Cardiology in the Young

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An 8-year single-centre experience of patients with subclinical rheumatic carditis

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Abstract

Objective: Transthoracic echocardiography is the gold standard method for screening and confirmation of acute rheumatic fever and subclinical rheumatic heart disease. Secondary antibiotic prophylaxis that is regularly employed in subclinical rheumatic heart disease may help to reverse mild rheumatic carditis lesions, delay the progression of the disease, reduce morbidity and mortality, and improve patients' quality of life. *Materials and Methods:* We retrospectively evaluated the outcomes of 180 patients with subclinical rheumatic heart disease who were followed up for a mean of 4.92 ± 2.0 (3.5–6.5) years. *Results:* Between 1 March 2015 and 31 December 2023, 180 patients diagnosed with subclinical rheumatic heart disease with a mean follow-up of 4.92 ± 2.0 (3.5–6.5) years were included in the study. Of the patients, 50.6% were male, 49.4% were female, mean age at diagnosis was 11.74 ± 3.18 (9.68–13.65) years, and mean follow-up period was 4.92 ± 2.0 (3.5–6.5) years. Further, 87.2 % of the patients had mitral valve regurgitation, 38.3% had aortic valve regurgitation, and 27.2% had both valve (aortic and mitral valve) regurgitation. Moreover, Sydenham chorea was also diagnosed in 7.8% the patients. Of the patients, 90% had mild rheumatic heart disease, 7.8% had moderate rheumatic heart disease, and 2.2% had severe rheumatic heart disease. After the diagnosis of rheumatic heart disease, 76.7% patients received regular and 23.3% irregular secondary benzathine penicillin G prophylaxis. *Conclusion:* We believe that echocardiography demonstrates its efficacy and safety profile in reducing the risk of rheumatic heart disease in patients diagnosed with subclinical rheumatic carditis and complying with regular secondary antibiotic prophylaxis.

Introduction

Rheumatic fever is an autoimmune disease that occurs as a result of group A β-hemolytic streptococcal infection in genetically susceptible individuals,[1] and in which carditis, arthritis, chorea, subcutaneous nodules, and erythema marginatum develop.[2] In 2015, changes were introduced in the Jones criteria in the intermediate- and high-risk population, including clinical and/or subclinical rheumatic heart disease, polyarthritis, monoarthritis, and polyarthralgia in the major criteria.[2,3] Echocardiography examination is currently the main diagnostic tool used to confirm, diagnose, and monitor valvular lesions in the course of rheumatic fever, especially in cases of subclinical rheumatic heart disease. Subclinical rheumatic heart disease is considered to be a condition in which no auscultatory murmur is heard on cardiac examination or recognised by the diagnosing clinician, but where echocardiography reveals mitral or aortic valve pathology. The prevalence of subclinical rheumatic heart disease varies between 0% and 53%.[2–6] The aim of early diagnosis may be considered to stop or reverse the progression of the disease to a more severe form with secondary benzathine penicillin G prophylaxis.[7]

However, recent studies have shown that globalisation, migration, and refugee crises have led to the development of rheumatic heart disease in developed countries, making rheumatic heart disease a global health problem.[8,9] In this study, we aimed to retrospectively evaluate the results of our mild, moderate, and severe rheumatic heart disease patients who presented to our centre for different reasons, who were diagnosed by echocardiography and followed up for a mean of 4.92 years (1–8 years).

Materials and methods

Between 1 March 2015 and 31 December 2023, 180 patients diagnosed with rheumatic heart disease with a mean follow-up of 4.92 ± 2.0 (3.5–6.5 years) years were included in the study. The rate of rheumatic heart disease among all acute rheumatic fever/rheumatic heart disease diagnosed during this period was 55.2% (n = 180) (total 326 patients). These patients were diagnosed according to American Heart Association and World Health Organization. The 8-year follow-up, treatment, and echocardiography of the patients were performed by the same paediatric cardiologist. Patients diagnosed with rheumatic heart disease were asymptomatic

patients who were referred to our paediatric cardiology outpatient clinic for other reasons such as pre-sports evaluation, chest pain, dizziness, Sydenham chorea, and syncope. Patients were evaluated with echocardiography at 6–12-month intervals. The study was conducted in accordance with the Declaration of Helsinki and ratified by the educational planning board of our hospital (approval no. 13.05.2024/09).

Populations at moderate and high risk for acute rheumatic fever: Populations where the incidence of acute rheumatic fever is >2 per 100,000 school-age children (usually 5–14 years) per year, or where the all-age prevalence of rheumatic heart disease is >1 per 1000 population, are moderate- to high-risk populations.[6] Subclinical rheumatic heart disease: Rheumatic valvular heart disease was detected on echocardiography scan in an asymptomatic population. Subclinical rheumatic heart disease refers exclusively to the circumstance in which classic auscultatory findings of valvar dysfunction either are not present or are not recognised by the diagnosing clinician, but echocardiography studies reveal mitral or aortic valvulitis.[2,4,6] Rheumatic mitral regurgitation and aortic regurgitation: Pathologic mitral regurgitation and aortic regurgitation were diagnosed according to the echocardiography criteria developed by The American Society of Echocardiography in 2023.[10] Pathologic mitral regurgitation on colour Doppler echocardiography was considered to be a pathologic mitral regurgitation when regurgitation was demonstrated on at least two different images, systolic jet length was ≥2 cm on at least one image, and peak velocity was >3 m/s. Pathologic aortic regurgitation on colour Doppler echocardiography was considered pathologic aortic regurgitation if aortic regurgitation was demonstrated on at least two different images, diastolic jet length was ≥1 cm on at least one image, and peak velocity was >3 m/s. Chronic mitral valve involvement on echocardiography was evaluated as thickening of the leaflets, fusions and thickening of the chorda tendinea, limited mobility of the leaflets, and calcifications. Patients diagnosed with valvulitis and cardiomegaly on echocardiography were evaluated as moderate carditis and severe carditis in the presence of heart failure, and mild/moderate/severe valve insufficiency was classified according to the severity of the valve insufficiency.[7,10] Benzathine penicillin G 600 thousand U for patients with a body weight <27 kg, 1.2 million U for those with a body weight between 27 and 65 kg, and 2.4 million U for those with a body weight >65 kg were administered by intramuscular injection every 21 days. In all patients, information about secondary prophylaxis was given by the parents and/or the patient. Although the statements of the patients and parents were essential, the written prescription was also checked. Those who complied with this rule were considered to have received regular benzathine penicillin G prophylaxis.

Results

Of the 326 patients we followed for acute rheumatic fever and acute rheumatic heart disease, 180 (55.21%) were evaluated as subclinical rheumatic heart disease. Among patients with rheumatic heart disease, 50.6% were male, 49.4% were female, mean age at diagnosis was 11.74 ± 3.18 years, mean follow-up was 4.92 ± 2.0 years, and 22.2% had a positive history of acute rheumatic fever. Rheumatic heart disease was mild in 90%, moderate in 7.8%, and severe in 2.2% of the patients. The rates of mitral regurgitation and aortic regurgitation were 87.2% and 38.3%, respectively. In addition, mitral regurgitation and aortic regurgitation coexisted in 27.2% patients. Mitral regurgitation regressed in 20.6% of patients, completely resolved in 7.8%, and in aortic regurgitation these rates were 12.8% and 3.4%, respectively. Mitral regurgitation increased in 8.3% patients. In addition, Sydenham chorea was diagnosed in 7.8% of the patients. Further, 23.3% patients were on irregular benzathine penicillin G prophylaxis. Patients with mitral valve stenosis and valve surgery were the patients with severe rheumatic heart disease clinically. Benzathine penicillin G allergy was present in only three female patients, and two of them used irregular secondary antibiotherapy prophylaxis. As allergic reactions, itching and widespread maculopapular rash developed in two patients, and syncope (anaphylaxis?) developed in one. Subsequently, the skin test performed by Pediatric Allergy showed positive penicillin allergy in all three patients. In benzathine penicillin G allergy, patients were started on macrolide group antibiotic prophylaxis (Table 1). The majority of patients with moderate and severe rheumatic heart disease were female, while in mild rheumatic heart disease cases, the number of males was found to be higher ($P = 0.057$). The prevalence of mitral regurgitation was 85.8% in mild rheumatic heart disease and 100% in moderate and severe rheumatic heart disease cases ($P = 0.231$). However, the prevalence of aortic regurgitation was 38.9% in mild rheumatic heart disease, 42.9% in moderate rheumatic heart disease, and aortic regurgitation was absent in severe rheumatic heart disease cases ($P = 0.269$). Heart failure was present in cases with moderate and severe rheumatic heart disease, and among three patients who underwent surgical intervention and mitral stenosis, all had severe rheumatic heart disease. It was observed that patients with increased mitral regurgitation significantly had irregular secondary antibiotic prophylaxis ($P < 0.001$) (Table 2).

Of the patients, 130 with mild rheumatic heart disease ($n = 130$) were found to have regular while 32 patients had irregular benzathine penicillin G prophylaxis. In moderate rheumatic heart disease, this ratio was seven patients each, and in severe rheumatic heart disease, three out of four patients were found to have irregular benzathine penicillin G prophylaxis. It was observed that patients with decreased mitral regurgitation significantly adhered to regular benzathine penicillin G prophylaxis ($P = 0.043$). Men showed a significant adherence to regular benzathine penicillin G prophylaxis ($P = 0.004$). Although not statistically significant, patients with Sydenham chorea tended to have a higher rate of adherence to regular benzathine penicillin G prophylaxis. Additionally, although not statistically significant, adherence to secondary prophylaxis was found to be lower in patients with a follow-up period of more than 5 years (Table 3).

Statistical evaluation

After encoding the data obtained from the study, they were transferred to the computer and analysed using the SPSS (Version 22 for Windows, SPSS Inc., Chicago, IL, USA) package programme. Continuous variables were expressed as mean ± standard deviation (1.quartile–3. quartile). Frequency data were expressed as numbers and percentages (%). For comparison of frequency data, the Pearson chi-square test or Fisher's exact test was used. A significance level of $p < 0.05$ was considered for all tests.

Discussion

In this study, we observed a decrease, improvement, or delay in the progression of rheumatic aortic regurgitation and mitral regurgitation in rheumatic heart disease patients who regularly underwent benzathine penicillin G prophylaxis. Conversely, we

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Table 1. Demographic characteristics of patients diagnosed with subclinical rheumatic carditis

Variables				
Age at diagnosis (years); mean ± ss(Q1–Q3)				11.74 ± 3.18 (9.68–13.65)
Follow-up duration (years); mean ± ss (Q1–Q3)				4.92 ± 2.00 (3.5–6.5)
Follow-up duration	Above 5 years			102 (56.7%)
	Below 5 years			78 (43.3%)
Gender		Male		91 (50.6%)
		Female		89 (49.4%)
Family history		Absent		140 (81,9%)
		Present		40 (22.2%)
Mitral regurgitation				157 (87.2%)
Aortic regurgitation				69 (38.3%)
Mitral and aortic regurgitation				49 (27.2%)
Decrease in mitral regurgitation				37 (20.6%)
Resolution of mitral regurgitation				14 (%7.8)
Increase in mitral regurgitation				15 (8.3%)
Decrease in aortic regurgitation				23 (12.8%)
Resolution of aortic regurgitation				6 (3.4%)
Mild degree of subclinical carditis				162 (90.0%)
Moderate degree of subclinical carditis				14 (7.8%)
Severe degree of subclinical carditis				4 (2.2%)
Sydenham chorea				14 (7.8%)
Benzathine penicillin G allergy positivity				3 (1.7%)
Seconder antibiotic prophylaxis			Regular	138 (76.7%)
			Irregular	42 (23.3%)

found a significant increase in valve insufficiencies in those who underwent benzathine penicillin G prophylaxis irregularly. It is known that without regular benzathine penicillin G prophylaxis application to rheumatic heart disease patients, deterioration in carditis may occur over time.[11–13] The purpose of early diagnosis can be considered to halt or regress the disease to a less severe form with secondary benzathine penicillin G prophylaxis. The main cause of morbidity and mortality resulting from acute rheumatic fever is recurrent acute rheumatic fever attacks and rheumatic heart disease with its associated complications (heart failure, arrhythmia, stroke, thromboembolic events, death).[11,12]

Although some studies suggest that rheumatic heart disease lesions may persist or worsen despite secondary antibiotic prophylaxis, the existing data are insufficient and of low quality, so reliable conclusions about the prognosis of rheumatic heart disease cannot be made. Until better studies are conducted, we don't have good evidence, but also we have to make evidence-based decisions. These decisions will have important practical implications, such as the use of echocardiography during the acute phase and follow-up, and the duration of secondary prophylaxis for acute rheumatic fever (ARF) diagnosis and rheumatic heart disease patients.[13] While reliable conclusions about the prognosis of rheumatic heart disease were not provided in some retrospective studies, we believe that the long-term follow-up of patients in our study by the same paediatric cardiologist for an average of 4.92 years (1–8 years) enhances the quality and reliability of the study. Meanwhile, the fact that some of our rheumatic heart disease patients with increased valve insufficiencies (although the number of cases is small) were in the group that applied irregular secondary antibiotic prophylaxis highlights the importance of antibiotic prophylaxis. Some rheumatic heart disease progressions can be prevented with regular benzathine penicillin G prophylaxis.[12,14] The prevalence of rheumatic heart disease in the population is five to ten times higher than clinical rheumatic heart disease.[15,16]

Incomplete adherence to secondary prevention measures increases the risk of recurrent acute rheumatic fever and worsening of rheumatic heart disease after each acute rheumatic fever recurrence. Optimising adherence and ensuring safe and adequate drug supply are key to the success of secondary prevention, and a distribution model involving special services, case management, and family support can enhance adherence to secondary prevention in the acute rheumatic fever/ rheumatic heart disease population.[17–19] In fact, penicillin has been the cornerstone of acute rheumatic fever treatment for decades, and there is no other proven treatment that alters the likelihood or severity of rheumatic heart disease after an acute rheumatic fever attack.[19]

Approximately 55% (180/326) of our acute rheumatic fever/ rheumatic heart disease patients, who were followed up for an average of 4.92 years, were diagnosed with rheumatic heart disease. The patients diagnosed with rheumatic heart disease were typically referred to our clinic with other complaints (pre-sports assessment, chest pain, Syn. chorea, dizziness, syncope, etc.) and were

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Table 2. Characteristics of patients diagnosed with subclinical rheumatic carditis

		Mild subclinical carditis (n = 162)	Moderate subclinical carditis (n = 14)	Severe subclinical carditis (n = 4)	P value
Gender	Male (n = 91)	86 (53.1%)	5 (35.7%)	0 (0.0%)	0.057*
	Female (n = 89)	76 (46.9%)	9 (64.3)	4 (100.0%)	
Family history (n = 40)		33 (20.4%)	4 (28.6%)	3 (75.0%)	0.029*
Mitral regurgitation (n = 157)		139 (85.8%)	14 (100.0%)	4 (100.0%)	0.231*
Decrease in mitral regurgitation (n = 37)		31 (22.3%)	6 (42.9%)	0 (0.0%)	0.119*
Resolution of mitral regurgitation (n = 14)		13 (9.4%)	1 (7.1%)	0 (0.0%)	1.00*
Increase in mitral regurgitation (n = 15)		8 (5.6%)	5 (35.7%)	2 (50.0%)	< 0.001*
Aortic regurgitation (n = 69)		63 (38.9%)	6 (42.9%)	0 (0.0%)	0.269*
Decrease in aortic regurgitation (n = 23)		22 (30.6)	1 (16.7)	–	0.664**
Resolution of AR (n = 6)		6 (8.2%)	0 (0.0%)	–	1.00**
Aortic and mitral regurgitation (n = 49)		43 (26.5%)	6 (42.9%)	0 (0.0%)	0.196*
Sydenham chorea (n = 14)		12 (7.4%)	2 (14.3%)	0 (0.0%)	0.550*
Mitral stenosis (n = 3)		0 (0.0%)	0 (0.0%)	3 (75.0%)	< 0.001*
Congestive heart failure (n = 8)		0 (0.0%)	4 (44.4%)	4 (100.0%)	< 0.001*
Valve replacement/repair/valvuloplasty (n = 3)		0 (0.0%)	0 (0.0%)	3 (75.0%)	< 0.001*
Benzathine penicillin G prophylaxis incompatibility (n = 40)		32 (19.8%)	7 (50.0%)	3 (75.0%)	0.002*

AR = aortic regurgitation; SBPGP = secondary benzathine penicillin G prophylaxis; MR = mitral regurgitation; *Pearson chi-square, **Fisher's exact test.

Table 3. Compliance with secondary antibiotic prophylaxis

		Regular benzathine penicillin G prophylaxis (n = 138)	Irregular benzathine penicillin G prophylaxis (n = 42)	P value
Mild degree subclinical carditis (n = 162)		130 (94.2%)	32 (76.2%)	0.002*
Moderate degree subclinical carditis (n = 14)		7 (5.1%)	7 (16.7%)	
Severe degree subclinical carditis (n = 4)		1 (0.7%)	3 (7.1%)	
Mitral regurgitation (n = 157)		116 (87.9%)	41(97.6%)	0.076**
Increase in mitral regurgitation (n = 15)		2 (1.4%)	13 (31.0%)	< 0.001**
Decrease in mitral regurgitation (n = 37)		33 (23.9%)	4 (9.5%)	0.043*
Resolution of mitral regurgitation (n = 14)		11 (8.0%)	3 (7.1%)	1.00**
Mitral stenosis (n = 3)		1 (0.7%)	2 (4.8%)	0.136**
Aortic regurgitation (n = 69)		57 (41.3%)	12 (28.6%)	0.137*
Decrease in aortic regurgitation (n = 23)		21 (15.2%)	2 (4.8%)	0.076*
Resolution of aortic regurgitation (n = 6)		5 (3.6%)	1 (2.4%)	1.00**
Gender	Male (n = 91)	78 (56.5%)	13 (31.0%)	0.004*
	Female (n = 89)	60 (43.5%)	29 (69.0%)	
Sydenham chorea (n = 14)		13 (9.4%)	1 (2.4%)	0.194**
Follow-up duration(n = 180)	Above 5 years	73 (40.1%)	29 (16.1%)	0.064*
	Below 5 years	65 (36.1%)	13 (7.2%)	
Family history positive acute rheumatic fever	Yes	25 (18.1%)	15 (35.7%)	0.016*
	No	113 (81.9%)	27 (64.3%)	

*Pearson chi-square, **Fisher's exact test.

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asymptomatic. Results from studies conducted over the past 20 years, using echocardiography effectively in the diagnosis of acute rheumatic fever, have reported rheumatic heart disease rates up to 53%. Despite the absence of auscultation findings in most studies related to rheumatic heart disease, echocardiography has demonstrated mitral or aortic valve insufficiency in acute rheumatic fever patients.[3,6,7,10,20] The high rate of rheumatic heart disease in our study suggests that the effectiveness and reliability of echocardiography in diagnosing rheumatic heart disease are higher than clinical examination. Both the World Health Organization and the World Heart Federation support rheumatic heart disease screening for rheumatic heart disease in moderate- and high-risk areas.[21–23]

Recent studies have strongly supported the use of portable echocardiography for rheumatic heart disease screening in developing countries. The detection rate of rheumatic heart disease patients by echocardiography has been shown to be 10 times higher compared to auscultation.[15] In some school screenings, this rate was found to be 2.3%, and in some studies using echocardiography for screening, the prevalence was detected to be 2.3 per 1000.[25–28] Optimising case detection in this way maximises the chance of preventing advanced rheumatic heart disease.[29] Adding echocardiography to rheumatic heart disease screening protocols leads to a much higher estimated prevalence, which is 10 times higher than that detected by clinical screening alone. However, in many echocardiographic screening studies, rheumatic heart disease prevalence has been found to range from 8 to 57 per 1000 children. Globally, it is estimated that there could be rheumatic heart disease in 62–78 million individuals, resulting in nearly 1.4 million deaths annually.[30] When the child population rates of the 27 European Union member states were examined, it was found that while the child population rate was 18.1% on average in the European Union in 2022, it was higher in Turkey at 26.5%. According to the Address-Based Population Registration System, as of the end of 2022, there were 22,578,378 children aged 0–17 in Turkey. Among these children, 16,911,205 (74.9%) are aged between 5 and 17.[30] Although there are many differences between countries (such as socio-economic status, genetic predisposition, possible pathogenicity of group A β-haemolytic streptococcal), when we adapt the rheumatic heart disease prevalence found in echocardiographic screening studies in medium- and high-risk countries like ours to Turkey, it is between 135,000 and 963,000 in the 5–17 age group. However, we think that more screening programmes and special studies should be conducted to investigate the incidence of rheumatic heart disease in Turkey.

In clinical practice, the use of echocardiography and Doppler technology has increased the detection rate of rheumatic heart disease, allowing for early diagnosis and intervention even in asymptomatic, latent rheumatic heart disease cases. This has contributed to the reduction of morbidity and mortality associated with rheumatic heart disease.[6]

Recent technological advancements in echocardiography and other diagnostic methods, along with the development of new and modified diagnostic criteria, have achieved significant progress in the diagnosis and monitoring of rheumatic heart disease. The use of echocardiography in rheumatic heart disease and acute phases of rheumatic carditis has proven beneficial, surpassing clinical examination alone. This is because the rate of detecting carditis on echocardiography is higher, even in cases of acute rheumatic fever without clinical symptoms.[11,12]

Although 7.8% of our patients had moderate rheumatic heart disease, these patients lacked symptoms and auscultatory findings. In studies reporting rheumatic heart disease, despite the absence of auscultatory findings, echocardiography has shown mitral regurgitation and aortic regurgitation in acute rheumatic fever patients.[10,20] Sydenham chorea is a hyperkinetic disorder characterised by irregular, jerky movements affecting the face, extremities, and trunk, associated with emotional variability and hypotonia. Sydenham chorea is a widely recognised post-streptococcal autoimmune disorder of the central nervous system.[32] Studies have reported the co-occurrence of rheumatic carditis with Sydenham chorea to range between 60% and 87.8% (34–36.)

Our patients had a clinical presentation of Sydenham chorea in 7.8% of cases, with no auscultatory findings or murmurs detected during cardiac examination. However, all patients referred due to Sydenham chorea were found to have subclinical rheumatic heart disease on echocardiography. The incidence of acute rheumatic fever varies greatly depending on socio-economic development, remaining a public health issue in low- and middle-income countries. The adherence to secondary antibiotic prophylaxis was found to be higher in patients with Sydenham chorea. This could be attributed to the physical and psychological impact of Sydenham chorea, which may affect patients more significantly than other clinical manifestations.

Preventing recurrent Group A streptococcal pharyngitis attacks is the most effective method to prevent the development of serious rheumatic heart disease. In populations where the incidence of rheumatic fever is particularly high, it is recommended to administer benzathine penicillin G every 3 weeks, as serum drug levels can fall below a protective level before the fourth week following the administration of this penicillin dose (Class I, Level of Evidence A).[36] In our patients, the frequency of irregular secondary benzathine penicillin G prophylaxis was 22.2%, and it was found that mitral valve insufficiency increased in these patients. Possible reasons for irregular secondary benzathine penicillin G prophylaxis in acute rheumatic fever include difficulties in accessing healthcare centres, painful intramuscular administration, lack of awareness about the importance of prophylaxis, freezing of the preparation in the syringe, concerns about allergic reactions to the medication, and the long duration of secondary penicillin prophylaxis.

Secondary prevention is a strategy aimed at preventing the recurrence of acute rheumatic fever and the progression of rheumatic heart disease to a severe form by continuing antibiotics in individuals who have previously experienced acute rheumatic fever or already have rheumatic heart disease. Regular administration of secondary benzathine penicillin G prophylaxis reduces the rates of streptococcal pharynx/tonsil infections and recurrence of acute rheumatic fever.[37,38] Early detection of acute rheumatic fever and antibiotic use for secondary prevention are essential in combating rheumatic heart disease. However, a treatment strategy involving intramuscular benzathine penicillin G prophylaxis injections every 4 weeks for at least 5–10 years becomes the key determinant of success in preventing acute rheumatic fever and rheumatic heart disease recurrence. Lack of funding, distance to facilities, shortage of medical resources, fear of side effects, painful injections, and lack of awareness about the importance of treatment have been reported as the main reasons for poor adherence to secondary prevention.[17,36]

The early detection of subclinical rheumatic heart disease can contribute to the reversal of mild lesions, delay the progression of the disease, reduce morbidity and mortality, and improve the quality of life for patients. Echocardiography is the gold standard method for screening and confirming latent rheumatic heart

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disease cases. Although there are doubts about the effectiveness of secondary antibiotic prophylaxis in randomised controlled trials,[39] we believe that adherence to secondary antibiotic prophylaxis following the diagnosis of subclinical rheumatic heart disease with echocardiography in children from regions with moderate to high risk for rheumatic heart disease, such as Turkey, demonstrates the effectiveness and safety profile of reducing the risk of rheumatic heart disease. Nevertheless, it is important to confirm these results with large-scale randomised controlled trials.

Further research is needed before implementing population level screening. Secondary benzathine penicillin G prophylaxis alone may not be sufficient to prevent rheumatic heart disease; therefore, there is a need for improvements in health literacy, access to adequate healthcare services, increasing community awareness about the disease through technology and internet tools, improving overcrowded conditions and housing, and addressing socio-economic conditions, along with advancements in group A streptococcus vaccination.

Limitations of the study may include its retrospective nature and the small number of cases.

Author's contributions. A.İ. designed the study. S.O.E., A.İ., and F.E.D. collected and analysed the data. A.İ. wrote the manuscript. All authors read and approved the final manuscript.

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