

Evaluation of clinical, demographic, and echocardiographic characteristics of patients with acute rheumatic fever diagnosed in the secondary care hospital

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ABSTRACT

Objective: Acute rheumatic fever remains a significant cause of morbidity and mortality, particularly in developing countries. According to the Modified Jones Criteria updated by the American Heart Association in 2015, populations with an annual incidence of fewer than 2 new cases per 100,000 individuals are considered low-risk. A nationwide multicenter study conducted in Türkiye reported an annual incidence of 8.8 per 100,000, classifying the country as being within the moderate-to-high-risk category. In this study, we aimed to evaluate the clinical, demographic, and echocardiographic characteristics of patients diagnosed with acute rheumatic fever at a secondary healthcare center.

Material and Methods: The clinical and demographic data of patients diagnosed with acute rheumatic fever at Denizli State Hospital between March 2015 and December 2024 were retrospectively evaluated. Patient records were accessed through the hospital's electronic database.

Results: A total of 60 patients were diagnosed with acute rheumatic fever during the study period. The most common presenting complaint was joint pain. Carditis and joint involvement (91.6% and 92.8%, respectively) were the most frequently observed major manifestations, while Sydenham chorea was diagnosed in 30% of the patients. According to the most recently modified criteria, the frequencies of polyarthritis, monoarthritis, and polyarthralgia as major manifestations were similar (30.1%, 28.6%, and 33.3%, respectively). Treatment-related complications included hepatotoxicity in four patients, and epistaxis, peptic ulcer, steroid-induced myopathy, esophageal candidiasis, and hyponatremia in one patient each.

Conclusion: Acute rheumatic fever remains a commonly encountered disease in Türkiye. With the recent updates to the Jones Criteria, the proportion of missed acute rheumatic fever cases in moderate-to-high-risk populations is expected to decline substantially. The high frequency and clinical significance of both the disease itself and its treatment-related complications underscore the importance of effective streptococcal eradication and early diagnosis.

Keywords: Acute rheumatic fever, arthritis, carditis, child, Sydenham chorea

Introduction

Acute rheumatic fever (ARF) is an autoimmune inflammatory reaction to pharyngitis and possibly superficial skin and skin structure infections in susceptible individuals after infection with group A β -hemolytic streptococcus. It is a serious but preventable public health problem in low- and middle-income countries and in indigenous populations of high-income countries (1,2). In 2021, rheumatic heart disease (RHD) affected an estimated 55 million people globally and caused 360,000 deaths (3-5).

There is currently no definitive diagnostic method, and diagnosis is made using the Jones criteria, first accepted in 1946 and last revised by the American Heart Association (AHA) in 2015 (3). Low risk is defined as an ARF incidence of <2 per 100,000 school-age children (usually 5–14 years of age) per year or a prevalence of RHD in the entire age group of ≤ 1 per 1000 population per year, where reliable epidemiological data are available. In Australia, the indigenous population has one of the highest reported incidences of ARF in the world, with 153 to 380 cases per 100,000 people per year

in the 5-14 age group, while in other Australian populations, the incidence is approaching European and North American levels (6). In a multicenter study covering the whole of Türkiye, the incidence was reported as 8.8 per 100,000 people, and it was determined as a moderate-high risk population (7).

The AHA made two main changes in the recent revision: First, different diagnostic criteria were defined for different incidence (risk) groups to prevent underdiagnosis in high-incidence populations and to reduce overdiagnosis in low-incidence populations. In moderate/high-risk populations, monoarthritis and polyarthralgia were considered major risk factors if other diagnoses were excluded. Second, valvular insufficiency detected by Doppler echocardiography was considered subclinical carditis in the diagnosis of carditis and was included among the major criteria (3).

Our study aimed to examine patients diagnosed with ARF according to the latest updated Jones Criteria in a secondary care hospital.

Material and Methods

Total of 60 patients diagnosed with a first episode of ARF at Denizli State Hospital between May 2015 and December 2024 were included in the study. All patients were evaluated by the same pediatric cardiologist. Data about age, gender, history of upper left respiratory tract infection, presenting symptoms, major and minor manifestations, supportive findings, and seasonal factors were collected from the medical records.

Laboratory tests (blood count, sedimentation rate, C-reactive protein, antistreptolysin O titers), telecardiography, and electrocardiography were obtained from the patients' hospital records.

The diagnosis of ARF was based on the Jones criteria as modified by the AHA in 2015 (3). Since our country is in the moderate-high risk group, we used the latest modified diagnostic criteria recommended by the AHA for these groups. The major criteria are arthritis, carditis, chorea, a characteristic rash called erythema marginatum, and subcutaneous nodules. The minor criteria include fever, arthralgia, elevated acute-phase reactants, and a prolonged PR interval on the electrocardiogram. Arthritis was defined either by redness, swelling, and hotness of joints, or by limitation in the range of joint movement due to tenderness and limping. Since our country is among the medium/high-risk countries, monoarthritis and polyarthralgia were accepted as major criteria in addition to polyarthritis in terms of joint findings. Carditis was characterized by the demonstration of valve involvement by echocardiography, with or without an audible murmur on physical examination. Sydenham chorea diagnosis was based on the exclusion of other possibilities and the presence of arthritis and/or carditis, together with evidence of a precedent group A streptococcal throat infection. The subcutaneous nodules were defined as small, varying in size from millimeters to 2 cm, and as firm, painless, freely movable lesions under the skin, mainly found on the extensor surface of the joints. Erythema marginatum, an uncommon manifestation, presented as a macular rash, sometimes coalescent with a serpiginous or circular form,

and was almost coppery pink at the border. It was mainly located on the trunk and inner surface of the proximal limbs, with a light-colored center. The diagnosis of recurrence of rheumatic fever in children with rheumatic heart disease was based on the presence of one major criterion, apart from carditis, or two minor criteria, in addition to the evidence of preceding streptococcal infection (1, 3, 8).

The pathological valve levels determined by echocardiography by the American Heart Association are as follows: in mitral valve regurgitation, a color jet length of >2 cm, the presence of a defined color jet in at least two planes, and the presence of a mosaic color jet with a peak velocity of >3 m/sec. In aortic valve regurgitation, holodiastolic regurgitation, a color jet length of >1 cm, the presence of a defined color jet in at least two planes, and the presence of a mosaic color jet with a peak velocity of >3 m/sec (9).

Patients whose ages were not between 5 and 15 years during the acute attack, and patients with recurrent attacks, were excluded from the study. All statistical analyses were performed using Systat statistical software (version 17.0 for Windows; SPSS Inc., Chicago, IL, USA). All variables were presented as the mean, standart deviation, range, frequency, and percentage. Data were tested for homogeneity of variance with the Kolmogorov-Smirnov test.

Results

Sixty patients met the Modified Jones Criteria, last modified in 2015. Of these patients, 29 (48.3%) were female, and 31 (51.6%) were male (male-to-female ratio: 1.07). The ages of the patients ranged from 7 to 18 years, with a mean age of 11.8 ± 2.1 years. Among those diagnosed with ARF, 25.0% presented during winter, 25.0% in spring, 26.7% in summer, and 23.3% in autumn. A total of 66.6% (40/60) of the patients presented with joint pain, 30.0% (18/60) with choreiform movements, one patient with isolated palpitations, and one patient with severe carditis presented with complaints of easy fatigability and dyspnea. Except for patients with chorea, all had elevated antistreptolysin-O (ASO) titers as evidence of streptococcal infection; however, none had a positive throat culture for group A β -hemolytic streptococcus.

Carditis was the most common major criterion of ARF, observed in 55 of 60 patients (91.6%), and 67.2% (37/55) of these had clinical carditis. The frequencies of other major manifestations—polyarthritis, aseptic monoarthritis, polyarthralgia, and Sydenham chorea—were 14/60 (23.3%),

Table I: Prevalence of carditis and associated joint manifestations

Findings	Count / Total	Rate (%)
Carditis	55/60	91.6
Clinical carditis	37/55	67.3
Subclinical carditis	18/55	32.7
Isolated carditis	16/55	29.1
Carditis + polyarthritis	14/55	25.4
Carditis + monoarthritis	12/55	21.8
Carditis + polyarthralgia	13/55	23.6

Table II: Valvular regurgitation profiles and subclinical carditis in acute rheumatic fever patients

Findings	Cases / Total	Rate (%)	Subgroups	Subgroup Rate (%)
Mitral regurgitation	55/60	91.7	Isolated mitral regurgitation	29/55 (52.7%)
Aortic regurgitation	27/60	45.0	Isolated aortic regurgitation	1/27 (3.7%)
Mitral + aortic regurgitation	26/60	43.3	—	—
Mitral regurgitation severity	—	—	Mild / Moderate / Severe	63.6 / 25.4 / 10.9
Aortic regurgitation severity	—	—	Mild / Moderate / Severe	85.1 / 11.1 / 3.7
Subclinical carditis	18/60	30.0	Mitral / Aortic / Both	94.4 / 11.1 / 5.5

Table III: Articular findings and their relationship to carditis in acute rheumatic fever

Findings	Case Count / Total	Rate (%)	Subgroups	Subgroup Rate (%)
Arthritis / Polyarthralgia	39/42	92.8	Isolated / With carditis	10.3 / 89.7
Isolated arthritis/polyarthralgia	4/39	10.3	—	—
Arthritis/polyarthralgia with carditis	35/39	89.7	—	—
Polyarthritits	13/42	30.1	With / Without carditis	83.3 / 16.7
Aseptic monoarthritis	12/42	28.6	With / Without carditis	91.6 / 8.4
Polyarthralgia	14/42	33.3	With / Without carditis	92.8 / 7.2

12/60 (20.0%), 15/60 (25.0%), and 18/60 (30.0%), respectively. The proportion of isolated carditis without joint involvement was 29.1% (16/55), while arthritis/polyarthralgia accompanied carditis in 70.9% (39/55). Carditis was accompanied by polyarthritits in 25.4% (14/55), by aseptic monoarthritis in 21.8% (12/55), and by polyarthralgia in 23.6% (13/55) of the patients as a major criterion Table I.

Mitral regurgitation was detected in 55/60 (91.7%) patients, and in 29 of 55 patients (52.7%), it was isolated mitral regurgitation. For aortic regurgitation, these rates were 27/60 (45.0%) and 1/27 (3.7%), respectively. A total of 26 patients (43.3%) had coexisting mitral and aortic regurgitation. The severity of mitral regurgitation was mild in 35/55 (63.6%), moderate in 14/55 (25.4%), and severe in 6/55 (10.9%) patients. For aortic regurgitation, the corresponding rates were 23/27 (85.1%), 3/27 (11.1%), and 1/27 (3.7%). Subclinical carditis was present in 18 (30%) patients, of which mitral regurgitation was found in 17/18 (94.4%) and aortic regurgitation in 2/18 (11.1%) patients, and only one patient (5.5%) had both mitral and aortic regurgitation Table II.

Among patients diagnosed with ARF, the rate of arthritis/poliarthralgia was 39/42 (92.8%). Of these, 10.3% (4/39) had isolated arthritis/poliarthralgia, while 89.7% (35/39) had arthritis/poliarthralgia associated with carditis. Polyarthritits was present in 13/42 (30.1%) patients; two (16.7%) of them had no carditis, while 10 (83.3%) had concomitant carditis. Aseptic monoarthritis was identified in 12/42 (28.6%) patients, 11 (91.6%) of whom had clinical carditis, while one patient (8.4%) did not. Polyarthralgia, another major criterion, was present in 14/42 (33.3%) patients; 13 (92.8%) had clinical carditis, and one (7.8%) did not Table III.

Sydenham chorea was identified in 18 patients (30.0%), with 10 (55.5%) being female and eight (44.5%) male. All patients with chorea had accompanying carditis. None had erythema marginatum or subcutaneous nodules. About 14.3% (6/42) of patients with ARF showed a prolonged

PR interval (first-degree atrioventricular block). Fever was present at admission in 4/42 (9.5%) patients, and only one (2.3%) experienced monoarthralgia. Acute-phase reactants were elevated in all patients except those diagnosed with chorea. One patient had Wenckebach-type second-degree Mobitz I AV block, and another had inappropriate sinus tachycardia upon admission. One patient with moderate morphologic carditis had mitral stenosis, and another had a history of surgery for a ventricular septal defect. Both erythrocyte sedimentation rate and C-reactive protein levels were elevated in all patients except those with chorea. The average sedimentation rate was 83.9 ± 25.6 mm/h, and the average CRP level was 77.4 ± 48.6 mg/dL (normal <5 mg/dL). The mean ASO titer was 814.2 ± 514.2 IU/mL. Acetylsalicylic acid (ASA) was started in patients with isolated arthritis or mild cardiac involvement. Prednisolone was given as initial therapy for patients with moderate or severe carditis. ASA was prescribed to 45.2% (19/42) and prednisolone to 54.8% (23/42). Nine patients experienced treatment-related complications necessitating therapy adjustments, including hepatotoxicity in four patients, and epistaxis, steroid-induced myopathy, esophageal candidiasis, peptic ulcer, and hyponatremia in one patient each.

Discussion

Our study evaluates patients diagnosed with ARF at a secondary-care hospital. The AHA defines high-risk populations as those with an annual incidence greater than 2 per 100,000 people (3). In studies previously conducted in Türkiye, the incidence of ARF was shown to decline from 56.6 to 21 per 100,000 over a decade (10,11). A multicenter study conducted in Türkiye in 2015 reported an annual incidence of 8.8 per 100,000 (7). In a recent study from Uganda, the incidence was reported to be 25 and 47.9 per 100,000 in two different cities (12). In Australia, the age-standardized incidence of ARF was markedly higher among the Indigenous population (71.9/100,000) compared with the non-Indigenous

population (0.6/100,000) (13). A very high incidence has also been reported in Malaysia (74.4/100,000) (14).

Denizli, where this study was conducted, is located in the Aegean Region of Türkiye. Therefore, we compared our data with the Aegean Region and national data. In this study, the frequency of carditis was similar to the average reported for the Aegean Region but higher than the national average (67.2%, 62.1%, and 53.5% respectively) (7). However, it was comparable to the global average reported by the World Health Organization (WHO) (67.2% and 59.5%) (5). The prevalence of subclinical carditis—defined as carditis without an audible murmur—was consistent with national data. The frequency of arthritis also aligned with WHO global estimates. While the prevalence of polyarthritis was lower than the averages reported for both the Aegean Region and Türkiye, the rates of aseptic monoarthritis and polyarthralgia were higher in our cohort. The prevalence of Sydenham chorea was notably higher than figures reported for the Aegean Region, Türkiye, and the WHO (30.0%, 6.0%, 7.9%, and 12.9% respectively) (5,7).

Consistent with the literature, arthralgia was the most common presenting complaint in our study, followed by choreiform movements (15-17). Although some studies report arthritis as the most common major manifestation and others report carditis as the predominant finding, carditis was likewise the most frequently observed major criterion in our cohort. Similar to WHO results, arthritis and carditis occur at approximately the same frequency (~60%) (5). Following the widespread adoption of echocardiography—including its recognition of subclinical carditis as a major criterion—the rate of carditis diagnoses has increased. WHO reports that echocardiography is substantially more sensitive than cardiac auscultation in detecting RHD, identifying 12.9 cases per 1,000 individuals in endemic regions, compared with 2.9 per 1,000 by auscultation (5).

Güler et al. (18) reported that, between 2015 and 2018, they were able to diagnose nine of the 50 patients (18%) using the updated criteria. A similar study conducted in Italy reported this rate as 20.7% (6). This finding suggests that the latest update will reduce the diagnostic difficulty in populations where ARF is common (18). Interestingly, the prevalence of Sydenham chorea in our cohort (30%) was substantially higher than WHO estimates and national multicenter data, although comparable rates have been reported in a study from Kayseri (25%) (5,7,15). Because many conditions can mimic the major and minor criteria of ARF, a meticulous differential diagnosis is essential. The presence of a single pediatric cardiologist at our center allowed patients to be regularly followed by the same physician. This continuity may have facilitated careful evaluation of diagnostically challenging cases, helping to prevent overdiagnosis. In this study, the higher proportion of Sydenham Chorea compared to other major findings and the different distribution of the joint conclusions compared to national and international reports can be explained by close follow-up of cases with diagnostic uncertainty and subsequent confirmation or exclusion of the ARF diagnosis (5, 7).

In line with the literature, isolated mitral regurgitation was the most common valvular involvement in both clinical and subclinical carditis, followed by combined mitral and aortic valve regurgitation (5, 15-19). Before the most recent revisions of the Jones criteria, polyarthritis was exceedingly common; however, following the inclusion of monoarthritis and polyarthralgia as major criteria in certain populations, the proportion of polyarthritis appears to have decreased (18, 20).

Hepatotoxicity is a well-known complication of high-dose acetylsalicylic acid therapy. In this study, four patients developed hepatotoxicity, and their treatment was switched to naproxen. Other complications included epistaxis, steroid-induced myopathy, esophageal candidiasis, peptic ulcer disease, and hyponatremia in a patient with concurrent heart failure. In a study reported by researchers from Central Anatolia, 27.2% of patients had elevated liver function tests, 6.8% experienced gastrointestinal side effects, 2% reported tinnitus, 2% developed rash and fever, one patient developed serum sickness, and one patient had epistaxis (10).

Limitations

It has some limitations. The presence of two centers in the same city does not reflect the entire population. Because it does not include patients before the final modified criteria, we were unable to compare the additional diagnostic benefit of the latest criteria.

Conclusion

In conclusion, ARF remains prevalent in Türkiye and continues to pose a significant public health concern due to its potential to cause rheumatic heart disease. Because Türkiye is among the medium- to high-risk countries, monoarthritis and polyarthralgia should be considered major criteria to prevent potential oversight. Furthermore, active echocardiography evaluation can help identify subclinical carditis. In addition, we believe that primary and secondary healthcare facilities play a pivotal role in ARF control, particularly through the implementation of more effective and widespread preventive measures against streptococcal infections.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Pamukkale University (12.11.2024, reference number: E-60116787-020-624004).

Contribution of the authors

AE: concept and design, data collection, analysis and interpretation of results, preparation of draft article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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