to 14 years was evaluated in this descriptive cross-sectional study, which took place at Abbasi Shaheed Hospital, Karachi Medical and Dental College, from January, 2023 to June 2023. Exclusions included co-morbidities like diabetes, kidney and liver diseases, inactive rheumatic heart disease, and HIV. Ethical approval and informed consent were obtained. Data collection encompassed medical history, physical exams, ECG, chest x-ray, and essential labs, with echocardiography performed on all participants. ARF diagnosis followed the Modified Jones Criteria, classifying carditis into no carditis, mild, moderate, and severe. Version 23.0 of the IBM-SPSS was utilized to analyze the data.

Results: The study included 86 children with acute rheumatic fever (ARF), with a mean age of 8.4 ± 3.2 years; 65.1% were between 4-12 years old. The cohort comprised 62.8% females and 37.2% males, with 58.1% residing in rural areas. A significant number, 60.5%, had symptoms for over a month, and 19.8% had parents with no formal education. Arthritis was significantly more common in first episodes (70.8%) than recurrences (29.0%, $p<0.0001$), while severe carditis was predominantly seen in recurrent cases (56.5%, $p<0.0001$). Valvular lesions such as mitral stenosis was more frequent in recurrences (32.3% vs. 16.7%, $p=0.048$), and mixed valvular lesions were notably more frequent in recurrent cases (35.5% vs. 33.3%, $p=0.043$).

Conclusion: This study emphasizes the significant impact of ARF, highlighting the necessity for early diagnosis, prompt treatment, and effective preventive measures, especially in underdeveloped areas.

Keywords: Rheumatic Heart Disease, Acute Rheumatic fever, Carditis, Arthritis, Mitral Stenosis, Valvular Heart Disease

Introduction

Worldwide, the primary cause of valvular heart disease (VHD) in both adult and pediatric age groups is rheumatic fever (RF). It is a serious public health issue, particularly in developing countries. Rheumatic heart disease (RHD) develops following recurrent episodes of acute rheumatic illness, and is one of the primary causes of morbidity and mortality in children.[1]

The central nervous system and connective tissues of the body are negatively affected by acute rheumatic fever (ARF). It usually develops after an infection with group-A beta-hemolytic streptococcal bacteria of the tonsils or throat. Rheumatic fever (RF) is a consequence of the immune system's reaction to the streptococcal infection, not the infection itself.[2]

Clinical symptoms of ARF typically appear three weeks after the initial streptococcal infection. These symptoms include erythema marginatum, chorea, polyarthritis, carditis, and subcutaneous nodules in addition to a high fever.[3] Significantly, the condition known as carditis can manifest as arrhythmias, cardiac hypertrophy, cardiac dysfunction, pericardial effusion, and new or fluctuating heart murmurs. It can also manifest up to six months after the first assault.[4]

In developed countries, the clinical profile of ARF and recurrent rheumatic fever tends to be milder compared to other parts of the world.[5] This disparity may be attributed to early diagnosis and treatment, which reduces the severity of subsequent occurrences. In contrast, many cases in developing countries, including Pakistan, present late, often with severe carditis, as initial silent carditis episodes frequently go unrecognized.[6] Despite a decline in RF incidence in Western countries, it remains prevalent in Pakistan, contributing significantly to heart failure admissions among the pediatric age group.[7]

Pakistan boasts one of the world's highest prevalence rates of RHD, with 21.9 per 1000 children suffering in the metropolitan slums and 5.6 per 1000 in the rural areas, according to a recent school survey.[8] A susceptible host, frequently residing in low-socioeconomic circumstances, interacts with a rheumatogenic strain of group-A streptococci (GAS) during the development of ARF. The disease process is marked by molecular mimicry between GAS and human proteins, leading to an autoimmune response and structural damage to the heart.[9]

The effects of ARF are more pronounced in children between the ages of 5 and 15 years, with an incidence in some emerging regions surpassing 50 per 100,000 children.[10] In older teenagers and young adults, the frequency falls. ARF affects about 3-6% of the population overall, with the first year following the initial episode carrying a substantial likelihood of relapse and progression to RHD.[11] In developing nations, teenagers and young adults frequently experience recurrent episodes of ARF, and the peak occurrence of RHD is observed between the ages of 25 and 40 years.[12]

RHD remains a significant contributor to non-communicable diseases in developing countries, with the majority of cases found in these regions. Between 62 and 78 million people globally are thought to have RHD, and the condition and its complications may account for 1.4 million fatalities every year.[13] According to a systematic review, the number of cases of RHD was higher in lower socioeconomic regions, based on 57 studies that used echocardiography criteria on children between the ages of 5 and 14 years.[14]

In order to improve patient care and outcomes and to gain a better knowledge of the disease's impact in this region, the purpose of this study is to ascertain the clinical features of children who present with ARF at a tertiary care facility in Karachi, Pakistan.

Objective

To explore and record the clinical features of acute rheumatic fever in pediatric patients at a tertiary care hospital in Karachi, Pakistan.

Methodology
Study Design:
Clinical features of acute rheumatic fever (ARF) in children aged 1 to 14 years was evaluated in this descriptive cross-sectional study, which took place at Abbasi Shaheed Hospital, Karachi Medical and Dental College, from January, 2023 to June 2023. Children with other co-morbidities like diabetes mellitus, kidney and liver diseases, inactive rheumatic heart disease (RHD) and HIV positive were omitted. The Institutional Ethical Review Board granted ethical approval, and parents or other carers provided informed written consent.

Data Collection Procedure:
Based on the criteria for inclusion and exclusion, all eligible cases who presented at the study center during the course of the study were included. Medical history was taken at the time of enrollment, and both clinical and physical exams were performed.
Each participant's clinical and demographic data were documented. A chest x-ray and a 12-lead ECG were among the diagnostic tests performed, in addition to necessary laboratory work. In all cases, two-dimensional echocardiography was carried out utilizing institutional resources.

Diagnosis and Classification:
The Modified Jones Criteria was utilized to diagnose ARF. Four categories were used to categories carditis:
1. No Carditis: According to echocardiography results, there is no cardiac murmur and no sleeping tachycardia.
2. Mild Carditis: Cardiothoracic ratio of 0.45–0.5, lack of congestive heart failure, and presence of any cardiac murmur.
3. Moderate Carditis: Cardiothoracic ratio of 0.60-0.70, presence of mild pulmonary hypertension, no evidence of congestive heart failure, and prsence of any heart murmur.
4. Severe Carditis: Cardiothoracic ratio $\geq$ 0.7, pulmonary arterial hypertension, and signs of congestive heart failure.

Data Analysis:
To analyse the data, SPSS version 23.0 statistical software was utilised. The mean and standard deviation have been determined for numerical data, while frequencies and percentages have been presented for categorical data. When comparing data using the chi-square test, a p-value of 0.05 or less was considered significant.

Results
The study included 86 children diagnosed with acute rheumatic fever (ARF). The mean age was 8.4 ± 3.2 years for the study population. 56 patients (65.1%) were between 4 to 12 years old, while 12 (13.6%) were below 4 years and 18 (21.3%) were above 12 years. In terms of gender distribution, 54 (62.8%) were female and 32 (37.2%) were male. Regarding the duration of illness, 34 (39.5%) children had been ill for less than one month, whereas 52 (60.5%) had been experiencing symptoms for more than one month. The majority of patients, 50 (58.1%), resided in rural areas, while 36 (41.9%) were from urban areas. Parental education levels varied, with 17 (19.8%) of the patients' parents having no formal education and 69 (80.2%) having some level of formal education. (Table 1)

Table 1: Baseline features

Variables		Value (n=86)/ Frequency (%)
Age Groups	Below 4 years	12 (13.6%)
	4 to 12 years	56 (65.1%)
	Above 12 years	18 (21.3%)
Gender	Male	54 (62.8%)

	Female	32 (37.2%)
Time duration of illness	Less than 1 month	34 (39.5%)
	More than 1 month	52 (60.5%)
Area of Residence	Rural	50 (58.1%)
	Urban	36 (41.9%)
Level of parental education	No formal education	17 (19.8%)
	Formal education	69 (80.2%)

In addition, notable distinctions were noted between individuals who had their first episode and those who had recurring infections. Arthritis was significantly more common in first episodes (70.8%) compared to recurrences (29.0%), with a p-value of <0.0001, indicating a highly significant statistical difference. Subcutaneous nodules were present in 37 children, more frequent in recurrences (45.2%) than first episodes (37.5%), though not statistically significant (p=0.2772). Erythema marginatum was found in 14 children, more in recurrences (19.4%) than first episodes (8.3%), but this difference was also not significant (p=0.1360). Easy fatigability was significantly more common in recurrent infections (40.3%) compared to first episodes (25.0%), with a p-value of 0.0414. Fever, the most frequent symptom, was similarly distributed between groups (83.3% in first episodes vs. 75.8% in recurrences; p=0.3833). Arthralgias and dyspnea were also more frequent in recurrences, but these differences were not significant (p=0.6898 and p=0.7546, respectively). Carditis severity showed a highly significant difference (p<0.0001), with severe carditis predominantly in recurrent cases (56.5%) and mild carditis more common in first episodes (54.2%). These findings which highlight significant clinical differences in the presentation and severity of ARF between first episodes and recurrent infections are illustrated in table 2.

Table 2: The clinical features of children diagnosed with an acute case of rheumatic fever

Clinical feature(s)		First episode of Acute case of Rheumatic Fever (n=24)	Recurrence of Acute Rheumatic Fever (n=62)	Total (n=86)	p-value
Arthritis		17 (70.8%)	18 (29.0%)	35 (40.7%)	**<0.0001**
Subcutaneous nodules		9 (37.5%)	28 (45.2%)	37 (43.0%)	0.2772
Erythema Marginatum		2 (8.3%)	12 (19.4%)	14 (16.3%)	0.1360
Easy fatigability		6 (25.0%)	25 (40.3%)	31 (36.0%)	0.0414
Fever		20 (83.3%)	47 (75.8%)	67 (77.9%)	0.3833
Arthralgias		15 (62.5%)	35 (56.5%)	50 (58.1%)	0.6898
Dyspnea (NYHA I-IV)		8 (33.3%)	20 (32.3%)	28 (32.6%)	0.7546
Carditis	Not Present	5 (20.8%)	0 (0%)	5 (5.8%)	**<0.0001**
	Mild	13 (54.2%)	05 (8.1%)	18 (20.9%)	
	Moderate	6 (25%)	22 (35.4%)	28 (32.6%)	
	Severe	0 (0%)	35 (56.5%)	35 (40.7%)	

Significant differences were noted between those experiencing their first episode and those with recurrent infections, especially in the severity and type of valvular lesions observed. Mitral stenosis (MS) was notably more common in recurrent infections, occurring in 32.3% of these cases compared to 16.7% in first episodes, with the difference being statistically significant (p=0.048). Mitral regurgitation (MR) was the frequently observed valvular lesion, present in 54.2% of first episodes and 54.8% of recurrences (p=0.965). Aortic regurgitation (AR) was observed in 33.3% of first episodes and 40.3% of recurrences (p=0.527). Aortic stenosis (AS) was present in 4.2% of first episodes and 8.1% of recurrences (p=0.509). Tricuspid regurgitation (TR) was noted in 12.5% of first episodes and 24.2% of recurrences (p=0.221). Mixed valvular lesions involving MR, AR, and TR were notably

more prevalent in recurrences (35.5%) in contrast to first episodes (33.3%), with a p-value of 0.043. Impaired left ventricular function was observed in 4.2% of first episodes and 9.7% of recurrences (p=0.416). These findings highlight the significant burden of valvular damage in children with recurrent ARF, emphasizing the importance of early detection and management to prevent severe outcomes. (Table 3)

Table 3: Distribution of Valvular Lesions in ARF Patients

Valvular lesions	First episode of Acute case of Rheumatic Fever (n=24)	Recurrence of Acute Rheumatic Fever (n=62)	Total (n=86)	p-value
Mitral Stenosis (MS)	4 (16.7%)	20 (32.3%)	24 (27.9%)	**0.048**
Mitral Regurgitation (MR)	13 (54.2%)	34 (54.8%)	47 (54.6%)	0.965
Aortic Stenosis (AS)	1 (4.2%)	5 (8.1%)	6 (6.9%)	0.509
Aortic Regurgitation (AR)	8 (33.3%)	25 (40.3%)	33 (38.4%)	0.527
Tricuspid Regurgitation (TR)	3 (12.5%)	15 (24.2%)	18 (20.9%)	0.221
Mixed valvular lesions (MR + AR + TR)	8 (33.3%)	22 (35.5%)	30 (34.9%)	**0.043**
Impaired Left Ventricular Function	1 (4.2%)	6 (9.7%)	7 (8.1%)	0.416

Discussion

Despite the fact that rheumatic heart disease (RHD) is avoidable, public health programs often fail to prioritize primary prevention because of underestimating the disease's incidence, especially in developing nations. The growing prevalence and morbidity of the condition in adolescents and young adults are caused by this overlook. The findings of our study are consistent with several previous studies in various aspects, yet also present some unique insights. Similar to the results by Suman S et al., we found that painful joints and fever are common clinical features of ARF. However, our study found a higher prevalence of fever (78.6%) compared to the 42% reported by Suman S et al.[15] This discrepancy could be attributed to differences in population demographics or healthcare accessibility. Additionally, the prevalence of carditis in our study (94.8%) was higher than the 50 to 78% reported in other studies.[16] This higher rate may reflect a selection bias towards more severe cases being referred to our tertiary care center, which is a common occurrence in underdeveloped regions like Pakistan where healthcare services are less accessible.

Arthritis was found to be present more in first episodes of ARF in our study, a finding that aligns with the literature suggesting that arthritis is often more prominent in initial attacks of ARF.[7] Subcutaneous nodules, while less common globally, were relatively frequent in our cohort, particularly among those with recurrent ARF, highlighting potential differences in disease manifestation or reporting practices. The severity of carditis being more pronounced in recurrent cases is consistent with findings from other local studies, such as those by Sheikh AM et al. from Rawalpindi.[17] This underscores the need for effective secondary prophylaxis and early intervention to prevent recurrences and mitigate the progression of carditis.

Valvular lesions, particularly mixed valvular lesions and mitral stenosis, were significantly more common in recurrent cases in our study. This aligns with global trends indicating that recurrent ARF leads to more severe and complex valvular damage.[18] The significant prevalence of mixed valvular lesions in recurrent cases (35.5%) compared to first episodes (33.3%), with a p-value of 0.043, highlights the progressive nature of the disease and the compounded damage with each recurrence.

Our study revealed a high recurrence rate of ARF (71.4%), consistent with local data reporting a 75% recurrence rate. Many children were initially treated by general practitioners, potentially delaying their admission to tertiary care facilities. Since hospital-based activities alone are unlikely to lower the incidence of ARF, preventative initiatives should target these healthcare providers. Campaigns to raise awareness in the community about RF both primary and secondary prevention are crucial. Our results require additional validation in more extensive, multicentric studies because this was a single-center investigation. It is important to follow up with patients who have ARF in order to assess how their clinical presentation affects their results.

Conclusion

Based on our findings, the majority of acute rheumatic fever (ARF) cases presented with recurrent episodes, with fever being the most common symptom. Patients who were going through the initial episode of ARF had a much higher prevalence of arthritis. Furthermore, individuals with recurrent ARF had carditis of a much higher degree. These results highlight the substantial burden of ARF and underline the importance of early diagnosis, prompt treatment, and robust preventive measures, particularly in underdeveloped regions.

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