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Acute Rheumatic Fever: A Five-year Tertiary Center Experience and Post-pandemic Trends

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Abstract

Objectives: Acute rheumatic fever (ARF) remains a significant cause of acquired heart disease among children in developing countries. This study aimed to evaluate the clinical, laboratory, and echocardiographic characteristics; treatment approaches; and outcomes of ARF patients followed in a tertiary pediatric cardiology center and to explore differences between pandemic and post-pandemic periods.

Materials and Methods: In this retrospective study, 122 patients diagnosed with ARF between May 2020 and August 2025 were analyzed. Using June 2022—when pandemic restrictions were eased—as a reference point, patients were divided into two groups: pandemic (n=41) and post-pandemic (n=81). Demographic characteristics, clinical findings, laboratory results, echocardiographic findings, treatments, and follow-up data were compared.

Results: The mean age was 12.8±2.4 years, and 62.3% of patients were male. The monthly number of cases increased from 1.58 to 2.13 in the post-pandemic period (p=0.048). Carditis was detected in 95% of patients, consistent with the tertiary referral profile of our study population. Although the rate of carditis was numerically higher in the post-pandemic period, the difference was not statistically significant (92% vs. 96%, p=0.403). Delayed presentation and elevated C-reactive protein levels were associated with carditis.

Conclusion: An apparent increase in ARF cases was observed in the post-pandemic period; however, this likely reflects referral dynamics rather than a true epidemiological shift. Delayed presentation and increased inflammatory burden were associated with more severe cardiac involvement.

Keywords: Acute rheumatic fever, rheumatic heart disease, coronavirus disease-2019

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Introduction

Acute rheumatic fever (ARF) is a multisystem inflammatory disease that develops after group A beta-hemolytic streptococcal (GABHS) pharyngitis and particularly affects children and adolescents[1]. Although its incidence has markedly decreased in developed countries, it remains the leading cause of acquired heart disease in developing countries and populations with low socioeconomic status[2]. The disease may progress to rheumatic heart disease (RHD) by causing permanent valvular damage, leading to significant morbidity and mortality. The diagnosis of ARF is based on the Jones criteria, which combine clinical and laboratory findings; these criteria were updated in 2015 to include echocardiographic findings[3].

The coronavirus disease-2019 (COVID-19) pandemic imposed unprecedented pressure on health systems worldwide, leading to disruptions in access to healthcare and difficulties in the follow-up of chronic diseases. Restrictions during the pandemic, quarantines, and public hesitancy to seek hospital care led to delays in the diagnosis of many childhood diseases[4,5]. In diseases such as ARF, where timely diagnosis and treatment directly affect prognosis, the consequences of delays are critical. The literature reports conflicting data regarding the course of GABHS infections and the trends in ARF case numbers during the pandemic[6,7].

This study aimed to describe the clinical, echocardiographic, and outcome characteristics of ARF patients followed at a tertiary pediatric cardiology center over five years and investigate differences in case volume, clinical presentation, and disease severity between the pandemic and post-pandemic periods.

Materials and Methods

This retrospective observational study reviewed data from newly diagnosed and subsequently followed patients in the pediatric cardiology clinic of a tertiary hospital between May 2020 and August 2025. Approval for the study was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinical Research Ethics Committee on October 22, 2025 (decision number 332).

The study periods were classified as the pandemic period (May 2020–June 2022, 26 months) and the post-pandemic period (July 2022–August 2025, 38 months), with June 2022 serving as the transition point, corresponding to the nationwide easing of major COVID-19 public health restrictions in Türkiye, including the lifting of mask mandates and travel restrictions, and the resumption of routine social, educational, and pediatric outpatient activities. Each calendar month was treated as an independent observational unit. This classification was also consistent with the approach used in similar studies[4].

Patients aged ≤18 years who were consecutively diagnosed with a first episode of ARF according to the 2015 Revised Jones Criteria during the study period were eligible for inclusion. No patients younger than 6 years of age were identified during the study period. Eligible patients were identified through the hospital electronic medical record system and the pediatric cardiology database. Only newly diagnosed cases were included to ensure a homogeneous study population and to avoid potential confounding related to previous disease episodes or long-term treatment. Patients with recurrent ARF attacks, established RHD, or incomplete clinical, laboratory, or echocardiographic data were excluded from the study.

Standard transthoracic echocardiography was performed using commercially available ultrasound systems according to current pediatric echocardiography recommendations. Two-dimensional imaging with color Doppler, pulsed-wave Doppler, and continuous-wave Doppler was routinely performed. Standard parasternal long-axis, parasternal short-axis, apical four-, five-, and two-chamber views, as well as subcostal views, were systematically acquired, and color Doppler interrogation was performed in all standard views to optimize the detection of valvular regurgitation. Carditis was defined as the presence of pancarditis, pericarditis, pathologic valvular regurgitation, or unexplained myocardial dysfunction according to the 2015 Revised Jones Criteria. Pathologic mitral regurgitation was diagnosed only when all four Doppler criteria were fulfilled: (1) visualization in at least two echocardiographic views, (2) a jet length ≥2 cm in at least one view, (3) a peak regurgitant velocity >3 m/s, and (4) a pansystolic jet on spectral Doppler. Pathologic aortic regurgitation required: (1) visualization in at least two views, (2) a jet length ≥1 cm in at least one view, (3) a peak regurgitant velocity >3 m/s, and (4) a pandiastolic jet on spectral Doppler. Regurgitation not fulfilling all four criteria was considered physiologic and was excluded from the analysis. Valvular regurgitation severity was graded according to current guideline recommendations. Multivalvular involvement was defined as the simultaneous presence of pathological mitral and aortic regurgitations that fulfill the 2015 Revised Jones Criteria. All echocardiographic examinations were performed and interpreted by experienced pediatric cardiologists with expertise in congenital heart disease, using standardized institutional imaging protocols[3,8,9].

Demographic characteristics (age, sex), clinical findings [(joint pain/swelling, fever, fatigue, palpitations, presence of carditis), laboratory results (complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), anti-streptolysin O (ASO) titer, leukocyte count], echocardiographic findings, treatment approaches, surgical requirements, and outcomes were retrospectively collected from the hospital information system and patient files. Patients were divided into three age groups: 6–10 years, 11–15 years, and 16–18 years. This categorization was based on the commonly reported epidemiological distribution for ARF, in which school-aged children and early adolescents constitute the group at highest incidence.

Blood samples were obtained at the time of initial hospital admission before initiation of anti-inflammatory therapy. Laboratory analyses were performed in the hospital's central clinical laboratory using standardized automated analyzers and following institutional quality-control procedures; results were interpreted using age-appropriate reference ranges. According to the 2015 Revised Jones Criteria, elevated acute-phase reactants were defined as an ESR ≥60 mm/h and/or a CRP level ≥ 3.0 mg/dL (30 mg/L). ASO titers were evaluated as supportive evidence of preceding group A streptococcal infection. Delayed presentation was defined as a hospital admission occurring more than 7 days after the first ARF-related symptom (most commonly joint symptoms or fever), based on the symptom onset documented in the medical records. Anti-inflammatory therapy followed current guideline recommendations: aspirin as first-line therapy; naproxen substituted in cases of aspirin intolerance; and prednisolone added for moderate-to-severe carditis, tapered based on clinical and echocardiographic response. Secondary prophylaxis with intramuscular benzathine penicillin G was initiated in all patients.

All patients were hospitalized during the acute phase. After discharge, follow-up visits were scheduled at 1, 3, and 6 months; patients with mild or no regurgitation were subsequently followed annually, while those with moderate-to-severe involvement were seen every 6 months. Clinical response was defined as resolution of fever and joint symptoms within 72 hours of treatment initiation. In patients with a documented prior episode, recurrent ARF was diagnosed according to the 2015 Revised Jones Criteria.

Statistical Analysis

Categorical variables are presented as n (%) and are compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables are presented as mean ± standard deviation; normality was assessed graphically, and comparisons were performed using the independent-samples t-test or Welch's t-test as appropriate. To identify factors associated with carditis, a multivariable binary logistic regression model was constructed using the Enter method. Candidate variables were selected based on clinical plausibility and univariate association with carditis at $p<0.10$; these included age, sex, delayed presentation (>7 days from symptom onset), CRP, ESR, ASO titer, and pandemic period. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Model fit was assessed using the Hosmer–Lemeshow test, and multicollinearity was checked with variance inflation factors.

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0. T wo-sided p-values were considered statistically significant (p<0.05).

Results

A total of 122 newly diagnosed ARF cases were included in the study. Among the patients, 62.3% were male and 37.7% were female. The 11–15-year age group was the most common, accounting for 66.4%, and the mean age was 12.8±2.4 years. The demographic characteristics of the patients are summarized in Table 1.

During the pandemic, 41 patients were evaluated, corresponding to a mean of 1.58 cases per month. In the post-pandemic period, 81 patients were evaluated, corresponding to a monthly mean of 2.13 cases. This 34.8% increase in the monthly mean number of cases was statistically significant (independent-samples t-test, p=0.048). Case numbers were lowest in 2020 and 2021, began increasing, peaked at 32 cases in 2023, and remained high in 2024.

At presentation, the most common symptoms and findings were joint involvement (arthritis/arthralgia) (87.7%), fever (71.3%), and fatigue (59%). Carditis was detected in 95% (n=116) of patients. Although the rate of carditis appeared higher in the post-pandemic period than in the pandemic period, the difference was not statistically significant (92% vs. 96%, p=0.403). The distribution of clinical findings by period is given in Table 2.

Echocardiographic evaluation of patients with carditis showed that the most common finding was mitral regurgitation (90.2%), followed by aortic regurgitation (75.4%). Multivalvular involvement was present in 70.4% of patients. The degree of regurgitation was mainly mild to moderate. Although there was a slight increase in valve involvement rates in the post-pandemic period, this increase did not reach statistical significance. Echocardiographic findings and valve involvement are given in Table 3.

Table 1. Demographic characteristics of the patients

Characteristic	Total (n=122)	Pandemic (n=41)	Post-pandemic (n=81)	p-value
Sex				0.856
Male	76 (62.3%)	26 (63.4%)	50 (61.7%)	
Female	46 (37.7%)	15 (36.6%)	31 (38.3%)	
Age groups				0.880
6–10 years	25 (20.5%)	9 (22.0%)	16 (19.8%)	
11–15 years	81 (66.4%)	26 (63.4%)	55 (67.9%)	
16–18 years	16 (13.1%)	6 (14.6%)	10 (12.3%)	
Mean age (years)	12.8±2.4	12.7±2.3	12.9±2.5	0.674

Data are presented as n (%)
**Mean ± standard deviation, Student's t-test*

Table 2. Comparison of clinical findings by period

Symptom/finding	Total (n=122)	Pandemic (n=41)	Post-pandemic (n=81)	p-value
Joint pain/swelling	107 (87.7%)	35 (85.4%)	72 (88.9%)	0.591
Fever	87 (71.3%)	28 (68.3%)	59 (72.8%)	0.600
Fatigue	72 (59%)	23 (56.1%)	49 (60.5%)	0.644
Palpitations	50 (41%)	15 (36.6%)	35 (43.2%)	0.492
Presence of carditis	116 (95%)	38 (92%)	78 (96%)	0.403

A marked elevation of acute-phase reactants was detected in the great majority of patients. Elevated ASO, CRP, and ESR were found in 89.3%, 73.8%, and 85.2% of subjects, respectively. The mean ESR value in the post-pandemic period was significantly higher than in the pandemic period (92±33 mm/h vs. 83±30 mm/h, p=0.034). No significant differences were found in other laboratory parameters. Laboratory findings and their distribution by period are given in Table 4.

All patients were started on benzathine penicillin G for secondary prophylaxis. As anti-inflammatory therapies, aspirin (81.1%) and steroids (31.1%) were used most frequently. The mean hospital stay was 11.5±4.8 days. During a mean follow-up of 28±18 months, no deaths occurred. Surgical intervention was required in 4.9% (n=6) of patients.

In multivariable logistic regression analysis, delayed presentation (>7 days from symptom onset) (adjusted OR: 13.76, 95% CI: 1.20–157.67, p=0.035) and elevated CRP levels (per 10 mg/L increase; adjusted OR: 1.13, 95% CI: 1.00–1.28, p=0.044) remained independently associated with the presence of carditis after adjustment for age, sex, ESR, ASO titer, and pandemic period (Table 5). Model fit was adequate according to the Hosmer–Lemeshow test (p=0.839), and no significant multicollinearity was detected.

Six patients required surgical intervention for refractory heart failure despite optimal medical therapy. Echocardiographic evaluation demonstrated severe rheumatic valvular regurgitation in all patients. Three patients had isolated severe mitral regurgitation and underwent mitral valve replacement; one patient had

Table 3. Echocardiographic findings in the overall study cohort according to pandemic and post-pandemic periods

Valvular regurgitation	Total (n=122)	Pandemic (n=41)	Post-pandemic (n=81)	p-value
Mitral regurgitation	110 (90.2%)	36 (87.8%)	74 (91.3%)	0.535
– Minimal/trace	37 (30.3%)	12 (29.2%)	25 (30.8%)	
– Mild	52 (42.6%)	17 (41.4%)	35 (43.2%)	
– Moderate	19 (15.5%)	6 (14.6%)	13 (16%)	
– Severe	2 (1.6%)	1 (2.4%)	1 (1.2%)	
Aortic regurgitation	92 (75.4%)	29 (70.7%)	63 (77.7%)	0.393
– Minimal/trace	30 (24.5%)	10 (24.3%)	20 (24.6%)	
– Mild	43 (35.2%)	13 (31.7%)	30 (37%)	
– Moderate	18 (14.7%)	6 (14.6%)	12 (14.8%)	
– Severe	1 (0.8%)	0 (0)	1 (1.2%)	
Multivalvular involvement	86 (70.4%)	27 (65.8%)	59 (72.8%)	0.424

Data are presented as n (%). Minimal/trace findings shown in the table reflect patients who additionally satisfied all four Jones Doppler criteria despite low-grade severity; trivial regurgitations not meeting these criteria were excluded. Multivalvular involvement was defined as the simultaneous presence of pathological mitral and aortic regurgitation fulfilling the 2015 Revised Jones Criteria. Percentages are calculated using the entire study cohort (n=122) as the denominator.
**Comparisons were performed using chi-square or Fisher's exact tests*

Table 4. Comparison of laboratory findings

Parameter	Total mean ± SD	Pandemic	Post-pandemic	p-value
ASO (IU/mL)	1285±445	1208±425	1325±455	0.161
CRP (mg/L)	118±78	106±74	125±80	0.184
ESR (mm/h)	89±32	83±30	92±33	0.034
Leukocytes (/µL)	12,100±3,800	11,400±3,500	12,400±3,900	0.156

ASO: Anti-streptolysin O, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, SD: Standard deviation
Data are presented as mean ± standard deviation
Continuous variables were compared using Student's t-test or Welch's t-test as appropriate

isolated severe aortic regurgitation requiring aortic valve replacement; and two patients had combined severe mitral and aortic regurgitation requiring combined mitral and aortic valve surgery. All surgically treated patients met echocardiographic criteria for severe rheumatic valvular disease and underwent multidisciplinary evaluation by pediatric cardiologists and cardiovascular surgeons before surgical intervention. Of the six patients requiring surgery, five were diagnosed during the post-pandemic period and one during the pandemic period.

No statistically significant differences were found between periods in terms of treatment and outcomes. A comparison of treatments is presented in Table 6.

Discussion

This study provides a comprehensive evaluation of a newly established tertiary pediatric cardiology center's five-year experience with ARF and of the effects of the COVID-19 pandemic on disease dynamics. The most striking finding of our study is the statistically significant increase in ARF cases following the easing of pandemic restrictions. The decline in ARF cases observed during the pandemic may be more plausibly explained by reduced transmission of group A streptococcal infections due to school closures, physical distancing, and decreased social contact than by changes in diagnostic or prescribing practices. However, the reopening of schools, the lifting of public health restrictions, increased social interaction, and renewed exposure among susceptible individuals may have contributed to a rise in GAS transmission and, consequently, in ARF presentations. Similarly, a Canadian study reported an increase in the number of ARF cases in the post-pandemic period[7]. The increase in ARF observed in our study is in line with observations reported in selected settings.

The demographic profile of our cohort is consistent with the classical epidemiological patterns of ARF, in which school-age children and early adolescents (predominantly aged 5–15 years) are most affected, and a modest male predominance is commonly observed[10]. These features are also consistent with previously published Turkish ARF series[11].

Table 5. Univariate and multivariable logistic regression analyses (Enter method) for factors associated with carditis

Variable	Carditis negative (n=6)	Carditis positive (n=116)	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Delayed presentation (>7 days)	1 (16.7%)	82 (70.7%)	14.91 (0.80–277.16)	13.76 (1.20–157.67)	0.035
CRP (mg/L) (per 10 mg/L increase)	24±20	58±43	1.14 (1.01–1.30)	1.13 (1.00–1.28)	0.044
Age (years)	11.6±2.6	12.9±2.4	1.24 (0.91–1.69)	1.13 (0.81–1.58)	0.458
Sex (male)	4 (66.7%)	72 (62.1%)	1.01 (0.20–5.04)	0.86 (0.14–5.18)	0.865
ESR (mm/h) (per 10 mm/h)	99±29	89±31	0.79 (0.61–1.01)	0.82 (0.63–1.06)	0.131
ASO titer (IU/mL) (per 100 IU/mL)	890±430	820±480	0.96 (0.80–1.14)	0.95 (0.79–1.14)	0.555
Post-pandemic period	3 (50.0%)	78 (67.2%)	2.04 (0.43–9.56)	2.53 (0.48–13.19)	0.271

Model fit was adequate (Hosmer–Lemeshow p=0.839), with no significant multicollinearity.
OR: Odds ratio, CI: Confidence interval, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate (mm/h); ASO: Anti-streptolysin O (IU/mL)

Table 6. Comparison of treatment characteristics of patients with acute rheumatic fever

Treatment/outcome	Total (n=122)	Pandemic (n=41)	Post-pandemic (n=81)	p-value
Aspirin	99 (81.1%)	32 (78%)	67 (82.7%)	0.562
Naproxen	31 (25.4%)	12 (29.3%)	19 (23.5%)	0.503
Steroid	38 (31.1%)	11 (26.8%)	27 (33.3%)	0.477
Surgical requirement	6 (4.9%)	1 (2.4%)	5 (6.2%)	0.410

The rate of carditis in our study was 95%, which is higher than the 50–80% range reported in developed countries[12,13] but similar to that in developing countries[14,15]. The rates of mitral (90.2%) and aortic (75.4%) regurgitation observed in our cohort are markedly higher than those reported in the literature. This discrepancy is most likely explained by the tertiary-referral nature of our center, which is enriched for more severe cases, and by the systematic use of echocardiography, which leads to the detection of subclinical valvular involvement in accordance with the 2015 Revised Jones Criteria. Therefore, the high prevalence of valvular involvement in our study should not be interpreted as representative of the general ARF population. The relatively high rate of carditis observed in both periods may be related to the tertiary referral nature of our center, which likely receives more severe or complicated cases. Subclinical valvular involvement detected on echocardiography using the 2015 Revised Jones Criteria may have contributed to the overall prevalence of carditis.

Although carditis and valve involvement rates were numerically higher in the post-pandemic period, these differences did not reach statistical significance. The relatively small sample size and uneven group distribution may have reduced statistical power to detect modest differences in clinical sub parameters.

Delayed presentation and elevated CRP levels were identified as factors associated with carditis in the multivariable analysis, supporting a role for inflammatory burden and diagnostic delay in disease severity. This finding is consistent with classic epidemiological data showing that early antibiotic treatment reduces disease severity[16]. Furthermore, high CRP and ESR values, reflecting the severity of the inflammatory response, have been associated with progression of valvular damage[17].

Although CRP did not differ significantly between periods, ESR was significantly higher in the post-pandemic group, possibly reflecting a more prolonged inflammatory burden given ESR's slower normalization kinetics relative to CRP. Variability in both markers on presentation may also be influenced by the timing of hospital admission, the prior use of anti-inflammatory medications, or the onset of subacute disease; the retrospective design precluded detailed time-based correlation analyses.

Secondary prophylaxis was initiated for all patients, and no deaths occurred. Notably, five of the six patients requiring surgery were diagnosed during the post-pandemic period. Although the number of surgical cases was small and the difference was not statistically significant, this observation may suggest a tendency toward more advanced valvular involvement during this period; however, this finding should be interpreted with caution. Previous studies have also identified inflammatory burden and delayed presentation as important determinants of persistent valvular disease and adverse outcomes in rheumatic carditis[18,19].

Study Limitations

This study has several important limitations. First, and most fundamentally, the cohort is subject to substantial selection and referral bias. Our hospital is a tertiary pediatric cardiology center that primarily receives patients with suspected or confirmed cardiac involvement; milder, non-carditic ARF cases managed in primary or secondary care settings are therefore not represented. Consequently, our rates of carditis (95%) and mitral and aortic regurgitation should be viewed as institution-specific patterns and must not be extrapolated to the general ARF population or to community-level epidemiology. Second, the center was newly established during the study period and its referral network expanded gradually; the post-pandemic increase in case volume therefore plausibly reflects institutional growth, increased outpatient clinic capacity, wider access to pediatric echocardiography, improved case capture, and evolving referral patterns, and any true temporal change in GAS transmission. We could not adjust for these confounders because a defined catchment denominator was not available. Third, comparisons between the pandemic and post-pandemic periods are descriptive; with only 41 pandemic-period patients, the power to detect modest between-period differences in clinical subparameters is limited. Fourth, although all regurgitations were classified according to the four 2015 Jones Doppler criteria to minimize misclassification between physiologic and pathologic regurgitation, residual misclassification nonetheless remains possible in a retrospective review of stored images and reports. Fifth, symptom duration was categorized rather than analyzed as a continuous variable, and long-term outcomes were reported descriptively without formal time-to-event analyses. Sixth, because only six patients were free of carditis, the multivariable logistic regression model should be interpreted with caution despite an acceptable goodness-of-fit (Hosmer–Lemeshow p=0.839). The limited number of outcome-negative patients may have reduced the stability of the estimated ORs and widened the CIs. Finally, single-center retrospective data preclude causal inference regarding pandemic effects on ARF biology.

Our findings underscore the importance of sustained awareness of GABHS pharyngitis management and secondary prophylaxis, particularly during health crises. Beyond temporal trends in case counts, this study contributes detailed clinical severity data, factors associated with carditis, and structured follow-up outcomes in a tertiary referral context.

Conclusion

In this single-center study, the number of ARF cases was higher in the post-pandemic period than in the pandemic period. A high prevalence of carditis was observed, reflecting the tertiary-referral nature of our center; therefore, this finding should not be generalized to the broader ARF population. Delayed presentation and elevated inflammatory markers were associated with cardiac involvement and the requirement for surgery. These findings should be interpreted within the limitations of a retrospective tertiary-center design.

Ethics

Ethics Committee Approval: Approval for the study was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinical Research Ethics Committee on October 22, 2025 (decision number 332).

Informed Consent: This retrospective study included pediatric cardiology patients followed between May 2020 and August 2025.

Footnotes

Authorship Contributions

Concept: Genç HZ, Güzelbağ AN, Öztürk E, Design: Genç HZ, Öztürk E, Data Collection and/or Processing: Güzelbağ AN, Çevlik B, Çoban Ş, Analysis and/or Interpretation: Genç HZ, Çevlik B, Öztürk E, Literature Search: Genç HZ, Güzelbağ AN, Writing: Genç HZ, Güzelbağ AN, Çoban Ş.

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