Indonesian Journal of Global Health Research
Volume 8 Number 5, October 2026
e-ISSN 2715-1972; p-ISSN 2714-9749
http://jurnal.globalhealthsciencegroup.com/index.php/IJGHR

ASSOCIATION BETWEEN ADHERENCE TO SECONDARY PROPHYLAXIS AND THE SEVERITY OF VALVULAR HEART DISEASE IN CHILDREN WITH RHEUMATIC HEART DISEASE

Ressa Hana Natasa Peranginangin[1], Tina Christina Lumban Tobing[1], Fathia Meirina[1], Muhammad Ichwan[2], Rizky Adriansyah[1], Gema Nazri Yanni[1]
[1]Department of Pediatrics, Faculty of Medicine, Universitas Sumatera Utara, Jl. Dr. Mansyur No.5, Padang Bulan, Medan Baru, Medan, Sumatera Utara 20155, Indonesia
[2]Department of Pharmacology and Therapeutics, Faculty of Medicine, Universitas Sumatera Utara, Jl. Dr. Mansyur No.5, Padang Bulan, Medan Baru, Medan, Sumatera Utara 20155, Indonesia
*ressahana@students.usu.ac.id

ABSTRACT
Rheumatic heart disease (RHD) is a complication of acute rheumatic fever that can cause progressive damage to the heart valves. Secondary prophylaxis is given to prevent recurrence of rheumatic fever and slow the progression of valve damage. However, the relationship between adherence to secondary prophylaxis and heart valve disease in children with RHD remains unclear. To determine the relationship between adherence to secondary prophylaxis medication use and the severity of heart valve disease in children with RHD. This study used a retrospective cohort design conducted at Haji Adam Malik General Hospital, Medan. Subjects were pediatric patients aged <18 years with a diagnosis of RHD who visited the Pediatric Heart Clinic between June and December 2025, had undergone routine secondary prophylaxis therapy for at least one year, and had complete echocardiographic data. Patients with congenital heart defects or other heart diseases were excluded. Data were obtained from patient registries and medical records, including age, gender, age at diagnosis, initial echocardiography results, adherence to secondary prophylaxis medication, and the severity of valve abnormalities after one year of follow-up. Data were analyzed using statistical software using univariate and bivariate analyses with a significance level of $p<0.05$. The most common valve lesion was severe mitral regurgitation (57,4%), and the mitral valve was the most frequently involved valve in children with RHD. Adherence to secondary prophylaxis was quite good, with 61.7% of patients compliant and 38.3% non-compliant. The analysis showed that adherence to secondary prophylaxis medication was not significantly associated with changes in heart valve severity during one year of follow-up ($p>0.05$). Adherence to secondary prophylaxis did not significantly correlate with changes in heart valve severity in children with RHD, although most patients maintained stable valve conditions throughout the follow-up period.

Keywords: adherence; children; heart valve severity; rheumatic heart disease; secondary prophylaxis

How to cite (in APA style)
Peranginangin, R. H., Tobing, T. C. L., Meirina, F., Ichwan, M., Adriansyah, R., & Yani, G. N. (2026). Association between Adherence to Secondary Prophylaxis and the Severity of Valvular Heart Disease in Children with Rheumatic Heart Disease. *Indonesian Journal of Global Health Research*, *8*(5), 835–844. https://doi.org/10.37287/ijghr.v8i5.2428.

INTRODUCTION

Rheumatic heart disease (RHD) is a long-term complication of acute rheumatic fever following pharyngeal infection with group A β-hemolytic Streptococcus and remains an important cause of morbidity and mortality among children (Liang et al., 2023; Ajeng et al., 2023). In Asia, approximately 1% of school-aged children show evidence of RHD, while the global incidence among children aged 5–14 years is estimated at 300,000–350,000 cases annually (Kazahura et al., 2021). The World Health Organization (WHO) has reported that approximately 18.1 million people are living with serious diseases caused by group A streptococcal infection, with approximately 347,000 deaths attributable to RHD each year (Peters et al., 2020; Mutagaywa et al., 2020). In Indonesia, the prevalence of RHD ranges from 0.3 to 0.8 per 1,000 children aged 5–15 years, while 72 pediatric cases were recorded at H. Adam Malik General Hospital in 2017 (Marpaung et al., 2021).

The primary manifestation of RHD is progressive valvular damage caused by recurrent inflammation. Valvular lesions may progress to severe regurgitation or stenosis, resulting in heart failure, pulmonary hypertension, arrhythmias, infective endocarditis, stroke, and death. Therefore, the severity of valvular involvement is an important determinant of prognosis, quality of life, the need for surgery, and mortality (Okello et al., 2013; Arafuri et al., 2022). Secondary prophylaxis with intramuscular benzathine penicillin G administered every 3–4 weeks, or an alternative antibiotic when indicated, is the primary strategy for preventing recurrent rheumatic fever (Liaw et al., 2022). The WHO and the World Heart Federation recommend long-term secondary prophylaxis because adequate treatment can reduce recurrent streptococcal infections, rheumatic fever recurrences, and the progression of valvular damage (Lilyasari et al., 2020).

The effectiveness of secondary prophylaxis largely depends on patient adherence. However, adherence may be affected by limited access to healthcare services, transportation costs, injection-related pain, inadequate family knowledge, and socioeconomic conditions. Adherence rates of approximately 50% in Bangladesh, 80.6% in Ethiopia, and approximately 90% in India and several other countries have been reported (Ilanchoorian et al., 2023; Alkan et al., 2022). Good adherence has been associated with reduced recurrence of rheumatic fever, progression of valvular lesions, heart failure, and the need for surgical intervention (Ilanchoorian et al., 2023; Alkan et al., 2022; Dass et al., 2024). Nevertheless, pediatric studies in Indonesia remain limited and generally have not evaluated structural valvular changes using echocardiography (Kumar et al., 2020). Therefore, this study aimed to analyze the association between adherence to secondary prophylaxis and the severity of valvular heart disease in children with RHD.

METHOD

Study Design and Setting

This retrospective cohort study used data from medical records and the RHD patient registry at the Pediatric Cardiology Outpatient Clinic of H. Adam Malik General Hospital, Medan, Indonesia. Data were obtained from patients who attended the clinic between June and December 2025.

Study Participants

The study population comprised 47 children younger than 18 years who had been diagnosed with RHD. Participants were selected using purposive sampling. The inclusion criteria were a diagnosis of RHD, receipt of secondary prophylaxis for at least one year, and complete baseline and one-year follow-up echocardiographic data. Patients who had recently been diagnosed, had congenital heart disease, or had another form of heart disease were excluded.

Variables and Operational Definitions

The collected data included sex, age, age at diagnosis, adherence to secondary prophylaxis, and the severity of mitral regurgitation, mitral stenosis, aortic regurgitation, pulmonary regurgitation, and tricuspid regurgitation. Adherence was assessed according to the proportion of prescribed doses received during the previous 12 months. Good adherence was defined as receiving more than 80% of the prescribed doses, whereas poor adherence was defined as receiving 80% or fewer. Valvular abnormalities were classified as absent, mild, moderate, or severe according to the echocardiographic reports. Changes after one year were categorized as improvement, no change, or worsening.

Statistical Analysis

Data were analyzed using statistical software. Categorical data are presented as frequencies and percentages, whereas numerical data are presented as means ± standard deviations or medians with minimum–maximum values, according to data distribution. Differences in the distribution of valvular severity between the baseline and follow-up examinations were analyzed using the marginal homogeneity test. Associations between patient characteristics, adherence, and changes in

valvular severity were analyzed using Fisher's exact test, one-way analysis of variance, or the Kruskal–Wallis test, as appropriate. A p-value <0.05 was considered statistically significant.

Ethical Approval

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara, under approval number: NO: 1422/KEPK/USU/2025

RESULT

A total of 47 children met the study eligibility criteria. Of these, 26 participants (55.3%) were male. The median age at the time of the study was 13.50 years, ranging from 7.92 to 17.92 years, while the median age at diagnosis was 13.58 years, ranging from 7.92 to 17.92 years. A total of 29 patients (61.7%) were classified as adherent to secondary prophylaxis (Table 1).

Table 1.
Characteristics of the study participants (n = 47)

Characteristic	n = 47
Sex, f (%)	
Male	26 (55,3)
Female	21 (44,7)
Age, years	
Median (Min – Max)	13,5 (7,92-17,92)
Age at diagnosis, years	
Median (Min – Max)	13,58 (7,92-17,92)
Adherence to secondary prophylaxis, n (%)	
Adherent	29 (61,7)
Nonadherent	18 (38,3)

Table 2.
Distribution of valvular lesion severity at baseline and after one year

Type of valvular lesion	Baseline examination	Follow-up examination	p-value*
Mitral regurgitation, n (%)			0.724
Absent	2 (4.3)	1 (2.1)	
Mild	3 (6.4)	8 (17.0)	
Moderate	20 (42.6)	11 (23.4)	
Severe	22 (46.8)	27 (57.4)	
Mitral stenosis, n (%)			0.343
Absent	41 (87.2)	38 (80.9)	
Mild	4 (8.5)	6 (12.8)	
Moderate	1 (2.1)	0 (0.0)	
Severe	1 (2.1)	3 (6.4)	
Aortic regurgitation, n (%)			0.866
Absent	23 (48.9)	21 (44.7)	
Mild	7 (14.9)	10 (21.3)	
Moderate	8 (17.0)	7 (14.9)	
Severe	9 (19.1)	9 (19.1)	
Pulmonary regurgitation, n (%)			0.414
Absent	39 (83.0)	41 (87.2)	
Mild	6 (12.8)	5 (10.6)	
Moderate	1 (2.1)	1 (2.1)	
Severe	1 (2.1)	0 (0.0)	
Tricuspid regurgitation, n (%)			0.655
Absent	20 (42.6)	23 (48.9)	
Mild	16 (34.0)	12 (25.5)	
Moderate	6 (12.8)	8 (17.0)	
Severe	5 (10.6)	4 (8.5)	

*Marginal homogeneity test.

At the follow-up examination, mitral regurgitation was the most common valvular abnormality, with 27 patients (57.4%) having severe mitral regurgitation. The distributions of severity at baseline and follow-up did not differ significantly for mitral regurgitation (p = 0.724), mitral stenosis (p =

0.343), aortic regurgitation (p = 0.866), pulmonary regurgitation (p = 0.414), or tricuspid regurgitation (p = 0.655) (Table 2). Most valvular lesions remained unchanged during follow-up. The highest proportion of stable lesions was observed in mitral stenosis (83.0%), followed by pulmonary regurgitation (78.7%). Adherence to secondary prophylaxis was significantly associated with changes in mitral regurgitation (p = 0.014), but not with changes in mitral stenosis, aortic regurgitation, pulmonary regurgitation, or tricuspid regurgitation. Among adherent patients, 9 of 29 patients (31.0%) experienced improvement in mitral regurgitation, whereas no improvement was observed among nonadherent patients (Table 3).

Table 3.
Changes in valvular lesion severity during the one-year follow-up

Change in valvular severity	n = 47
Mitral regurgitation, f (%)	
Improvement	9 (19.1)
No change	30 (63.8)
Worsening	8 (17.0)
Mitral stenosis, f (%)	
Improvement	3 (6.4)
No change	39 (83.0)
Worsening	5 (10.6)
Aortic regurgitation, f (%)	
Improvement	7 (14.9)
No change	32 (68.1)
Worsening	8 (17.0)
Pulmonary regurgitation, f (%)	
Improvement	6 (12.8)
No change	37 (78.7)
Worsening	4 (8.5)
Tricuspid regurgitation, f (%)	
Improvement	9 (19.1)
No change	30 (63.8)
Worsening	8 (17.0)

Age and age at diagnosis were significantly associated with changes in mitral regurgitation, with p-values of 0.049 and 0.023, respectively, and with changes in mitral stenosis, with p-values of 0.047 and 0.016, respectively. Patients who experienced worsening mitral regurgitation were younger than those whose condition remained stable or improved. Sex was not significantly associated with changes in any of the valvular lesions analyzed (Table 4).

Table 4.
Associations of patient characteristics and adherence to secondary prophylaxis with changes in the severity of mitral regurgitation

Variable	Worsening	No change	Improvement	p-value
Sex, n (%)				0.450[a]
Male	3 (11.5)	18 (69.2)	5 (19.2)	
Female	5 (23.8)	12 (57.1)	4 (19.0)	
Age, years	11.55 ± 1.94	13.53 ± 2.39	13.99 ± 1.37	0.049[b]
Age at diagnosis, years	9 (8–12)	11.91 ± 2.37	12.34 ± 1.82	0.023[c]
Adherence to secondary prophylaxis, n (%)				0.014[a]
Nonadherent	3 (16.7)	15 (83.3)	0 (0.0)	
Adherent	5 (17.2)	15 (51.7)	9 (31.0)	

[a]Fisher's exact test; [b]one-way analysis of variance; [c]Kruskal–Wallis test. Data are presented as n (%), mean ± standard deviation, or median (range).

Table 5 shows that age and age at diagnosis were significantly associated with changes in the severity of mitral stenosis, with p-values of 0.047 and 0.016, respectively. Patients who experienced improvement had a higher mean age of 16.39 ± 1.38 years and a higher mean age at diagnosis of 15.20 ± 1.63 years than those whose condition worsened or remained unchanged. Sex and adherence to secondary prophylaxis were not significantly associated with changes in mitral stenosis, with p-values of 0.062 and 1.000, respectively.

Table 5.
Associations of patient characteristics and adherence to secondary prophylaxis with changes in the severity of mitral stenosis

Variable	Worsening	Fixed	Improvement	p-value
Sex, f (%)				0,062[a]
Male	5 (19,2)	20 (76,9)	1 (3,8)	
Female	0 (0,0)	19 (90,5)	2 (9,5)	
Age, years	13,02 ± 2,90	13,08 ± 2,11	16,39 ± 1,38	0,047[b]
Age at diagnosis, years	11,77 ± 2,65	11,34 ± 2,10	15,20 ± 1,63	0,016[b]
Prophylaxis adherence, n (%)				1,000[a]
Non-adherent	2 (11,1)	15 (83,3)	1 (5,6)	
Adherent	3 (10,3)	24 (82,8)	2 (6,9)	

[a]Fisher's exact test; [b]one-way analysis of variance. Data are presented as n (%) or mean ± standard deviation.

Table 6 shows that Sex, age, age at diagnosis, and adherence to secondary prophylaxis were not significantly associated with changes in the severity of aortic regurgitation, with all p-values >0.05. Nevertheless, the proportion of patients who experienced worsening was numerically lower among adherent than nonadherent patients, at 10.3% and 27.8%, respectively. The adherent group also had a higher proportion of improvement than the nonadherent group, at 17.2% and 11.1%, respectively, although the differences were not statistically significant.

Table 6.
Associations of patient characteristics and adherence to secondary prophylaxis with changes in the severity of aortic regurgitation

Variable	Worsening	No change	Improvement	p-value
Sex, n (%)				0.678[a]
Male	4 (15.4)	17 (65.4)	5 (19.2)	
Female	4 (19.0)	15 (71.4)	2 (9.5)	
Age, years	13.01 ± 2.80	13.22 ± 2.40	13.57 ± 0.80	0.934[b]
Age at diagnosis, years	11.24 ± 2.50	11.73 ± 2.46	11.62 ± 1.24	0.867[b]
Adherence to secondary prophylaxis, n (%)				0.321[a]
Nonadherent	5 (27.8)	11 (61.1)	2 (11.1)	
Adherent	3 (10.3)	21 (72.4)	5 (17.2)	

[a]Fisher's exact test; [b]one-way analysis of variance. Data are presented as n (%) or mean ± standard deviation.

Table 7 shows that no significant associations were found between sex, age, age at diagnosis, or adherence to secondary prophylaxis and changes in the severity of pulmonary regurgitation, with all p-values >0.05. Numerically, adherent patients had a lower proportion of worsening than nonadherent patients, at 3.4% and 16.7%, respectively. The proportion of improvement was also higher among adherent patients than among nonadherent patients, at 17.2% and 5.6%, respectively, although the differences were not statistically significant.

Table 7.
Associations of patient characteristics and adherence to secondary prophylaxis with changes in the severity of pulmonary regurgitation

Variable	Worsening	No change	Improvement	p-value
Sex, n (%)				0.877[a]
Male	2 (7.7)	20 (76.9)	4 (15.4)	
Female	2 (9.5)	17 (81.0)	2 (9.5)	
Age, years	14.94 ± 1.48	13.01 ± 2.30	13.89 ± 2.27	0.217[b]
Age at diagnosis, years	12.56 ± 2.34	11.52 ± 2.35	11.74 ± 2.11	0.691[b]
Adherence to secondary prophylaxis, f (%)				0.169[a]
Nonadherent	3 (16.7)	14 (77.8)	1 (5.6)	
Adherent	1 (3.4)	23 (79.3)	5 (17.2)	

[a]Fisher's exact test; [b]one-way analysis of variance. Data are presented as n (%) or mean ± standard deviation.

Table 8 shows that sex, age, age at diagnosis, and adherence to secondary prophylaxis were not significantly associated with changes in the severity of tricuspid regurgitation, with all p-values >0.05. Numerically, the proportion of worsening was lower among adherent than nonadherent patients, at 13.8% and 22.2%, respectively. Conversely, improvement was more frequent among adherent patients than among nonadherent patients, at 24.1% and 11.1%, respectively, although this difference did not reach statistical significance.

Table 8.
Associations of patient characteristics and adherence to secondary prophylaxis with changes in the severity of tricuspid regurgitation

Variable	Worsening	No change	Improvement	p-value
Sex, f (%)				0.834[a]
Male	4 (15.4)	16 (61.5)	6 (23.1)	
Female	4 (19.0)	14 (66.7)	3 (14.3)	
Age, years	12.25 ± 2.76	13.67 ± 1.92	12.91 ± 2.81	0.255[b]
Age at diagnosis, years	9.46 (8–17)	12.02 ± 1.94	11.53 ± 2.72	0.103[c]
Adherence to secondary prophylaxis, f (%)				0.517[a]
Nonadherent	4 (22.2)	12 (66.7)	2 (11.1)	
Adherent	4 (13.8)	18 (62.1)	7 (24.1)	

[a]Fisher's exact test; [b]one-way analysis of variance; [c]Kruskal–Wallis test. Data are presented as n (%), mean ± standard deviation, or median (range).

DISCUSSION

Characteristics of the Study Participants

Most participants were male (55.3%), with a mean age of 13.28 ± 2.27 years. Most patients were adherent to secondary prophylaxis (61.7%), and the severity of most valvular lesions remained unchanged during the one-year follow-up period (Passos et al., 2022). The mean age in this study is consistent with previous reports indicating that RHD is commonly identified among children aged 10–15 years. Repeated exposure to streptococcal infections in this age group may increase the risk of permanent valvular damage (Wirth et al., 2022). Adherence to secondary prophylaxis is essential for preventing reinfection with group A *Streptococcus*, recurrent rheumatic fever, and the progression of valvular damage (Karthikeyan et al., 2023; Dass et al., 2026). Nevertheless, 38.3% of patients in this study were classified as nonadherent. Poor adherence may be influenced by inadequate patient and family knowledge, pain associated with benzathine penicillin G injections, limited access to healthcare services, financial constraints, and insufficient social support (Bimerew et al., 2024; Areri et al., 2024).

Changes in Valvular Lesion Severity

Most valvular lesions remained relatively stable during the one-year follow-up period. No change was observed in 63.8% of patients with mitral regurgitation and tricuspid regurgitation, 83.0% of those with mitral stenosis, and 78.7% of those with pulmonary regurgitation. Approximately 19.1% of patients with mitral regurgitation and tricuspid regurgitation experienced improvement. Such stability or improvement may be related to reduced inflammatory activity, improved hemodynamic status, and the prevention of recurrent streptococcal infections through secondary prophylaxis (Karthikeyan et al., 2023; Bimerew et al., 2024; Ambari et al., 2024). The absence of significant changes in most valvular lesions may also reflect the chronic nature of RHD. Structural valvular changes generally progress slowly and are more likely to be detected over follow-up periods of 3–10 years than during a single year of observation (Watkins et al., 2018).

Mitral Regurgitation

Age, age at diagnosis, and adherence to secondary prophylaxis were significantly associated with changes in the severity of mitral regurgitation. Patients who experienced worsening tended to be younger and had been diagnosed at an earlier age. These findings may reflect an earlier disease onset, more active inflammation, and a longer period of exposure to the disease process. Mitral

valve lesions are the most common valvular abnormalities in RHD and may progressively worsen because of recurrent inflammation, fibrosis, chordal deformity, and structural alterations of the valve leaflets (Zimmerman et al., 2022; Rwebembera et al., 2026; Beaton et al., 2022; Gomes et al., 2022). Improvement in mitral regurgitation was observed only among patients who were adherent to secondary prophylaxis. This finding supports the role of secondary prophylaxis in preventing recurrent rheumatic fever and limiting further valvular damage (Beaton et al., 2022; Gomes et al., 2022).

Mitral Stenosis

Age and age at diagnosis were significantly associated with changes in the severity of mitral stenosis, whereas sex and adherence to secondary prophylaxis were not. Patients who experienced improvement had a higher mean age and were older at diagnosis. Mitral stenosis develops through chronic fibrosis, commissural fusion, and thickening of the subvalvular structures over an extended period. Therefore, disease onset at a younger age may indicate a more aggressive clinical course (Alahmadi et al., 2026). The lack of an association between adherence and changes in mitral stenosis may be attributable to the nature of the lesion, which is more strongly influenced by permanent structural changes than by acute inflammatory activity. In developing countries, rheumatic mitral stenosis may progress more rapidly and can occur during the first decade of life (Bray et al., 2024; Tadele et al., 2013).

Aortic Regurgitation

Sex, age, age at diagnosis, and adherence to secondary prophylaxis were not significantly associated with changes in the severity of aortic regurgitation. Nevertheless, adherent patients had a numerically lower proportion of worsening and a higher proportion of improvement than nonadherent patients. These findings are consistent with the role of secondary prophylaxis in preventing recurrent rheumatic fever and maintaining stable valvular function (Tadele et al., 2013).

Previous studies have shown that complete or partial regression may occur in both mitral and aortic valve lesions following secondary prophylaxis, although improvement is more frequently observed in the mitral valve (Torres et al., 2021). Studies conducted in Pakistan and Brazil have also demonstrated that adherence to secondary prophylaxis is associated with regression or stabilization of valvular lesions, whereas nonadherence is associated with disease recurrence, lesion progression, the development of new valvular lesions, and increased mortality (Haran et al., 2018; Araújo et al., 2012).

Pulmonary Regurgitation

No significant associations were found between patient characteristics or adherence to secondary prophylaxis and changes in the severity of pulmonary regurgitation. Pulmonary valve involvement in RHD is uncommon and generally occurs in conjunction with other valvular lesions. RHD predominantly affects left-sided heart valves, particularly the mitral and aortic valves. Right-sided valvular involvement is usually related to the hemodynamic consequences of left-sided valvular disease (Kumar et al., 2020; Agasthi et al., 2024). Although the differences were not statistically significant, adherent patients had a lower proportion of worsening and a higher proportion of improvement. These findings suggest a possible clinical benefit of prophylaxis in maintaining valvular stability.

Tricuspid Regurgitation

Sex, age, age at diagnosis, and adherence to secondary prophylaxis were not significantly associated with changes in the severity of tricuspid regurgitation. In patients with RHD, tricuspid regurgitation is more commonly secondary to the hemodynamic effects of mitral or aortic valve disease than to primary rheumatic damage of the tricuspid valve. It frequently accompanies chronic rheumatic mitral valve disease and may require simultaneous correction during valvular surgery (García-

Villarreal et al., 2017). Tricuspid regurgitation rarely occurs as an isolated lesion and may initially be asymptomatic. Severe regurgitation may result in right-sided heart failure, characterized by elevated central venous pressure, jugular venous distension, peripheral edema, ascites, and organ dysfunction (Saputri et al., 2024). Numerically, adherent patients had a lower proportion of worsening and a higher proportion of improvement, although the differences were not statistically significant.

CONCLUSION

Most children with RHD maintained stable valvular lesion severity during the one-year follow-up period. Adherence to secondary prophylaxis was significantly associated with changes in mitral regurgitation, with a higher proportion of improvement among adherent patients. However, adherence was not significantly associated with changes in mitral stenosis, aortic regurgitation, pulmonary regurgitation, or tricuspid regurgitation. Strengthening adherence programs and ensuring long-term echocardiographic monitoring remain important, particularly for patients with mitral valve involvement.

REFERENCES

Agasthi, P., Saji, A. M., & Sharma, S. (2024). Pulmonary regurgitation. In StatPearls. StatPearls Publishing.

Ajeng, R. N., Rahman, M. M., Said, A. B., Adenan, A. S. B., Ameenudeen, M., Choo, G. M. G. K., et al. (2023). Determinants of rheumatic heart disease: Findings from qualitative research approach. Paediatrica Indonesiana, 63, 483–491.

Alahmadi, M. H., Haleem, S. M., & Sharma, S. (2026). Mitral stenosis. In StatPearls. StatPearls Publishing.

Alkan, F., Yigit, E., Sapmaz, S. Y., & Coskun, S. (2022). Clinical and psychosocial factors affecting treatment adherence in children with rheumatic heart disease. Cardiology in the Young, 32, 1668–1674.

Ambari, A. M., Radi, B., Dwiputra, B., Arityanti, D., Rikl, T., Inggriani, M. P., et al. (2024). Adherence to penicillin treatment is essential for effective secondary prevention of rheumatic heart disease: A systematic review and meta-analysis. Annals of Medicine and Surgery, 86, 2116–2123.

Araújo, F. D. da R., Goulart, E. M. A., & Meira, Z. M. A. (2012). Prognostic value of clinical and Doppler echocardiographic findings in children and adolescents with significant rheumatic valvular disease. Annals of Pediatric Cardiology, 5, 120–126. https://doi.org/10.4103/0974-2069.99610

Arafuri, N., Murni, I. K., Julia, M., Nugroho, S., & Soehadi, N. (2022). Survival of rheumatic heart disease in Indonesian children. Global Heart, 17, Article 71.

Areri, H. A., Tadele, H., & Workneh, S. (2024). Barriers and facilitators of benzathine penicillin G adherence among rheumatic heart disease patients: A mixed-methods systematic review using the COM-B capability, opportunity, and motivation for behavior model. Systematic Reviews, 13, Article 297.

Beaton, A., Okello, E., Rwebembera, J., Grobler, A., Engelman, D., Alepere, J., et al. (2022). Secondary antibiotic prophylaxis for latent rheumatic heart disease. The New England Journal of Medicine, 386, 230–240.

Bimerew, M., Araya, F. G., & Ayalneh, M. (2024). Adherence to secondary antibiotic prophylaxis among patients with acute rheumatic fever and/or rheumatic heart disease: A systematic review and meta-analysis. BMJ Open, 14, Article e082191.

Bray, J. J., Thompson, S., Seitler, S., Ali, S. A., Yiu, J., Salehi, M., et al. (2024). Long-term antibiotic prophylaxis for prevention of rheumatic fever recurrence and progression to rheumatic heart disease. Cochrane Database of Systematic Reviews, 2024(9), Article CD015779.

Dass, C., & Kanmanthareddy, A. (2024). Rheumatic heart disease. In StatPearls. StatPearls Publishing.

Dass, C., & Kanmanthareddy, A. (2026). Rheumatic heart disease. In StatPearls. StatPearls Publishing.

García-Villarreal, O. A., & Heredia-Delgado, J. A. (2017). Left atrial appendage in rheumatic mitral valve disease: The main source of embolism in atrial fibrillation. Archivos de Cardiología de México, 87, 286–291.

Gomes, N. F. A., Silva, V. R., Levine, R. A., Esteves, W. A. M., de Castro, M. L., Passos, L. S. A., et al. (2022). Progression of mitral regurgitation in rheumatic valve disease: Role of left atrial remodeling. Frontiers in Cardiovascular Medicine, 9, Article 862382.

Haran, S., Crane, N., Kazi, S., Axford-Haines, L., & White, A. (2018). Effect of secondary penicillin prophylaxis on valvular changes in patients with rheumatic heart disease in Far North Queensland. Australian Journal of Rural Health, 26, 119–125.

Ilanchoorian, D., Thakur, J. S., Vijayvergiya, R., Jindal, A. K., Gandhi, A., & Sagar, V. (2023). Treatment adherence and its determinants among rheumatic fever/rheumatic heart disease patients during the COVID-19 pandemic: A cross-sectional study from Chandigarh, India. Journal of Family Medicine and Primary Care, 12, 3254.

Karthikeyan, G., Watkins, D., Bukhman, G., Cunningham, M. W., Haller, J., Masterson, M., et al. (2023). Research priorities for the secondary prevention and management of acute rheumatic fever and rheumatic heart disease: A National Heart, Lung, and Blood Institute workshop report. BMJ Global Health, 8.

Kazahura, P. T., Mushi, T. L., Pallangyo, P., Janabi, M., Kisenge, R., Albaghdadi, M., et al. (2021). Prevalence and risk factors for subclinical rheumatic heart disease among primary school children in Dar es Salaam, Tanzania: A community-based cross-sectional study. BMC Cardiovascular Disorders, 21, Article 610.

Kumar, R. K., Antunes, M. J., Beaton, A., Mirabel, M., Nkomo, V. T., Okello, E., et al. (2020). Contemporary diagnosis and management of rheumatic heart disease: Implications for closing the gap: A scientific statement from the American Heart Association. Circulation, 142, e337–e357.

Liang, Y., Yu, D., Lu, Q., Zheng, Y., & Yang, Y. (2023). The rise and fall of acute rheumatic fever and rheumatic heart disease: A mini review. Frontiers in Cardiovascular Medicine, 10, Article 1183606.

Liaw, J., Gorton, S., Heal, C., & White, A. (2022). Adherence to secondary prevention of rheumatic fever and rheumatic heart disease in young people: An 11-year retrospective study. Australian and New Zealand Journal of Public Health, 46, 758–763.

Lilyasari, O., Prakoso, R., Kurniawati, Y., Roebiono, P. S., Rahajoe, A. U., Sakidjan, I., et al. (2020). Clinical profile and management of rheumatic heart disease in children and young adults at a tertiary cardiac center in Indonesia. Frontiers in Surgery, 7, Article 47.

Marpaung, L. N. S. M., Tobing, T. C. L., & Saragih, R. A. C. (2021). Characteristic quality of life children with rheumatic heart disease. Open Access Macedonian Journal of Medical Sciences, 9, 270–273.

Mutagaywa, R. K., Wind, A. M., Kamuhabwa, A., Cramer, M. J., Chillo, P., & Chamuleau, S. (2020). Rheumatic heart disease anno 2020: Impacts of gender and migration on epidemiology and management. European Journal of Clinical Investigation, 50, Article e13374.

Okello, E., Wanzhu, Z., Musoke, C., Twalib, A., Kakande, B., Lwabi, P., et al. (2013). Cardiovascular complications in newly diagnosed rheumatic heart disease patients at Mulago Hospital, Uganda. Cardiovascular Journal of Africa, 24, 80–85.

Passos, L. S. A., Nizet, V., Levine, R. A., & Aikawa, E. (2022). Can we diagnose acute rheumatic fever early to maximize the success of secondary prophylaxis in rheumatic heart valve disease? Cardiovascular Research, 118, e62–e65.

Peters, F., Karthikeyan, G., Abrams, J., Muhwava, L., & Zühlke, L. (2020). Rheumatic heart disease: Current status of diagnosis and therapy. Cardiovascular Diagnosis and Therapy, 10, 305–315.

Rwebembera, J., Beaton, A., Kado, J., & Kumar, R. K. (2026). Rheumatic heart disease in children and adolescents, part 1: Epidemiology, pathogenesis, and diagnosis. BMJ Paediatrics Open, 10, Article e003435.

Saputri, V. L., & Yogibuana, V. (2024). Isolated rheumatic tricuspid valve regurgitation: It is only rare, not just a myth: A rare case report. The Egyptian Heart Journal, 76, Article 56.

Tadele, H., Mekonnen, W., & Tefera, E. (2013). Rheumatic mitral stenosis in children: A more accelerated course in sub-Saharan patients. BMC Cardiovascular Disorders, 13, Article 95.

Torres, R. P. de A., Torres, R. F. de A., de Crombrugghe, G., Moraes da Silva, S. P., Cordeiro, S. L. V., Bosi, K. A., et al. (2021). Improvement of rheumatic valvular heart disease in patients undergoing prolonged antibiotic prophylaxis. Frontiers in Cardiovascular Medicine, 8, Article 676098.

Watkins, D. A., Beaton, A. Z., Carapetis, J. R., Karthikeyan, G., Mayosi, B. M., Wyber, R., et al. (2018). Rheumatic heart disease worldwide: JACC scientific expert panel. Journal of the American College of Cardiology, 72, 1397–1416.

Wirth, S., Sika-Paotonu, D., Beaton, A., Raghu, A., Steer, A., & Carapetis, J. (2022). Acute rheumatic fever and rheumatic heart disease. In J. J. Ferretti, D. L. Stevens, & V. A. Fischetti (Eds.), Streptococcus pyogenes: Basic biology to clinical manifestations (2nd ed.). University of Oklahoma Health Sciences Center.

Zimmerman, M., Kitooleko, S., Okello, E., Ollberding, N. J., Sinha, P., Mwambu, T., et al. (2022). Clinical outcomes of children with rheumatic heart disease. Heart, 108, 633–638.