JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1562094
J Contemp Med 202x;xx(x):xxx-xxx

Original Article / Orijinal Araştırma

Evaluation of Patients with Acute Rheumatic Fever: 13-Year Experience of a Single Center

Akut Romatizmal Ateş Tanılı Hastaların Değerlendirilmesi: 13 Yıllık Tek Merkez Deneyimi

Fatma İssi Irlayıcı[1], Embiya Dilber[2]

[1]Department of Pediatric Gastroenterology, Denizli State Hospital, Denizli, Turkiye
[2]Department of Pediatric Cardiology, Karadeniz Technical University Faculty of Medicine, Trabzon, Turkiye

Abstract

Aims: This study aims to retrospectively evaluate acute rheumatic fever's epidemiological and clinical characteristics in the Eastern Black Sea Region.

Material and Method: Demographic, clinical and laboratory characteristics of patients diagnosed with acute rheumatic fever in our clinic between January 2005 and December 2017 were evaluated from archival records.

Results: Included in the study were 175 patients with a mean age of 11±3.52 years (26 months–17 years), with a female/male ratio of 1.38. Patients are most frequently presented in February, May and August. Carditis was the most common (80%) major finding, while arthritis was seen in 51.4% and chorea in 16%. Erythema marginatum was present in only one patient. While isolated mitral valve involvement (54.3%) was most common in the patients with carditis, simultaneous mitral and aortic valve involvement was found in 30.7% of the patients, and isolated aortic valve involvement in 10%. Tricuspid regurgitation was seen in three (2.1%) patients with mitral involvement. Recurrence was detected in four (57.1%) of the seven patients who were incompatible with secondary prophylaxis. During clinical follow-up, two patients underwent mitral and aortic valve replacement. No mortality was observed in the patients.

Conclusion: Despite improving socio-economic conditions in Turkiye in recent years, acute rheumatic fever remains a significant health problem for the Eastern Black Sea Region.

Keywords: Acute rheumatic fever, carditis, children, rheumatic heart disease

Öz

Amaç: Bu çalışmada, Doğu Karadeniz Bölgesi'nde akut romatizmal ateşin epidemiyolojik ve klinik özelliklerini retrospektif olarak değerlendirmeyi amaçlanmıştır.

Gereç ve Yöntem: Kliniğimizde Ocak 2005 ile Aralık 2017 tarihleri arasında akut romatizmal ateş tanısı alan hastaların demografik, klinik ve laboratuvar özellikleri arşiv kayıtlarından değerlendirildi.

Bulgular: Çalışmaya yaş ortalaması 11±3,52 yıl (26 ay-17 yıl), kadın/erkek oranı 1,38 olan 175 hasta dahil edildi. Hastalar en sık Şubat, Mayıs ve Ağustos aylarında başvurdu. En sık görülen majör bulgu kardit (%80) iken, artrit %51,4, kore ise %16 oranında görüldü. Sadece bir hastada eritema marjinatum mevcuttu. Kardit hastalarında en sık izole mitral kapak tutulumu (%54,3) görülürken, eş zamanlı mitral ve aort kapak tutulumu hastaların %30,7'sinde, izole aort kapak tutulumu ise %10 oranında saptandı. Mitral tutulumu olan üç (%2,1) hastada triküspit yetersizliği görüldü. Sekonder profilaksi ile uyumsuz olan yedi hastanın dördünde (%57,1) nüks tespit edildi. Klinik takip sırasında iki hastaya mitral ve aort kapak değişimi uygulandı. Hastalarda mortalite görülmedi.

Sonuç: Türkiye'de son yıllarda sosyo-ekonomik koşullardaki iyileşmeye rağmen akut romatizmal ateş, Doğu Karadeniz Bölgesi için önemli bir sağlık sorunu olmaya devam etmektedir.

Anahtar Kelimeler: Akut romatizmal ateş, kardit, çocuk, romatizmal kalp hastalığı

Corresponding *(İletişim)*: Fatma İssi Irlayıcı, Denizli State Hospital, Department of Pediatric Gastroenterology, Denizli, Turkiye
E-mail *(E-posta)*: fatmaissi@gmail.com
Received *(Geliş Tarihi)*: 06.10.2024 **Accepted *(Kabul Tarihi)*:** 26.11.2024

INTRODUCTION

Acute rheumatic fever (ARF) is a late autoimmune response secondary to tonsillopharyngitis due to group A streptococci. The disease is characterized by such widespread systemic involvement as migratory joint involvement, carditis, chorea, erythema marginatum, subcutaneous nodules and fever.[1]

Although most of the clinical findings in the acute period improve with short-term medical treatments, cardiac valve damage can be permanent. Rheumatic heart disease is the main cause of ARF-related mortality and morbidity.[2] Deaths are most common in low- and middle-income countries.[3]

In developed countries, the frequency of ARF and the prevalence of rheumatic heart disease developing secondary to the disease have decreased significantly since the 20th century.[4] This decrease has been associated with improved medical care, the widespread use of benzathine penicillin in the treatment of streptococcal tonsillopharyngitis, a decrease in the number of households and other socioeconomic improvements.[5]

According to the latest Jones criteria, which were revised due to differences between countries, populations with ARF frequency ≤2/100,000 in school-age children, and rheumatic heart disease prevalence ≤1/1000 at all ages were low-risk; others were defined as moderate- to high-risk. In addition, it has been suggested that populations for which sufficient reliable epidemiological data are not available should be included in the moderate- to high-risk group.[6]

There is limited data on the incidence of ARF in Turkiye, and it is in the moderate-high risk group according to the 2015 Jones criteria.[7] We aimed to evaluate the clinical, laboratory results, demographic data and prognosis of the patients who were followed up with the diagnosis of ARF in our Pediatric Cardiology Clinic between 2005 and 2017.

MATERIAL AND METHOD

We present here a retrospective analysis of cases diagnosed with ARF in our Pediatric Cardiology Clinic between January 2005 and December 2017.

The cases included in the study were diagnosed according to the modified Jones criteria from 1992 until 2015, and according to the revised Jones criteria after 2015.

The patients' age at the time of hospital admission, gender, month of admission, socioeconomic status, complaint and history were ascertained from the records, along with (i) whether or not the patient had a history of tonsillopharyngitis, (ii) whether or not the patient consulted a doctor for tonsillopharyngitis (iii) whether or not antibiotics were recommended to the patient (iv) the duration/dose, if recommended; and (v) family history of acute rheumatic fever.

Since the start date of the study in January 2005, transthoracic echocardiography was performed by a pediatric cardiologist in our department on all patients with suspected ARF, as well as the presence or absence of a murmur. The criteria recommended by the World Heart Federation were used to define pathological valve regurgitation and to rate the severity of cardiac involvement.[8]

The hemogram, CRP, ESR, anti-streptolysin O titer and throat swab culture results of the patients were recorded. PR distance was evaluated from electrocardiogram recordings.

A single dose of benzathine penicillin was administered to all patients as primary prophylaxis, and salicylate was used for the treatment of arthritis. In the acute period, strict bed rest was applied to all patients. Although steroid treatment in mild carditis cases is controversial, our clinical observations are that mild carditis did not regress with salicylate, and all cases with carditis were treated with steroids. Haloperidol treatment was started in all cases diagnosed with chorea. In the follow-up, secondary prophylaxis was given to all cases.

Compliance used for patients receiving regular secondary prophylaxis. Recurrence defined as a new episode of ARF with group A streptococcal infection two months after the end of treatment.

Ethical approval was obtained from the local ethics committee of our hospital (Decision Number: 2017/99) and was conducted by the Declaration of Helsinki. Informed consent was obtained from the families of all children participating in the study.

IBM SPSS Statistics (Version 23.0. Armonk, NY: IBM Corp.) was used for the statistical analysis of the findings obtained in the study. While evaluating the data, in addition to complementary statistical approaches (mean, standard deviation, frequency), a Chi-Square test and Fisher's Exact Chi-Square test were used to compare qualitative data. In evaluating the results; p-values below 0.05 were considered to be statistically significant. Variables were presented as mean±standard deviation (SD), number (n), and percent (%).

RESULTS

Included in the study were 175 patients with a mean age of 11±3.52 years (2–17 years), of which 102 (58.2%) were female. When compared according to age groups, the largest group was between the ages of 10-14 with 82 (46.8%) patients (**Figure 1**).

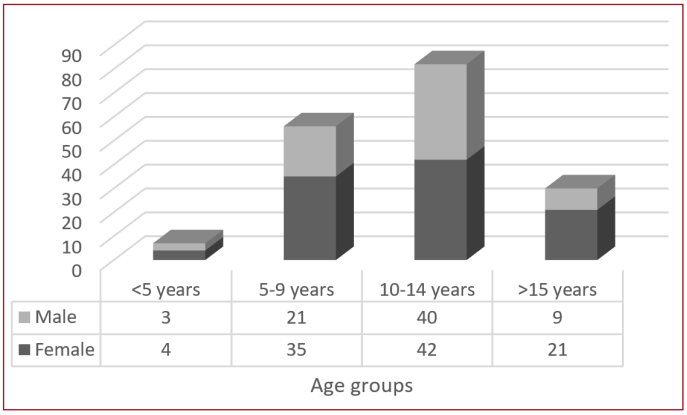

Figure 1. Distribution of ARF cases by age groups

The analysis of the distribution of cases by the years of diagnosis revealed the highest annual number of cases (n=28) was in 2017, while the lowest number of cases (n=7) was presented in 2005 (**Figure 2**). The disease was observed more often in spring (30%) and winter (29%), and mostly in February (13%), May (12%) and August (9%).

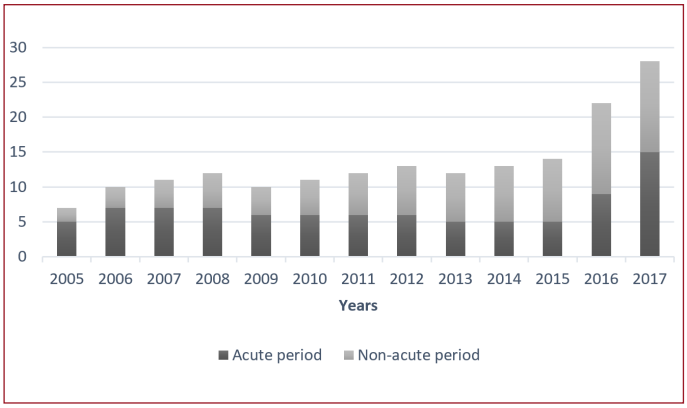

Figure 2. Distribution of ARF cases according to the years of diagnosis

Among the 47 (26.8%) patients with a history of tonsillopharyngitis before the diagnosis of acute rheumatic fever, 43 (24.6%) stated that they had consulted a doctor, and 28 (65.1%) of these were recommended antibiotics.

While 89 (51%) of the cases were in the acute period at the time of diagnosis, 86 (49%) cases were not in the acute period. Among the cases that were not in the acute period, 28 (16%) were referred to our department for chorea, and 18 (10.2%) incidentally detected murmur on physical examination. In these cases, valve involvement that could not be attributed to any other cause was diagnosed, and they were followed up with a diagnosis of acute rheumatic fever. Among the cases, 40 (22.8%) were diagnosed in another health center and administered to our hospital for follow-up. These cases were also included in the group not in the acute period. While the most common presenting complaint of cases diagnosed with acute rheumatic fever was joint pain/swelling (51%), other complaints were; involuntary movements (16%), palpitations/chest pain (12%), murmur (10%), fever (9%), fatigue (1.5%), rash (0.5%).

Carditis (n=140, 80%) was the most common major finding, followed by arthritis/polyarthralgia (n=90, 51.4%). Sydenham's chorea was observed in 28 (16%) cases, and erythema marginatum in one case, while no subcutaneous nodules were detected. When evaluated for the presence of more than one major criterion, carditis and arthritis were found to be coexistent in 65 (37.1%) cases, while chorea and valve involvement were coexistent in 18 (10.2%) cases (**Table 1**).

Table 1. Distribution of Major Manifestations in ARF Cases

Major manifestations	(n)	(%)
Carditis	140	80
Arthritis/Polyarthralgia	90	51.4
Chorea	28	16
Erythema marginatum	1	0.5
Subcutaneous nodules	-	-
Multiple major criteria		
Arthritis+Carditis	65	37.1
Chorea+Carditis	18	10.2

When the distribution of major findings by gender was examined, Sydenham's chorea was more common in females (F/M: 1.8/1), but the difference was not statistically significant ($p > 0.05$).

When the cases diagnosed with carditis were evaluated in terms of valve involvement; mitral regurgitation was present in 125 (89.3%), aortic regurgitation in 57 (40.7%), and tricuspid regurgitation in three (2.1%). The most common form of involvement was isolated mitral regurgitation (76 cases - 54.3%), while mitral and aortic regurgitation were observed concurrently in 43 (30.7%) cases, and isolated aortic regurgitation was observed in 14 (10%) cases. All three of the cases with tricuspid regurgitation had coexistent mitral regurgitation.

When the grade of valve involvement in echocardiography was evaluated; grade I mitral regurgitation was observed in 61 (43.6%) cases, grade II mitral regurgitation in 33 (23.6%) cases, grade III mitral regurgitation in 26 (18.6%) cases, and grade IV mitral regurgitation in five (3.6%) cases. In aortic valve involvements, grade I aortic regurgitation was detected in 48 (34.2%), grade II aortic regurgitation in seven (5%), and grade III aortic regurgitation in two (1.4%) cases (**Table 2**).

Table 2. Echocardiographic Evaluation of Valve Involvements

	Grade I- AR* n (%)	Grade II- AR n (%)	Grade III- AR n (%)	Isolated MR† n (%)
Grade I- MR	17 (12.1)	1 (0.7)	-	43 (30.7)
Grade II- MR	10 (7.1)	1 (0.7)	-	22 (15.7)
Grade III- MR	8 (5.7)	1 (0.7)	-	17 (12.1)
Grade IV- MR	1 (0.7)	2 (1.4)	2 (1.4)	-
Isolated AR	12 (8.6)	2 (1.4)	-	-

*AR: Aortic regurgitation, †MR: Mitral regurgitation

The severity of carditis was determined based on clinical and echocardiographic examinations. When carditis was classified according to clinical severity; mild carditis was observed in 94 (67%), moderate carditis in 31 (22%) and severe carditis in 15 (11%) cases.

When the 89 cases in the acute period were evaluated in terms of minor findings, monoarthralgia was observed in one (1.1%) case, while prolonged PR interval was found in four (9.5%) of 42 cases with accessible electrocardiogram recordings. While fever was detected in 17 (19%) cases, elevated CRP and/or ESR were present in all cases in the acute period.

Among the supporting findings, high anti-streptolysin O titer was detected in 100 (57.1%) cases. Group A streptococci was detected in six (9.2%) of the 65 patients from whom throat swab cultures were obtained.

All cases with cardiac involvement were treated with steroids. Supportive treatment was given to 15 (10.7%) cases with congestive heart failure. Mitral and aortic valve replacements were performed in two (1.7%) patients with grade IV mitral regurgitation and grade III aortic regurgitation that could not be controlled with medical treatment.

In terms of secondary prophylaxis, records of 112 cases were evaluated. While 115 (94.2%) of these cases had good treatment compliance, 7 (5.8%) cases had insufficient compliance. A single daily oral macrolide treatment was recommended for three of the cases due to penicillin allergies and for four cases who declined benzathine penicillin prophylaxis due to pain. Clarithromycin was used as macrolide therapy since erythromycin could not be supplied.

In the clinical follow-up, improvement in valve involvement was observed in 59 (48.3%) cases. In 45 (36.9%) of these cases, the grade of valve regurgitation regressed, while in 14 (11.4%) cases the valve involvement disappeared completely. The median time to the disappearance of valve regurgitation was 4 months (1–6 months). In the first month, improvement in valve regurgitation was detected in 37 (26.4%) cases. While no recurrence was observed in our patients with secondary prophylaxis compliance, it was detected in 4 (57.1%) of 7 non-compliant patients. While surgical intervention was required in two cases due to severe valve insufficiency and uncontrolled congestive heart failure, no mortality was observed in our cases.

DISCUSSION

Acute rheumatic fever and rheumatic heart disease are among the most common preventable reasons for cardiovascular mortality and morbidity, particularly in low- and middle-income countries.[9]

The incidence of ARF is estimated to be 8-51/100.000 worldwide.[10] The lowest incidence was reported as 0.5-3.1/100,000 in Western Europe and the United States.[11] Despite being developed countries, ARF is common among Aborigines in Australia, Maoris in New Zealand, and natives of the Pacific islands.[12] In a study in Australia between 1997 and 2010, the incidence of ARF was reported as 194/100,000 in Indigenous children aged 5-14 years.[13] However, it is not possible to state the true incidence worldwide, since sufficient data cannot be obtained from the African and Asian regions, where the disease is common.

Until 2015, mostly regional data was available on the incidence of ARF in Turkey. Saraçlar et al.[14] found the frequency of ARF to be 20/100.000 between 1972 and 1976. According to other studies, the incidence of the disease varies between 7.4/100.000 and 107.7/100.000.[15,16] The 2016 records of the Turkish National Statistics Institute were used to determine the incidence of ARF by various provinces and regions. The estimated incidence rate of ARF in Turkey is 8.84/100.000.[7]

We were unable to determine the incidence of the disease in our province and region for the years 2005–2017. During this period, the temporary presence of a second pediatric cardiologist in the region made our incidence assessment impossible. Again, since our center provides tertiary healthcare services, we observe that complicated carditis cases are often referred to our center.

Acute rheumatic fever is most commonly observed in the 5–15 years age group, being the period in which the risk of group A streptococci tonsillopharyngitis is highest. While the incidence of the disease before the age of 5 years is around 5%, cases under the age of 2 years are very rare.[17] In the study by Örün et al.[15] involving the highest number of cases in our country, 98.3% of cases were between the ages of 5 and 15 years, while 1.7% were under the age of 5 years. The youngest case in the literature is a nine-month-old female patient; she was diagnosed with fever, arthritis, and a 3/6 pansystolic murmur at the apex and mitral regurgitation.[18] Among the cases in the present study, 78.8% were in the 5–15 years age range. The youngest of the seven (4%) patients under the age of 5 years was 26 months old. She was admitted to the hospital with migratory arthralgia and fever. While acute phase reactants and anti-streptolysin O titers were high, the patient's echocardiography was normal. Although the diagnosis of ARF was considered in the patient, she was hospitalized and followed up, as migratory polyarthralgia was not among the major findings at the time of diagnosis. Due to the continued increase in anti-streptolysin O titers during follow-up and the progressive mitral regurgitation identified on repeated echocardiography, the patient was diagnosed with ARF and treatment was started.

In parallel with the fact that group A streptococci tonsillopharyngitis is observed mostly in the spring and winter, ARF is mostly observed in these seasons.[19] Concurring with the literature, the disease was observed mostly in spring (30%) and winter (29%) in our study. In the distribution according to months, the cases applied primarily in February (13%) and May (12%). In our study, it was seen that the cases were diagnosed during the summer season as well. These cases were not usually in acute period, and the majority of them were patients who were admitted with the diagnosis of Sydenham's chorea.

The history of tonsillopharyngitis undergone before ARF ranges from 24–81%.[20] In our study, a history of tonsillopharyngitis before ARF was noted in 26.8% of the cases, 24.6% of whom had consulted a doctor due to tonsillopharyngitis. The reasons why the rate of tonsillopharyngitis history is so low were; a significant portion of cases, tonsillitis resolves asymptomatically or were not admitted to hospital due to infection. Antibiotics

were recommended for 65.1% of the cases admitted to the health institution. According to the results of our study, the most important reasons for the high frequency of ARF in our region were: (i) asymptomatic group A streptococci tonsillopharyngitis or, (ii) antibiotic treatment was not recommended, or (iii) the treatment was not complied with in the appropriate dose and duration, although antibiotics were recommended. The preference of benzathine penicillin for primary prophylaxis in only four cases in the study group is quite low, and we believe that increasing the single dose of benzathine penicillin treatment will lead to significant improvements in the incidence of ARF.

Örün et al.[15] found the most common major finding to be carditis with a rate of 61.7%, followed by arthritis in 59.1%, chorea in 14.1%, erythema marginatum in 0.8%, and subcutaneous nodule in 0.6%, respectively. In our study, carditis was observed in 80%, arthritis in 51.4%, chorea in 16% and erythema marginatum in one case, while no subcutaneous nodule was detected.

The most common major coexisting findings were carditis and arthritis, while in a study conducted in Bursa between 1994 and 2000, coexisting arthritis and carditis was observed in 37% of 207 cases.[21] In the present study, the coexistence of carditis and arthritis was found at a rate of 37.1%. Carditis is reported in more than half of chorea patients in literature.[22] In a study by Caldas et al.[23] carditis was found in 64% of patients with chorea and the importance of performing echocardiography in patients with chorea was emphasized. Similarly in our study, carditis was detected in 64.2% of the patients with chorea.

Carditis is the most significant major finding of ARF due to its potential to cause sequelae.[24] In the study conducted by Erdem et al.[25] isolated mitral regurgitation was observed in 54.9% of cases, mitral and aortic regurgitation concurrently in 34% of cases and isolated aortic regurgitation in 5.7% of cases. In the same study, pericardial effusion with pancarditis was detected in 5.7% of cases, while tricuspid regurgitation was not observed. Similarly in our study, isolated mitral regurgitation was observed in 54.3% of cases with cardiac involvement, mitral and aortic regurgitation were observed concurrently in 30.7%, while isolated aortic regurgitation was detected in 10%. Furthermore, tricuspid regurgitation, among the rare involvements, was present in three (2.1%) cases with mitral regurgitation, while no pericardial effusion was observed.

Mild carditis is observed mostly in terms of clinical severity of carditis. In the study by Ekici et al.[26] between 2005 and 2008, 63% of 193 cases were evaluated as mild, 30.2% as moderate and 6.7% as severe carditis. When the 140 cases with carditis in the present study were classified according to clinical severity, the condition was evaluated as mild in 67%, moderate in 22% and severe in 11% of cases.

A review of literature assessing the frequency of minor findings, arthralgia was reported at rates in the range of 54.6–81.1%, fever in 40–62%, prolonged PR interval in 15.9–23%, ESR elevation in 81.8–95%, and CRP elevation in 72–81.8%.[27,28] These data, however, were reported according to the Jones criteria prior to the 2015 revision. In our study; monoarthralgia 1.1%, PR prolongation 9.5%, fever 19% and increased acute phase reactants were present in all cases. While acute phase reactants are the most common minor finding similar to the literature, monoarthralgia has been under-detected since it has been included in the diagnostic criteria since 2015.

As an indicator of previous group A streptococci infection, Güngör et al.[29] found elevated anti-streptolysin O titers in 92,2% of patients and group A streptococci in throat swab culture in 4.4%. In our study, while elevated anti-streptolysin O titers was observed in all of the cases in the acute period, group A streptococci was present in the throat culture of 9.2%.

One of the most important factors that cause mortality and morbidity in the follow-up of ARF is recurrences. Benzathine penicillin prophylaxis is the most effective prevention method to prevent recurrent attacks and severe consequences of the disease such as valve replacement.[30] In the study of Ekici et al.[26] compliance with secondary prophylaxis was 83.6%, and recurrence was observed in 16.7% of the cases. While the recurrence rate was 4.8% in cases that were compliant with prophylaxis, this rate was found to be 78% in non-compliant cases. In our study, compliance with secondary prophylaxis was 94.2%, recurrence as carditis was observed in 3.3% of our cases. Recurrence was not observed in our patients with secondary prophylaxis compliance, whereas recurrence was found in 57.1% of non-adherent patients.

Concerning the prognosis of ARF, among the 702 cases in Brazil that were followed for 1.3–16.9 years, the valve lesions resolved completely in 34.4% of the cases with mild carditis.[31] Bozabali et al.[32] reported that among 62 cases with mitral regurgitation who were followed up for an average of 3.4±2.7 years after treatment, 32.2% experienced a regression in the grade of valve involvement, while complete recovery was observed in 11.3%. In the present study, a regression in the grade of valve involvement was detected in 36.9% of cases, while complete improvement was observed in 11.4% of the cases. The median time to the disappearance of valve involvement was 4 months (1-6), while improvement in valve involvement in the first month occurred in 26.4% of the cases.

Although congestive heart failure is relatively rare (4.4–13.8%) in patients with ARF carditis, it can be observed.[33] Bostan et al.[21] reported that surgical intervention was performed in four (2%) patients whose levels of severe aortic insufficiency and progressive mitral stenosis. In our study, medical treatment was applied to 10.7% of the cases due to congestive heart failure, and mitral and aortic valve replacement was performed in two (1.7%) cases due to 4th degree mitral regurgitation and 3rd degree aort regurgitation that did not respond to treatment. No mortality was observed in our cases.

Subclinical carditis has gained importance after the revised Jones criteria. For this purpose, an echocardiographic screening study was conducted among Turkish school children, including 2550 students. The incidence of rheumatic heart disease is 15/1000, which is similar to studies in intermediate- and high-risk populations.[34] It has been emphasized that echocardiographic screening studies are necessary to reduce the burden of rheumatic heart disease and long-term follow-up of children diagnosed with subclinical rheumatic heart disease is necessary.

CONCLUSION

ARF remains a significant health concern in the Eastern Black Sea Region. The most important reasons for the high frequency of ARF are the fact that in most patients the group A streptococci tonsillopharyngitis is asymptomatic, that they do not admit to health institutions due to infection and do not use antibiotic therapy at the appropriate dose and time. We consider that increasing the single-dose benzathine penicillin treatment will lead to significant improvements in the incidence of ARF. In addition, increasing echocardiographic screening studies will contribute to reducing the burden of rheumatic heart disease.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of **XXXXXXXXXXXXXXX** Ethics Committee (Date: **XXXXXXXXXX**, Decision No: 2017/99).

Informed Consent: Informed consent was obtained from the families of all children participating in the study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Webb RH, Grant C, Harnden A. Acute rheumatic fever. BMJ 2015;351:h3443.
2. Arvind B, Ramakrishnan S. Rheumatic fever and rheumatic heart disease in children. Indian J Pediatr 2020;87:305-11.
3. Zühlke LJ, Beaton A, Engel ME, et al. Group A Streptococcus, acute rheumatic fever and rheumatic heart disease: epidemiology and clinical considerations. Curr Treat Options Cardiovasc Med 2017;19:15.
4. Woldu B, Bloomfield GS. Rheumatic Heart Disease in the Twenty-First Century. Curr Cardiol Rep 2016;18:96.
5. Lahiri S, Sanyahumbi A. Acute Rheumatic Fever. Pediatr Rev 2021;42:221-32.
6. Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. Circulation 2015;131:1806-18.
7. Gürses D, Koçak G, Tutar E, Özbarlas N. Turkish ARF study group. Incidence and clinical characteristics of acute rheumatic fever in Turkey: Results of a nationwide multicentre study. J Paediatr Child Health 2021;57:1949-54.
8. Reményi B, Wilson N, Steer A, et al. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease--an evidence-based guideline. Nat Rev Cardiol 2012;9:297-309.
9. Karthikeyan G, Guilherme L. Acute rheumatic fever. Lancet 2018;392:161-74.
10. Kumar RK, Tandon R. Rheumatic fever & rheumatic heart disease: the last 50 years. Indian J Med Res 2013;137:643-58.
11. de Loizaga SR, Beaton AZ. Rheumatic Fever and Rheumatic Heart Disease in the United States. Pediatr Ann 2021;50:98-104.
12. Rising Ethnic Inequalities in Acute Rheumatic Fever and Rheumatic Heart Disease, New Zealand, 2000-2018. Emerg Infect Dis 2021;27:36-46.
13. Oliver J, Osowicki J, Cordell B, Hardy M, Engelman D, Steer AC. Incidence of acute rheumatic fever and rheumatic heart disease in Melbourne, Australia from 1937 to 2013. J Paediatr Child Health 2020;56:1408-13.
14. Saraçlar M, Ertuğrul A, Özme ve Ajun A. Akut romatizmal ateş insidansı ve romatizmal kalp hastalıklarının prevalansı. Türk Kardiyoloji Dern Arş 1978;7:50-5.
15. Orün UA, Ceylan O, Bilici M, et al. Acute rheumatic fever in the Central Anatolia Region of Turkey: a 30-year experience in a single center. Eur J Pediatr 2012;171:361-8.
16. Narin N, Mutlu F, Argun M, et al. Incidence and clinical features of acute rheumatic fever in Kayseri, Central Anatolia, 1998-2011. Cardiol Young 2015;25:745-51.
17. Tani LY, Veasy LG, Minich LL, Shaddy RE. Rheumatic fever in children younger than 5 years: is the presentation different? Pediatrics 2003;112:1065-8.
18. Abdin ZH, Eissa A. Rheumatic fever and rheumatic heart disease in children below the age of 5 years in the tropics. Ann Rheum Dis 1965;24:389-91.
19. Bono-Neri F. Acute Rheumatic Fever: Global Persistence of a Preventable Disease. J Pediatr Health Care 2017;31:275-84.
20. Bennett J, Rentta N, Leung W, et al. Structured review of primary interventions to reduce group A streptococcal infections, acute rheumatic fever and rheumatic heart disease. J Paediatr Child Health 2021;57:797-802.
21. Bostan MÖ, Çil E. Bursa ilindeki çocuklarda akut romatizmal ateşin değerlendirilmesi. T Klin Kardiyoloji 2001;14:276-81.
22. Teixeira AL, Vasconcelos LP, Nunes MDCP, Singer H. Sydenham's chorea: from pathophysiology to therapeutics. Expert Rev Neurother 2021;21:913-22.
23. Caldas AM, Terreri MT, Moises VA, et al. What is the true frequency of carditis in acute rheumatic fever? A prospective clinical and Doppler blind study of 56 children with up to 60 months of follow-up evaluation. Pediatr Cardiol 2008;29:1048-53.
24. Hung LC, Nadia R. A Review of Acute Rheumatic Fever and Rheumatic Heart Disease Research in Malaysia. Med J Malaysia 2016;71:79-86.
25. Erdem S, Demir F, Ayana M, et al. Acute rheumatic fever in south-east of Turkey: clinical features and epidemiological evaluation of the patients over the last 25 years. Cardiol Young 2020;30:1086-94.
26. Ekici F, Kale Y, Kocabaş A. Changing face of acute rheumatic fever: our clinical observations. Anadolu Kardiyol Derg 2013;13:506-7.
27. Grassi A, Fesslovà V, Carnelli V, et al. Clinical characteristics and cardiac outcome of acute rheumatic fever in Italy in the last 15 years. Clin Exp Rheumatol 2009;27:366-72.
28. Yildirim A, Aydin A, Demir T, et al. Acute rheumatic fever: a single center experience with 193 clinical cases. Minerva Pediatr 2016;68:134-42.
29. Güngör Ş, Doksöz O, Fettah A, Nacaroğlu HN, Örün UA, Karademir S. Akut romatizmal ateş tanısı ile izlenen hastaların geriye dönük olarak değerlendirilmesi: Beş yıllık tek merkez deneyimi. İzmir Dr. Behçet Uz Çocuk Hast. Dergisi 2014; 4:87-96.
30. Bennett J, Rentta NN, Leung W, et al. Early diagnosis of acute rheumatic fever and rheumatic heart disease as part of a secondary prevention strategy: Narrative review. J Paediatr Child Health 2021;57:1385-90.

31. Mota CC, Meira ZM, Graciano RN, Graciano FF, Araújo FD. Rheumatic Fever prevention program: long-term evolution and outcomes. Front Pediatr 2015;2:1-5.
32. Bozabalı S, Mammadova A, Turan C, Sahan YO, Levent E. Akut Romatizmal Ateşe Bağlı Kardit Gelişen Hastalarda Penisilin Profilaksisinin Etkinliğinin Değerlendirilmesi. Türkiye Çocuk Hast Derg 2016;1:7-12.
33. Leal MTBC, Passos LSA, Guarçoni FV, et al. Rheumatic heart disease in the modern era: recent developments and current challenges. Rev Soc Bras Med Trop 2019;52:e20180041.
34. Atalay S, Tutar E, Uçar T, Topçu S, Köse SK, Doğan MT. Echocardiographic screening for rheumatic heart disease in Turkish schoolchildren. Cardiol Young. 2019;29(10):1272-7.