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CLINICAL PROFILE OF ACUTE RHEUMATIC FEVER IN CHILDREN IN PAKISTAN: A STUDY AT A TERTIARY CARE HOSPITAL

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Abstract

Introduction: Acute rheumatic fever (ARF) is a significant cause of cardiovascular morbidity in children, in particular those from low and middle-income countries like Pakistan. This study aims to examine the clinical profile and management outcome of children diagnosed with ARF.

Objectives: This study aimed to describe the clinical features, laboratory findings, and treatment outcomes of children admitted to a tertiary care hospital with acute rheumatic fever in Pakistan.

Materials and methods: A cross-sectional study was carried out at Lady Reading Hospital Peshawar, Pakistan in the duration from November, 2023 to October, 2024. The study included children aged 5–15 years old diagnosed with ARF by the modified Jones criteria. Clinical, laboratory tests and echocardiographic findings were recorded and analyzed descriptively.

Results: 120 children were included; migratory arthritis with carditis was most commonly present. In 70% of cases, the throat infection was caused by streptococcus. Appropriate antibiotic prophylaxis and anti-inflammatory treatment were given to most patients.

Conclusion: Early diagnosis and treatment of ARF are crucial to prevent progression to rheumatic heart disease. Follow-up, long and short, and education of the public is indispensable.

Keywords: Acute rheumatic fever, rheumatic heart disease, streptococcal infection, pediatric cardiology, Pakistan, public health.

INTRODUCTION

Acute Rheumatic Fever (ARF) is a relevant problem in pediatric healthcare, especially in developing countries where its prevalence continues to affect many children, resulting in severe long-term consequences, for example, rheumatic heart disease (RHD). This inflammatory disorder most commonly follows a group A streptococcal throat infection attack and may show as carditis, arthritis, erythema marginatum, and Sydenham's chorea. It has been recognized for many years as a significant cause of preventable cardiovascular morbidity in children in low and middle-income countries,

including Pakistan, where acquired heart disease in children is a leading cause (1). Since Pakistan has a high burden of infectious diseases, it provides a unique context for studies of ARF with a clinical profile. While they have been proven, preventive antibiotics for streptococcal throat infection have not been effective because of different socioeconomic and delivery of healthcare challenges that characterize the disease. Some of the reasons behind the continuation of ARF as a disease among Pakistani children include poor access to health care facilities, lack of laboratory infrastructure, delay in starting treatment, and low public awareness. This strengthens the need for further extensive studies in clinical aspects, diagnostic modalities and management strategies in local settings (2).

Rheumatic heart disease is a significant public health problem in Pakistan, and rheumatic heart disease develops from an ARF infection that is not appropriately treated. ARF can have long-term sequelae, including valve damage in lifetime management, such as surgery that can impair the quality of life in a child substantially. Therefore, this makes ARF an important field of pediatric cardiology research in Pakistan, and screening of ARF with early detection and prevention strategies is a reason (3). Sadiq et al. (2024) conducted a study to evaluate the effectiveness of several regimens of treatment, Naproxen and Aspirin, for treating acute inflammatory phases of ARF and the importance of early and effective intervention to prevent the development of RHD. Therefore, pharmacological treatment and prompt management reduce complications (3). Additionally, echocardiographic studies have shown that the diagnosis of RHD in children who developed ARF should include the detection of valvular involvement in the early stages (2).

Making diagnosis and treating the ARF patients in Pakistan hasn't been easy; there is a broad spectrum of the presenting symptoms of patients. Common manifestations include migratory arthritis, carditis, carditis, and chorea, and they require different therapeutics. The high variability in the clinical presentation of ARF in children is a very significant issue in the diagnosis and treatment of ARF in children in resource-limited settings. Finally, children with ARF are not followed with consistency for long-term outcomes, which may lead to the development of RHD (6). There is also a large amount of literature mentioning the importance of the socio-demographic factors in the prevalence of ARF. Among Pakistan, some of the key factors leading to the development of ARF include the lack of health input of ARF-affected children belonging to the lower socioeconomic groups of people as ARF-affected children in Pakistan have more chances of being malnourished, overcrowded, and deprived of health facilities. Despite the fact that the incidence of ARF is greater in young people, this demographic divergence significantly contributes to the importance of public health strategies, including health education, secondary prophylaxis, and early diagnosis and treatment of streptococcal pharyngitis (4). Moreover, the wave studies have also pointed out that at a regional level, ARF incidence in Pakistan does vary, but in rural areas, the rates of reported cases of ARF are higher due to deficient health infrastructure and awareness in rural areas. (7)

Similarly, clinical profiles of ARF and its complications have been studied globally in Australia and Ghana. For example, the studies by Owusu et al. (2022) in Ghana have shown that it is possible to identify risk factors early and conserve well, which will lead to a reduction in RHD occurrence among children. Other such ARF cases, which occur in developed countries, also follow similar trends slowed down by early intervention. As a result, the disease persists in Pakistan because of its role in social, economic, and health care. Additionally, other factors, such as genetic and environmental factors responsible for clinical manifestation in particular geographical areas, determine the clinical profile of ARF in individual geographical settings. Current thinking on ARF incidence is that it has decreased in developed countries, but the disease is still important and is common in low and middle-income countries, for example, Pakistan, where environmental healthcare factors cannot be fully eradicated, which makes ARF a major problem (14).

A multidimensional strategy to control and prevent ARF in Pakistan will be required. The initiatives include facilities for healthcare centres to facilitate their diagnostic prowess on throat infection, public health consciousness-raising, and the handing out of antibiotics to prevent streptococcal throat infection. Similarly, ARF disease burden reduction, decrease in ARF to RHD progression, and ARF exacerbations are of similar magnitude in reducing the ARF disease burden (5). This study aimed to identify the comprehensive clinical profile of children with ARF admitted to a tertiary health care

hospital in Pakistan and to improve the management strategies and outcomes in affected children (15). The objective of this research is to have more specific data to prepare less biased policies or strategies for ARF and RHD reduction among the Pakistani pediatric population (12). The data presented in this study constitute the first decisive step towards the improvement in all aspects of ARF outcomes and preventable complications of ARF in the country.

Objective: This study aimed to evaluate the clinical profile, demographic features, and outcomes of management of acute rheumatic fever children being cared for at one of the tertiary care hospitals established in Pakistan.

MATERIALS AND METHODS

Study Design: Cross-sectional study

Study setting: The study was at Lady Reading Hospital Peshawar, Pakistan in the duration from November, 2023 to October, 2024.

Inclusion Criteria:

These studies included 5 to 15-year-old children who were modified by Jones criteria as having acute rheumatic fever. They chose only patients with classic symptoms such as migratory arthritis, carditis, erythema marginatum, and Sydenham's chorea. Furthermore, infant siblings of cases were enrolled if they had a confirmed streptococcal throat infection or report of sore throat within 2 to 4 weeks prior to enrollment. Only subjects who were seen by their initial management at the hospital and gave their informed consent were subjects.

Exclusion Criteria

Children with known congenital heart disease, other autoimmune disorders, juvenile idiopathic arthritis, or systemic lupus erythematosus were not included in the study if they did not have complete medical records or if they were not diagnosed with acute rheumatic fever. Additionally, they excluded people who already had already had severe complications of rheumatic fever, such as valvular stenosis or heart failure.

Methods

Clinical data of children attending Lady Reading Hospital Peshawar, Pakistan with acute rheumatic fever was collected. Demographic and medical history, from a structured questionnaire, was collected by which way of clinical symptoms. Clinical features of migratory arthritis, carditis (erythema marginatum), Sydenham's chorea associated with a previous streptococcal throat infection, and streptococcal throat culture or rapid antigen test were used to make the diagnosis. An echocardiographic study of the cardiac involvement of the patients was carried out. Laboratory tests, including complete blood counts and acute phase reactants (CRP, ESR), confirmed the diagnosis and the assessment of the inflammatory status. Descriptive statistics were used to analyze the results and summarize the presentation and outcomes. The hospital's ethics committee approved data collection, and informed consent for the data collection was obtained from all the participants' guardians.

RESULTS

The study included all 120 children diagnosed with acute rheumatic fever. The patients were, in fact, very young, with a mean age of 9.3 ± 3.4 years, and most patients aged between 7 and 12 years. Of these, 60% were male, 40% were female, and a slightly higher incidence occurred in boys. The patients showed a diverse clinical presentation, with the most common symptom being migratory arthritis in 85%. Fifty percent of patients had carditis, 15 percent Sydenham's chorea, and 10 percent erythema marginatum.

The clinical features observed in the study population are distributed as shown in Table 1.

Clinical Feature	Frequency (%)
Migratory Arthritis	85
Carditis	50
Sydenham's Chorea	15
Erythema Marginatum	10

The sore throat or upper respiratory tract infection most children had had 2 to 4 weeks before symptoms could be regarded as a clear association with streptococcal infections. Group A streptococcus was reported positive in throat cultures in 70%, and rapid antigen tests were positive in 72% of patients. All patients had elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in the laboratory findings, with the mean CRP level being 38.7 ± 16.4 mg/L, and ESR of 58.5 ± 11.1 mm/hr.

The laboratory test results of the study cohort are also given in Table 2.

Test Parameter	Mean Value
C-reactive Protein (mg/L)	38.7 ± 16.4
Erythrocyte Sedimentation Rate (mm/hr)	58.5 ± 22.3

Echocardiographic findings included 40% mitral regurgitation, 30% mild mitral stenosis, and 20% aortic regurgitation. In 25% of cases, severe carditis required long-term follow-up. There were no patients who required emergency valve surgery during the study period. However, 10% of patients showed signs of chronic valvular changes in follow-up. Treatment was appropriate antibiotic prophylaxis; 100% of patients received it, while 80% were prescribed anti-inflammatory treatment, mainly with aspirin or naproxen, for treatment of the acute inflammatory phase of the disease.
A summary of the treatment regimen given to the study population is shown in Table 3.

Treatment Regimen	Frequency (%)
Antibiotic Prophylaxis	100
Anti-inflammatory Treatment (Aspirin/Naproxen)	80

The results were generally favorable, although more than half of patients improved clinically within 6 weeks. Nevertheless, 5% of children cleared the infection but continued to suffer from persistent arthritis symptoms that required ongoing treatment. All patients were advised that long-term follow-up includes preventing recurrences and monitoring for possible development of rheumatic heart disease.

DISCUSSION

Acute rheumatic fever (ARF) is a significant cause of morbidity and mortality in the child in low and middle-income countries, including Pakistan. In conclusion, this study provides an essential clinical picture, laboratory findings, and management outcome of ARF in children at a tertiary care institution in Karachi, Pakistan. The findings underscore the relevance of the disease despite the steady improvements in medical care, indicating the difficulties in the prevention and treatment of ARF in such settings. The clinical manifestations of ARF in this cohort are similar to what is often described in the literature. The most common symptom was that of migratory arthritis, as this symptom has been described in the previous studies on pediatric ARF (1). One hallmark feature of ARF is this transient form of arthritis that typically affects the large joints - knees and ankles in the case of this type. The high frequency of migratory arthritis in this study reflects the usual course of the disease as seen in other such studies conducted in Pakistan and developing countries elsewhere (2, 3). Furthermore, half of the children involved the heart, specifically carditis, which is consistent with ARF key complication (4).
Forty per cent of the patients had carditis, specifically mitral regurgitation, as has been shown in other studies on ARF in Pakistani children (5). Carditis in ARF patients is a significant risk factor for long-

term cardiac complications, including rheumatic heart disease (RHD). From our study, in 25% of children, severe carditis required long-term follow-up, implying early and appropriate management of acute and refractory RHD to prevent progression from ARF to chronic RHD. This further emphasizes the need for early antiseptic prophylaxis and anti-inflammatory treatment to decrease the odds of chronic valvular damage. ARF has been controversially managed, particularly regarding the use of non-steroidal inflammatory drugs (NSAIDs). For this study, 80% of children received NSAIDs like aspirin or naproxen to control inflammation during the acute phase of ARF (6,7). NSAIDs are effective in reducing inflammation, although it is vital to watch for potential side effects like gastrointestinal irritation, especially in children who are also having an infection.

It is well known that ARF is associated with streptococcal throat infections, and this study revealed that many patients had a history of sore throat or upper respiratory tract infections before the event. 70% of throat cultures of patients were positive for group A streptococcus, and rapid antigen tests confirmed the bacteria in 72 per cent of cases. This reflects previous research regarding the association between untreated or inadequately treated streptococcal infections and ARF (8). However, the study highlights the need for effective public health strategies toward improving the diagnosis and treatment of streptococcal throat infections, especially in ARF endemic areas. To this end, antibiotics, e.g., penicillin, are effective in preventing the development of ARF following a streptococcal infection. However, noncompliance with treatment regimens and limited accessibility to healthcare facilities are key barriers to effective prevention in Pakistan (9, 10).

In this study, the laboratory findings resulted in the elevation of C reactive protein (CRP) and erythrocyte sedimentation rate (ESR), both being systemic inflammatory markers that commonly are elevated in patients with ARF (11). The mean CRP level of 38.7 mg/L and ESR of 58.5 mm/hr in this cohort are similar to other reported values for patients with ARF in children (12). Besides aiding in confirming the diagnosis of it, increased levels of CRP and ESR also serve as a marker of anti-inflammatory therapy. Such markers also show clinicians how far to go with treatment (discontinue or alter regimen) based on the patient's inflammatory response (13). In this study, 40% of patients had mitral regurgitation, a typical finding for ARF-related carditis (14). Early valve involvement is present in 30% of cases, in which mild mitral stenosis suggests that the valve will eventually contribute to symptoms as time goes on. Detection of valvular involvement early in the course of the disease is critical to avoid further complications, like failure of the heart and surgical intervention. All patients diagnosed with ARF should undergo regular follow-up with echocardiography and for monitoring of the progression of the cardiac involvement and management decisions. At follow-up, 10 per cent of patients developed chronic valvular changes, and the study concluded that long-term monitoring is needed to diagnose and treat these complications (15).

The main finding of this study is the high use of antibiotic prophylaxis at almost 100% prophylactic use of antibiotics to prevent the recurrence of streptococcal infection. This is in agreement with the international guidelines that suggest the use of secondary prophylaxis with various antibiotics, including penicillin, to prevent the recurrence of ARF and the development of RHD (16). Prophylactic antibiotics are available, although recurrence of ARF is a problem, especially when regimens and care systems are not strictly followed (17). Therefore, preventing recurrent ARF and RHD effectively relies on the wide use of prophylactic antibiotics and public health education, as well as ensuring early diagnosis and treatment of the disease.

The study points out the value of early detection and quick treatment of ARF in avoiding progression to RHD. This fellow was generally well, and most children improved clinically, with long follow-ups needed for possible complications. This study finally suggests that further research needs to be carried out into possible effective preventive approaches and management strategies for ARF in Pakistan and rural areas, which have limited access to medical facilities. Generations of awareness of streptococcal throat infection and the value of early treatment of ARF may be instrumental in reducing the incidence of the disease and its complications in the pediatric population. Discussed here is the remaining significant health problem in Pakistan for children: the ARF result. The findings of this study provide important information about the clinical profile of these patients, their laboratory findings, and the

management of ARF necessary to assist in advising further healthcare policies and decreasing the incidence of this preventable disease. To reduce the burden of these ARF and rheumatic heart disease among the Pakistan pediatric population, further attempts to increase healthcare access, public health initiatives, early diagnosis as well as treatment of streptococcal infections are needed.

CONCLUSION

Acute rheumatic fever (ARF) in the pediatric age group is still an important health problem in Pakistan, as migratory arthritis and carditis are still prevalent. The importance of early diagnosis and treatment to avoid incurable ARF that could lead to RHD in a setting of low resources is highlighted. The findings draw attention to the importance of early antibiotic prophylaxis for eradicating recurrent streptococcal infections and appreciable inflammatory treatment of recurrent acute inflammatory infections. Monitoring the patients' echocardiography is essential to detect early valvular involvement and avoid later chronic heart disease. Improved healthcare in Pakistan. However, it resolve some challenges, such as limited access to healthcare facilities, poor patient adherence to treatment, and late diagnoses, requiring a multidisciplinary approach consisting of public health education, health infrastructure, and effective management of ARF and RHD.

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