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Clinical Profile, Complications, and Factors Associated with Mortality among Children with Rheumatic Mitral Stenosis in a Resource-Limited Setting: A Retrospective Cohort Study

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Abstract

Background

Rheumatic mitral stenosis remains an important cause of morbidity and mortality among children in low-resource settings. In Tigray, Ethiopia, where access to cardiac surgical and catheter-based interventions is limited, children are managed primarily with medical therapy, and the clinical profile and outcomes of the disease remain poorly characterized. This study aimed to assess the clinical characteristics, complications, and factors associated with mortality among pediatric patients with rheumatic mitral stenosis in this setting.

Methods

A retrospective cohort study was conducted using medical records of children younger than 18 years with echocardiographically confirmed rheumatic mitral stenosis diagnosed between April 2019 and April 2024. A total of 98 eligible children were included. Data were collected using a structured data abstraction tool, entered into EpiData version 3.0.0.1, and analyzed using SPSS version 27. Multivariable binary logistic regression was performed to identify factors independently associated with mortality. Statistical significance was defined as a p-value < 0.05.

Results

A total of 98 children with rheumatic mitral stenosis were included, with a mean age at diagnosis of 13.7 ± 3.0 years; the youngest child diagnosed with mitral stenosis was 5 years old. Severe mitral stenosis was present in 60.2% of children at diagnosis. Congestive heart failure was common (84.7%), and a high echocardiographic probability of pulmonary hypertension was documented in 61 of 75 children with available TR velocity measurements (81.3%). Atrial fibrillation and infective endocarditis were each identified in 9.2% of cases. Malnutrition was highly prevalent, with 75.6% of children exhibiting moderate-to-severe thinness and 52.0% having stunting. Sixteen children (16.3%) died during the study period. Factors independently associated with mortality included atrial fibrillation (AOR 10.5, 95% CI: 1.7–63.8; p = 0.011), peripheral edema (AOR 8.0, 95% CI 2.0–32.8; p = 0.004), and infective endocarditis (AOR 7.6, 95% CI 1.2–46.8; p = 0.029).

Conclusions

This study demonstrates that pediatric rheumatic mitral stenosis in a resource-limited setting is characterized by early onset of disease, advanced disease at presentation, and a high burden of malnutrition, complications, and mortality. Atrial fibrillation, peripheral edema, and infective endocarditis were independently associated with mortality. Strengthening early detection, improving adherence to

secondary prophylaxis, integrating nutritional support, and expanding access to timely cardiac intervention are essential to improve outcomes.

1. Background

Rheumatic heart disease (RHD) is a chronic acquired valvular disorder caused by an autoimmune-mediated inflammatory response following group A streptococcal pharyngitis, typically acquired during childhood (1). Despite being almost entirely preventable through timely diagnosis and treatment of streptococcal pharyngitis, RHD remains a major public health challenge in many low- and middle-income countries (2, 3).

Rheumatic mitral stenosis (MS) is a severe manifestation of rheumatic heart disease and remains a major cause of morbidity and mortality among children in low-resource settings following recurrent episodes of acute rheumatic fever (2). Unlike many other valvular lesions that may arise from diverse etiologies, isolated mitral stenosis alone or in combination with other valvular abnormalities is almost exclusively attributable to rheumatic heart disease (4, 5). Progressive leaflet thickening, commissural fusion, and subvalvular fibrosis result in obstruction of left ventricular inflow, leading to elevated left atrial pressure, pulmonary venous congestion, and eventually pulmonary hypertension and right-sided heart failure.

Echocardiography is the cornerstone for the diagnosis and assessment of rheumatic MS. It provides comprehensive evaluation of mitral valve morphology, disease severity, subvalvular involvement, associated valvular lesions, and hemodynamic consequences (6, 7). Two-dimensional planimetry and Doppler-derived pressure half-time are among the commonly used echocardiographic methods for estimating mitral valve area (8). Additional investigations, including electrocardiography, chest radiography, and cardiac catheterization, may provide complementary diagnostic and prognostic information in selected patients (6).

Rheumatic mitral stenosis is associated with several potentially life-threatening complications, including atrial fibrillation, thromboembolic events, pulmonary hypertension, congestive heart failure, and stroke. Mortality is primarily attributable to progressive heart failure, severe pulmonary hypertension, pulmonary edema, systemic thromboembolism, and infective endocarditis (9, 10).

Rheumatic heart disease continues to impose a substantial public health burden worldwide, affecting an estimated 40.2 million people and causing approximately 306,000 deaths annually. The burden is disproportionately concentrated in sub-Saharan Africa, which has the highest regional prevalence among school-aged children. In Ethiopia, RHD remains a major cause of cardiovascular morbidity, with a recent systematic review reporting a pooled prevalence of 3.19% in the general population (2, 11–13).

Mitral stenosis (MS) is one of the most common manifestations of RHD in low- and middle-income countries. However, its reported prevalence varies considerably across Africa because of differences in study populations, diagnostic methods, and the limited availability of epidemiological data. In Ethiopia,

MS has been reported in 7% to 56.4% of patients with RHD, reflecting substantial heterogeneity across study settings (14–16).

Despite the significant burden of disease, current knowledge regarding the clinical course and outcomes of rheumatic MS is largely derived from historical cohorts established before the widespread availability of valve interventions, studies involving adults who declined surgery, or limited reports from resource-constrained settings (9, 10, 17, 18). Consequently, evidence describing the natural history, complications, and factors associated with mortality among children with rheumatic MS remains scarce, particularly in low-income countries.

This knowledge gap is especially relevant in northern Ethiopia, where pediatric cardiac surgical and catheter-based interventions are unavailable. Children with rheumatic MS are predominantly managed with medical therapy. This setting provides an opportunity to characterize the clinical course and outcomes of rheumatic MS among children managed without definitive valve intervention.

Therefore, this study aimed to determine the clinical profile, echocardiographic characteristics, complications, and factors associated with mortality among children with rheumatic mitral stenosis who have follow-up at Ayder Comprehensive Specialized Hospital.

Evidence describing pediatric rheumatic MS in Ethiopia remains limited, particularly regarding mortality and its determinants. Although previous Ethiopian studies have examined the epidemiology and complications of rheumatic heart disease and a few have described mitral stenosis, none have specifically evaluated factors associated with mortality among children with rheumatic MS. Furthermore, to our knowledge, no published study has investigated this condition among pediatric patients with rheumatic MS in the Tigray region (16, 19).

In addition, the study provides locally generated evidence that may support health system planning and advocacy for improving access to specialized pediatric cardiac care. Given the limited availability of cardiac surgery services in Ethiopia, which remain largely concentrated in the capital city, these findings may contribute to efforts aimed at expanding equitable access to advanced cardiac interventions and improving outcomes of children with rheumatic heart disease (20).

2. Methods

2.1 Study design and setting

We conducted a hospital-based retrospective cohort study among children diagnosed with echocardiographically confirmed rheumatic mitral stenosis between April 2019 and April 2024. Participants were followed through available medical records until death, the last documented clinical assessment, or the end of the study observation period.

The study was conducted at Ayder Comprehensive Specialized Hospital (ACSH), a tertiary referral and teaching hospital located in Mekelle, Tigray Regional State, northern Ethiopia, approximately 778 km from Addis Ababa. Since its establishment in 2008, ACSH has provided both referral and non-referral healthcare services to an estimated catchment population of approximately nine million people from the Tigray, Afar, and northeastern Amhara regions, as well as Eritrean refugees. The hospital has approximately 500 inpatient beds and serves as one of Ethiopia's largest tertiary healthcare institutions.

The Department of Pediatrics comprises pediatric emergency, inpatient, and pediatric intensive care units with a total capacity of 95 beds. A therapeutic feeding unit provides nutritional rehabilitation for children younger than five years, while nutritional support for older children is limited and primarily focuses on high-protein dietary supplementation.

The pediatric cardiac unit is staffed by three pediatricians trained in diagnostic echocardiography, four cardiac nurses, and rotating pediatric residents. The unit provides comprehensive inpatient and outpatient cardiac services and serves as the principal pediatric echocardiography center in the Tigray region, receiving referrals from neighboring regions. Diagnostic facilities include one electrocardiography (ECG) machine and two transthoracic echocardiography machines (SonoAce X8 and GE Vivid S5). Definitive cardiac surgical and catheter-based interventions for rheumatic mitral stenosis were not available at the hospital during the study period, and patients were managed medically.

2.2 Study Population

Source population

The source population comprised all pediatric patients with rheumatic heart disease (RHD) who attended the pediatric cardiac clinic for follow-up or were admitted to the pediatric emergency department, pediatric intensive care unit (PICU), or pediatric wards at Ayder Comprehensive Specialized Hospital between April 2019 and April 2024.

Study population

The study population comprised children younger than 18 years with echocardiographically confirmed rheumatic mitral stenosis (MS) who attended the pediatric cardiac clinic or were admitted to the pediatric emergency department, PICU, or pediatric wards during the study period and fulfilled the predefined eligibility criteria.

Study unit

The study unit was the individual eligible child with echocardiographically confirmed rheumatic mitral stenosis, represented by their medical record.

2.3 Cohort entry and eligibility

Medical records of children diagnosed with rheumatic mitral stenosis between April 2019 and April 2024 were reviewed. Children younger than 18 years with echocardiographically confirmed rheumatic mitral stenosis were included, whether they survived or died during the study period. Patients with congenital mitral stenosis or previous surgical or percutaneous intervention for mitral stenosis were excluded.

2.4 Study variables

Dependent variable

- Mortality documented during the study period

Independent variables

- Sociodemographic characteristics: age and sex.
- Clinical characteristics: presenting symptoms, duration of symptoms, New York Heart Association functional class, physical examination findings, and comorbid conditions.
- Nutritional status: wasting and stunting based on World Health Organization (WHO) growth standards.
- Echocardiographic findings: mitral valve area, left atrial size, left ventricular ejection fraction, pulmonary hypertension, and associated valvular lesions.
- Disease-related complications: congestive heart failure, atrial fibrillation, atrial flutter, infective endocarditis, left atrial thrombus, systemic embolism, stroke, and cardiogenic shock.

2.5 Sample size determination and sampling technique

Sample size determination

Pediatric rheumatic mitral stenosis is relatively uncommon; therefore, all eligible cases identified during the study period were included. A total of 209 medical records were screened, of which 93 were patients with RHD without mitral stenosis and were excluded. Among the 116 patients with mitral stenosis, 2 had congenital MS, 10 had incomplete records, and 6 lacked echocardiography reports. Thus, 98 eligible patients were included in the study.

Sampling technique

All children with echocardiographically confirmed rheumatic mitral stenosis who met the predefined inclusion criteria between April 2019 and April 2024 were included. Eligible patients were identified from children with RHD who attended the pediatric cardiac clinic or were admitted to the pediatric emergency department, PICU, or pediatric wards during the study period. All 98 eligible patients were included in the final analysis.

2.6 Data collection procedures

Medical records of eligible children diagnosed between April 2019 and April 2024 were reviewed.. Mortality was ascertained from documented clinical records during this period. Data were extracted using a structured data abstraction tool based on the study objectives and relevant literature. The tool included sociodemographic characteristics, clinical presentation, physical examination findings, anthropometric measurements, laboratory investigations, electrocardiographic findings, echocardiographic parameters, chest radiographic findings, treatment, complications, and clinical outcomes, including mortality.

Electrocardiographic findings were extracted from physicians' documented interpretations. Chest radiographic findings were obtained from official radiology reports.

Data were collected by three pediatric residents and three medical interns after receiving training on study objectives, data abstraction procedures, and confidentiality requirements. The principal investigator supervised the data collection process and reviewed all completed data abstraction forms daily for completeness, consistency, and accuracy before data entry.

2.7 Data quality assurance

Data quality was ensured through several measures. The data abstraction tool was pretested using approximately 5% of medical records outside the study period to assess completeness, clarity, and consistency. Based on the findings of the pretest, minor modifications were made before the commencement of data collection.

All data collectors received standardized training before data collection. Throughout the study period, the principal investigator closely supervised the data collection process, reviewed completed abstraction forms daily for completeness and internal consistency, and provided immediate feedback whenever discrepancies or ambiguities were identified. Regular meetings were also conducted with the data collectors to resolve uncertainties and maintain uniformity in data abstraction.

2.8 Statistical analysis

Data were coded, cleaned, and verified for completeness before entry into EpiData Manager version 3.0.0.1 and subsequently exported to IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY, USA) for analysis.

Descriptive statistics were used to summarize the characteristics of the study population. Continuous variables were summarized using means and standard deviations (SD) or medians and interquartile ranges (IQR), as appropriate, while categorical variables were presented as frequencies and percentages.

Because the primary objective was to identify factors associated with mortality during the defined observation period, binary logistic regression was used as the primary analytical approach. Logistic regression was considered appropriate because the outcome was mortality during the study period

(yes/no), whereas the timing of diagnosis, follow-up, and documentation of clinical factors varied among participants.

Although participants were required to have at least six months of documented follow-up, the exact dates of diagnosis, last clinical assessment, and death were not consistently available for all participants. The interval from diagnosis to death could be reliably established for only 13 of the 16 deceased patients. Therefore, a formal time-to-event analysis was not performed, and mortality was analyzed as a binary outcome.

Associations between categorical variables and mortality were initially assessed using the chi-square test or Fisher's exact test, as appropriate. Bivariable logistic regression was then performed, and variables with a p-value < 0.20 were considered for inclusion in the multivariable logistic regression model. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated to estimate the strength of association. Statistical significance was defined as a two-sided p-value < 0.05.

Multicollinearity among variables included in the multivariable model was assessed using variance inflation factor and tolerance statistics. Model fit was evaluated using the Hosmer–Lemeshow goodness-of-fit test.

Cardiogenic shock was not included as a candidate variable in the mortality regression model because it was considered a terminal or proximal manifestation of severe cardiac decompensation rather than an independent prognostic characteristic. In this cohort, all patients who developed cardiogenic shock subsequently died, further supporting its interpretation as a terminal clinical event rather than an independent factor associated with mortality.

2.9 Operational and standard definitions

Rheumatic mitral stenosis: Obstruction of blood flow from the left atrium to the left ventricle secondary to rheumatic heart disease, confirmed by transthoracic echocardiography. Mitral stenosis severity was classified according to mitral valve area as mild (> 1.5 cm^2), moderate (1.0–1.5 cm^2), and severe (< 1.0 cm^2).

Echocardiographic probability of pulmonary hypertension

The echocardiographic probability of pulmonary hypertension was assessed using peak tricuspid regurgitation velocity (TR Vmax) measured by Doppler echocardiography. A TR Vmax ≤ 2.8 m/s indicated low probability, 2.9–3.4 m/s indicated intermediate probability, and > 3.4 m/s indicated high probability of pulmonary hypertension.

Cardiomegaly

Cardiomegaly was defined based on the documented radiological interpretation of an enlarged cardiac silhouette.

Left atrial enlargement: Left atrial systolic dimension above the normal reference range adjusted for body surface area.

Index date

The index date was defined as the date of the first echocardiographically confirmed diagnosis of rheumatic mitral stenosis at ACSH.

Atrial fibrillation: Physician-diagnosed atrial fibrillation confirmed by electrocardiography, characterized by an irregularly irregular rhythm without identifiable P waves.

Complications of rheumatic mitral stenosis: Clinical complications attributable to rheumatic mitral stenosis, including congestive heart failure, pulmonary hypertension, atrial fibrillation, atrial flutter, left atrial thrombus, systemic embolism, stroke, infective endocarditis, and cardiogenic shock.

Infective endocarditis: Only patients fulfilling the diagnostic criteria for definite infective endocarditis were included.

Cardiogenic shock: Heart failure accompanied by persistent hypotension requiring inotropic or vasopressor support despite appropriate fluid resuscitation, together with clinical evidence of tissue hypoperfusion, including oliguria, cyanosis, cold extremities, altered mental status, or hypotension, and documented physician diagnosis.

Nutritional status

Nutritional status was assessed using BMI-for-age and height-for-age z-scores based on the WHO 2007 Growth Reference for children and adolescents aged 5–19 years. Thinness was classified according to BMI-for-age, while stunting was assessed using height-for-age.

New York Heart Association functional class: Functional status was classified according to the New York Heart Association classification.

Anemia: Hemoglobin concentration below the age- and sex-specific lower reference limits based on World Health Organization recommendations.

Worsening of mitral stenosis: A documented reduction in mitral valve area (MVA) on serial echocardiographic examinations compared with the earliest available echocardiographic measurement.

Incomplete medical record: A medical record lacking essential clinical, anthropometric, or echocardiographic information required for the study..

2.10 Ethical considerations

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board with reference number of MU-IRB 2323/2024

from the College of Health Sciences, Mekelle University, before commencement of the study. Permission to access patient medical records was obtained from Ayder Comprehensive Specialized Hospital.

As this was a retrospective review of existing medical records, the requirement for informed consent was waived by the Institutional Review Board. Patient confidentiality was maintained throughout the study by using anonymized data collection forms, excluding personal identifiers, and restricting access to the collected data to the research team only.

3. Results

3.1 Participant selection

A total of 209 medical records were screened during the study period. Of these, 93 were patients with rheumatic heart disease without mitral stenosis and were excluded. Among the remaining 116 patients with mitral stenosis, 2 had congenital mitral stenosis, 10 had incomplete medical records, and 6 lacked echocardiography reports. The remaining 98 patients met the eligibility criteria and were included in the final analysis. The participant selection process is illustrated in Fig. 1.

3.1 Demographic and clinical characteristics at presentation

A total of 98 children with rheumatic mitral stenosis who met the eligibility criteria were included in the analysis. The mean age at diagnosis was 13.7 ± 3.0 years (range, 5–17 years), with more than four-fifths (86.7%) aged 11–17 years. Males accounted for 55 (56.1%) of the study participants.

Only 20 (20.4%) children had a documented history of acute rheumatic fever. The mean duration of symptoms before diagnosis was 16.7 ± 13.4 months, ranging from a few months to six years.

At presentation, 83 (84.7%) children had congestive heart failure. Among these, 11 (13.3%), 18 (21.7%), and 54 (65.0%) were classified as NYHA II, III, and IV, respectively. Palpitations were the most frequently reported symptom (88.8%), followed by shortness of breath (75 (76.5%)) and cough (66 (67.3%)). Peripheral edema and hepatomegaly were documented in 22 (22.4%) and 53 (54.1%) of patients, respectively.

Hemoglobin measurements were available for 95 children, among whom 43 (45.2%) were anemic. Nutritional assessment demonstrated a substantial burden of malnutrition: 74 (75.6%) children had moderate-to-severe thinness, while 51 (52.0%) had moderate-to-severe stunting at the time of diagnosis.

Chest radiographs were available for 86 patients. Cardiomegaly was the most common radiographic abnormality, observed in 62 (72.1%) patients, followed by pulmonary edema 36 (41.8%) and pleural effusion 23 (26.7%). The baseline demographic and clinical characteristics of the study participants are presented in Table 1.

Table 1
Demographic and clinical characteristics of children with rheumatic mitral stenosis at presentation, Ayder Comprehensive Specialized Hospital, Mekelle, Ethiopia, April 2019–April 2024 (N = 98)

Variable	n (%)
Sex	
Male	55 (56.1)
Female	43 (43.9)
Age group (years)	
5–10	13 (13.3)
11–17	85 (86.7)
History of acute rheumatic fever	20 (20.4)
Duration of symptoms before diagnosis (months)	
0–5	22 (22.4)
6–11	17 (17.3)
12–23	20 (20.4)
≥ 24	39 (39.8)
Symptoms at presentation	
Palpitations	87 (88.8)
Shortness of breath	75 (76.5)
Cough	66 (67.3)
Hemoptysis	26 (26.5)
Physical examination findings	
NYHA functional class, among children with heart failure (n = 83)	
NYHA class II	11 (13.3)
NYHA class III	18 (21.7)
NYHA class IV	54 (65.0)
Hepatomegaly	53 (54.1)
Peripheral edema	22 (22.4)
Pneumonia	14 (14.3)

Variable	n (%)
Sex	
Anemia (n = 95)	43 (45.2)
Nutritional status (BMI-for-age)	
Normal	24 (24.5)
Moderate thiness	27 (27.6)
Severe thinness	47 (48.0)
Height-for-age	
Normal	47 (48.0)
Moderate stunting	26 (26.5)
Severe stunting	25 (25.5)
Chest radiographic findings (n = 86)	
Cardiomegaly	62 (72.1)
Pulmonary edema	36 (41.8)
Pleural effusion	23 (26.7)

3.2 Echocardiographic characteristics

Severe rheumatic mitral stenosis (mitral valve area < 1.0 cm^2) was identified in 59 (60.2%) children at diagnosis, while 25 (25.5%) had moderate stenosis and 14 (14.3%) had mild stenosis. Mitral valve area was assessed by two-dimensional planimetry in all patients, with a mean value of 1.06 ± 0.47 cm^2. Mean transmitral diastolic pressure gradient assessment was available in 50 patients and averaged 18.1 ± 6.1 mmHg. Left ventricular systolic function was preserved in most patients, with 88 (89.8%) having an ejection fraction ≥ 55%; the mean left ventricular ejection fraction was 63.3 ± 8.0% (range, 36–83%).

Left atrial enlargement was present in 88 (89.8%) children, with a mean left atrial diameter of 4.8 ± 0.87 cm (range, 2.8–8.1 cm). Among the 75 patients with available tricuspid regurgitation velocity measurements, 61 (81.3%) had a high echocardiographic probability of pulmonary hypertension (TR Vmax > 3.4 m/s). Tricuspid regurgitation was the most common associated valvular lesion, occurring in 78 (79.5%) patients, followed by mitral regurgitation (48.0%) and aortic regurgitation (38.8%). The echocardiographic characteristics of the study participants are summarized in Table 2.

Table 2
Echocardiographic characteristics of children with rheumatic mitral stenosis at diagnosis, Ayder Comprehensive Specialized Hospital, Mekelle, Ethiopia, April 2019–April 2024 (N = 98)

Variable	n (%)
Associated valvular lesions*	
Isolated mitral stenosis	31 (31.6)
Mitral regurgitation	47 (48.0)
Aortic regurgitation	38 (38.8)
Aortic stenosis	10 (10.2)
Tricuspid stenosis	7 (7.1)
Tricuspid regurgitation	78 (79.5)
Cardiac morphology	
Left atrial enlargement	88 (89.8)
Probability of Pulmonary hypertension (TR Vmax) (n = 75)	
≤ 2.8 m/s (Low probability)	4 (5.3)
2.9–3.4 m/s (Intermediate probability)	10 (13.3)
> 3.4 m/s (High probability)	61 (81.3)
Severity of mitral stenosis (mitral valve area)	
Severe (< 1.0 cm^2)	59 (60.2)
Moderate (1.0–1.5 cm^2)	25 (25.5)
Mild (> 1.5 cm^2)	14 (14.3)
Left ventricular ejection fraction	
< 40%	1 (1.0)
40–54%	9 (9.2)
≥ 55%	88 (89.8)
Mean transmitral diastolic pressure gradient (n = 50)	
< 10 mmHg	4 (8.0)
11–20 mmHg	28 (56.0)

* Patients could have more than one associated valvular lesion; therefore, percentages do not sum to 100%. Abbreviations: MVA = Mitral valve area; MS = Mitral stenosis; AR = Aortic regurgitation; AS = Aortic stenosis; MR = Mitral regurgitation; TS = Tricuspid stenosis; TR = Tricuspid regurgitation; TR Vmax = Maximal tricuspid regurgitation velocity; LA = Left atrium

Variable	n (%)
21–30 mmHg	14 (28.0)
> 30 mmHg	4 (8.0)

* Patients could have more than one associated valvular lesion; therefore, percentages do not sum to 100%. Abbreviations: MVA = Mitral valve area; MS = Mitral stenosis; AR = Aortic regurgitation; AS = Aortic stenosis; MR = Mitral regurgitation; TS = Tricuspid stenosis; TR = Tricuspid regurgitation; TR Vmax = Maximal tricuspid regurgitation velocity; LA = Left atrium

3.3 Complications

During the study period, all 98 patients had at least one documented clinical or echocardiographic manifestation associated with rheumatic mitral stenosis. Worsening of mitral stenosis, defined as a documented reduction in mitral valve area on serial echocardiographic examinations, was documented in 25 (25.5%) patients.

Heart failure was the most common complication, among the 83 children with heart failure, 11 (13.3%) were classified as NYHA class II, 18 (21.7%) as class III, and 54 (65.0%) as class IV; thus, 72 (86.7%) had class III or IV symptoms. A high echocardiographic probability of pulmonary hypertension was documented in 61 of 75 patients (81.3%) with available TR Vmax measurements.

Atrial fibrillation occurred in 9 patients (9.2%; 95% CI: 4.1–13.8). Left atrial thrombus was detected in 5 patients, while systemic embolism occurred in 4 patients. Infective endocarditis was identified in 9 patients (9.2%; 95% CI: 4.1–14.8). Cardiogenic shock developed in 11 patients (11.2%; 95% CI: 7.1–19.9), and all affected patients died. Stroke and atrial flutter were each documented in two patients. Bar chart illustrating the complications of rheumatic mitral stenosis in children is presented in Fig. 2.

3.4 Mortality

During the study period, 16 of the 98 children died, resulting in an overall mortality proportion of 16.3%. The mean age at death was 14.4 ± 1.4 years. The interval between diagnosis and death could be reliably determined for 13 of the 16 children who died during the study period and was 26 ± 22 months (range, 2–65 months). This interval was not available or sufficiently reliable for the remaining three patients because of incomplete or inconsistent documentation of the date of diagnosis.

Cardiogenic shock was the leading immediate documented cause of death, accounting for 11 (68.8%) of the 16 deaths, followed by thromboembolic events (3 deaths) and infective endocarditis (2 deaths).

3.5 Factors associated with mortality among pediatric patients with rheumatic mitral stenosis

Variables with a p-value < 0.20 in the bivariable logistic regression analysis were considered for inclusion in the multivariable logistic regression model to identify factors independently associated with mortality. Given the limited number of mortality events, the multivariable model was interpreted cautiously. In the

bivariable analysis, atrial fibrillation, peripheral edema, and infective endocarditis were associated with mortality. The severity of mitral stenosis showed a borderline association with mortality (COR = 3.4, 95% CI: 0.9–12.8; p = 0.072) and was included in the multivariable model because of its clinical relevance.

In the multivariable logistic regression analysis, children with atrial fibrillation had higher odds of mortality than those without atrial fibrillation (AOR = 10.5, 95% CI: 1.7–63.8; p = 0.011). Similarly, children with peripheral edema had eightfold higher odds of mortality (AOR = 8.0, 95% CI: 2.0–32.8; p = 0.004). Infective endocarditis was also independently associated with mortality, with affected children having 7.6-fold higher odds of death compared with those without infective endocarditis (AOR = 7.6, 95% CI: 1.2–46.8; p = 0.029). Although mitral stenosis severity was included in the multivariable model because of its clinical significance and borderline association in the bivariable analysis, it was not statistically significantly associated with mortality after adjustment for the other variables.

The final model demonstrated good calibration, as indicated by the Hosmer–Lemeshow goodness-of-fit test (p = 0.136). The clinical outcomes and mortality characteristics of the study participants are presented in Table 3.

Table 3
Bivariable and multivariable logistic regression analyses of factors associated with mortality among children with rheumatic mitral stenosis at Ayder Comprehensive Specialized Hospital, Mekelle, Tigray, Ethiopia, 2019–2024.

		Mortality, n		COR [95% CI]	p-value	AOR [95% CI]	p-value
Predictors		Yes	No				
Pneumonia	Yes	1	13	0.35 [0.04, 2.83]	0.354		
	No	15	69	1			
Peripheral edema	Yes	8	14	4.9 [1.6, 15.1]	0.006	8.0 [2, 32.8]	0.004*
	No	8	68	1		1	
Anemia	Yes	10	33	2.3 [0.7, 6.9]	0.146		
	No	6	45	1			
Pleural effusion	Yes	3	20	0.58 [0.15, 2.17]	0.42		
	No	13	50	1			
Mitral stenosis severity (cm^2)	Severe	13	46	3.4 [0.9,12.8]	0.072		
	Mild to Moderate	3	36	1			
Atrial fibrillation	Yes	5	4	8.9 [2, 38.1]	0.003	10.5 [1.7, 63.8]	0.011*
	No	11	78	1		1	
Embolism	Yes	2	2	5.7 [0.7, 44]	0.094		
	No	14	80	1			
Infective endocarditis	Yes	4	5	5.1 [1.2, 21.9]	0.027	7.6 [1.2, 46.8]	0.029*
	No	12	77	1		1	

Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; CI, confidence interval; MVA, mitral valve area; MS, mitral stenosis; MR, mitral regurgitation; AR, aortic regurgitation; AS, aortic stenosis. $P < 0.05$ indicates statistical significance.

4. Discussion

To our knowledge, this is the first study to evaluate the clinical profile, complications, and factors associated with mortality among pediatric patients with rheumatic mitral stenosis (RMS) in Tigray, Ethiopia, a setting where surgical intervention for valve disease is unavailable. Our findings demonstrate that rheumatic MS remains a severe pediatric health problem in this context, characterized by early presentation, advanced disease at diagnosis, substantial nutritional impairment, and considerable mortality. The children in this cohort were diagnosed at a mean age of 13.7 ± 3 years, with some diagnosed as early as five years of age. Notably, some children were diagnosed as early as five years of age, highlighting that rheumatic valve disease may progress to clinically significant mitral stenosis during childhood in this setting. Most patients presented after prolonged symptoms, with a mean symptom duration of more than one year, and 60.2% had severe mitral stenosis at diagnosis. Furthermore, malnutrition was highly prevalent, with three-quarters of patients having moderate-to-severe thinness and more than half having stunting. During the study period, mortality occurred in 16.3% of patients, and peripheral edema, atrial fibrillation, and infective endocarditis were independently associated with mortality.

4.1 Characteristics of rheumatic mitral stenosis

In this study, rheumatic MS affected children at a relatively young age, with a mean age at diagnosis of 13.7 ± 3 years, and 13.3% of patients were diagnosed before 10 years of age. In high-income countries, rheumatic MS is uncommon in childhood, as effective prevention, early diagnosis, and access to advanced cardiac care have substantially reduced progression to severe rheumatic valve disease; consequently, it is often detected later in adolescence or adulthood (21). In contrast, studies from low- and middle-income countries have demonstrated earlier onset and more rapid progression of rheumatic valve disease, leading to significant complications during childhood and adolescence (22, 23).

Isolated rheumatic MS was present in 31.6% of our patients, a finding comparable to reports from India (24) and South Africa (25). However, this proportion was considerably higher than that reported from the Addis Ababa Cardiac Center, where isolated rheumatic MS accounted for only 9.5% of cases (16), as well as other African studies reporting proportions ranging from 7.8% to 13.4% (26–28). The higher proportion observed in our study may reflect differences in referral patterns, disease severity at presentation, and access to early diagnosis and intervention. In a setting where patients frequently present late with advanced disease, isolated mitral valve involvement may represent a later stage of rheumatic valve progression.

Severe rheumatic MS, defined as a mitral valve area (MVA) < 1.0 cm^2, was observed in 60.2% of our patients. This proportion was lower than the 72.8% reported in a prospective cohort study from Tanzania that included both children and adults with rheumatic MS (26), but substantially higher than the 18.1% reported among pediatric patients from Addis Ababa (16). Differences in age distribution, referral patterns, disease severity at enrollment, and availability of early cardiac evaluation may explain these variations. Importantly, most previous studies included older populations or mixed pediatric and adult cohorts, whereas our study specifically focused on children and adolescents with rheumatic MS.

The high burden of isolated and severe rheumatic MS among young patients in our study suggests an accelerated disease trajectory in this population. Several factors may contribute to this pattern, including poverty, overcrowding, limited awareness of RHD prevention, delayed healthcare seeking, and inadequate adherence to secondary penicillin prophylaxis (29–31). Similar to other studies from resource-limited settings, many patients in our study did not recall a previous episode of rheumatic fever (16, 27), suggesting that undiagnosed or untreated streptococcal infections and subclinical rheumatic episodes may contribute to progressive valve damage before clinical recognition. These findings emphasize the importance of strengthening primary prevention, improving early detection through echocardiographic screening where feasible, and ensuring access to secondary prophylaxis to prevent progression to advanced rheumatic valve disease.

4.2 Malnutrition in children with rheumatic mitral stenosis

Malnutrition is an important but relatively underrecognized complication among children with rheumatic heart disease, particularly among those with advanced valvular lesions. Data specifically describing nutritional status among pediatric patients with rheumatic MS remain limited. We identified only two Ethiopian studies that evaluated malnutrition among children with RHD: one from Haramaya (32) and another from Addis Ababa (19). Both studies reported substantially lower rates of severe acute malnutrition compared with our findings, with severe acute malnutrition observed in 12.8% of patients in each study. The Addis Ababa study additionally reported moderate malnutrition in 32.9% of pediatric RHD patients (19). In contrast, our study found that more than three-quarters of children with rheumatic MS had moderate-to-severe thinness, and nearly half had severe thinness. Similarly, chronic nutritional impairment was common, with 52% of patients experiencing stunting and 25.5% having severe stunting, compared with only 3.7% stunting and 0.8% severe stunting reported in the Addis Ababa cohort (19).

The markedly higher prevalence of malnutrition in our cohort may reflect the advanced stage of cardiac disease among our patients. Chronic rheumatic MS may contribute to malnutrition through mechanisms related to reduced nutritional intake, increased metabolic demands, chronic inflammation, and complications of heart failure. Furthermore, recurrent infections, prolonged illness duration, and delayed presentation may further worsen nutritional status. In our setting, these effects may be compounded by the already high burden of childhood malnutrition in Tigray, where rates of wasting and stunting remain above national averages (33).

However, the nutritional burden observed in this study appears substantially higher than expected based solely on regional nutritional trends. This may indicate the additional contribution of advanced rheumatic MS, recurrent rheumatic activity, and limited access to timely cardiac care. The relationship between malnutrition and rheumatic MS is likely bidirectional: advanced cardiac disease may contribute to nutritional deterioration, while malnutrition may further impair immune function, increase susceptibility to infection, and reduce physiological reserve, potentially worsening clinical outcomes. These findings highlight the need to integrate nutritional assessment and rehabilitation into the comprehensive management of children with advanced RHD.

4.3 Complications and mortality of rheumatic mitral stenosis

Contemporary data on mortality among patients with medically managed rheumatic mitral stenosis are limited, largely because surgical and interventional therapies have become standard in many settings with advanced cardiac care (21). Sixteen (16.3%) patients died during the five-year study period. A prospective cohort study from Tanzania involving medically managed patients with rheumatic MS reported a mortality rate of 10.4% over one year (26). Direct comparison between these studies should be interpreted cautiously because of differences in follow-up duration, patient characteristics, disease severity, and healthcare settings. The relatively high mortality observed in both studies likely reflects the advanced disease burden among patients managed without definitive valve intervention.

Historical studies from high-income countries provide important context regarding the natural history of untreated rheumatic MS during the pre-intervention era. Studies from the 1960s in the United States reported mortality rates of 39% and 80% at 10 and 20 years, respectively (9), while a Danish cohort reported similarly high long-term mortality rates of 64% and 84% (10). However, these findings are difficult to directly compare with our study because of differences in diagnostic methods, treatment approaches, population characteristics, and duration of follow-up.

In Ethiopia, published data on rheumatic MS-related mortality remain scarce. A study from Tikur Anbassa Teaching Hospital reported that RHD accounted for 26.5% of cardiovascular-related deaths (34), while Günther et al. documented an annual mortality rate of 12.5% among patients with RHD in rural communities (13). However, these studies involved broader RHD populations and had methodological differences that limit direct comparison with our pediatric rheumatic MS cohort.

In our study, AF was independently associated with mortality; children with AF had approximately 10 times the odds of death compared with those without AF. This finding is comparable with reports from Ethiopia (9.1%) (19) and Nigeria (10%) (27). However, it was higher than the 4.4% reported from another Ethiopian pediatric RHD study (16), although this difference was not statistically significant. Studies involving predominantly adult or mixed-age populations have reported substantially higher AF prevalence, ranging from 20.3% to 57% (10, 26, 28).

The observed differences in AF prevalence across studies are likely related to variations in age distribution, disease severity, referral patterns, and diagnostic practices. AF is strongly associated with age and chronic atrial enlargement; therefore, studies including older patients generally report higher rates. Differences in routine ECG screening practices may also influence detection, as studies performing ECG evaluation in all patients may identify asymptomatic AF more frequently than those investigating only clinically suspected cases. Despite being lower than rates reported in adult populations, the presence of AF in nearly one in ten children with rheumatic MS is clinically concerning, given its association with advanced disease and poor outcomes.

In our study, AF was independently associated with mortality, with affected patients having approximately tenfold higher odds of documented mortality compared with those without AF. The pathophysiological basis for this association is well established. Rheumatic MS causes impaired left ventricular filling by restricting blood flow across the mitral valve, reducing end-diastolic volume and cardiac output. The development of AF further compromises ventricular filling by eliminating effective atrial contraction and shortening diastolic filling time, resulting in worsening heart failure and increased mortality risk.

Our finding is consistent with previous evidence. A Tanzanian prospective cohort of 145 medically managed rheumatic MS patients reported a 2.44-fold increased mortality risk among patients with arrhythmias compared with those without arrhythmia (26). Similarly, the African REMEDY registry, which included 3,343 patients with RHD from 14 developing countries, demonstrated a 1.4-fold higher mortality risk among patients with AF (35). The stronger association observed in our study may be related to the smaller sample size, younger population, advanced disease at presentation, and the exclusive focus on rheumatic MS rather than the broader spectrum of RHD. Historical data also support the adverse prognostic role of AF; among patients with rheumatic MS in the United States, mortality was substantially higher among those with AF (9), and the Danish cohort reported poor long-term survival among patients with AF (10).

Infective endocarditis was also independently associated with mortality in our study. This finding differs from previous studies, including a prospective cohort from Uganda and multicenter studies such as REMEDY (35) and VALVAFRIC (28), where IE was not identified as an independent predictor of mortality. Several factors may explain this discrepancy, including differences in diagnostic criteria, patient selection, disease severity, and access to timely diagnosis and treatment.

The prevalence of IE in our cohort was 9.2%, which was comparable to findings from Tanzania (26) and Nigeria (27). It was higher than the 4.2% reported from Addis Ababa (19). Differences in reported prevalence may be related to variation in inclusion criteria, as some studies included possible IE cases, whereas our study included only definite IE diagnoses. The strong association between IE and mortality in our cohort emphasizes the vulnerability of children with advanced rheumatic MS to severe infectious complications and highlights the importance of early recognition, appropriate antibiotic therapy, and preventive strategies.

Peripheral edema was observed in 22% of patients and was independently associated with mortality. This finding is consistent with previous study demonstrating that peripheral edema is an indicator of advanced cardiac dysfunction and increased risk of adverse outcomes (36). Clinically, peripheral edema reflects systemic venous congestion and often indicates progression to right-sided heart failure, severe pulmonary hypertension, or advanced valvular disease. Therefore, its presence should prompt urgent assessment and optimization of heart failure management.

Previous studies have identified additional factors associated with mortality among patients with RHD, including age, sex, heart failure, New York Heart Association (NYHA) functional class, and multivalvular

disease (26, 31, 35). In contrast, these factors were not significantly associated with mortality in our study. This difference may be explained by the distinct characteristics of our cohort, which included only pediatric patients with predominant mitral stenosis, whereas many previous studies enrolled broader RHD populations involving multiple valve lesions and a wider age range. Furthermore, the single-center design and relatively small sample size may have limited the statistical power to detect additional predictors.

5. Strengths and limitations of the study

5.1 Strengths

This study has several important strengths. First, it specifically focuses on pediatric patients with rheumatic mitral stenosis, a population that remains underrepresented in the existing literature despite the substantial burden of rheumatic heart disease in low- and middle-income countries. Second, the study was conducted in a setting where surgical and interventional management for advanced rheumatic valve disease is not available, providing valuable insight into the clinical course, complications, and outcomes of rheumatic MS under predominantly medical management. Third, the study provides baseline data on the severity of disease, nutritional burden, complications, and factors associated with mortality that may support future research and inform strategies for improving pediatric RHD care in similar resource-limited settings.

5.2 Limitations

The findings of this study should be interpreted considering several limitations.

The retrospective design limited the completeness of longitudinal follow-up data, and exact dates of diagnosis and death were inconsistently recorded; diagnosis-to-death intervals were available for only 13 of 16 deceased patients, precluding formal time-to-event analysis.

Second, important socioeconomic determinants, including household conditions, healthcare access, and adherence to secondary penicillin prophylaxis, could not be adequately assessed because of limited availability of reliable records. These factors may have contributed to disease progression and outcomes but could not be evaluated.

Third, as a single-center study conducted at a tertiary referral hospital, the findings may be affected by referral bias and may not be fully generalizable to all children with RHD in Ethiopia.

Finally, the relatively small number of mortality events limited the number of variables that could be included in multivariable analysis and resulted in wide confidence intervals around some estimates; therefore, the identified associations should be interpreted cautiously.

6. Conclusions

This study highlights the substantial burden of rheumatic mitral stenosis among children in a resource-limited setting without access to surgical intervention. The findings demonstrate that children may present with advanced rheumatic valve disease at a young age, accompanied by a high prevalence of acute and chronic malnutrition, severe mitral stenosis, and life-threatening complications. Atrial fibrillation, infective endocarditis, and peripheral edema were independently associated with mortality.

These findings underscore the need for strengthening primary and secondary prevention of rheumatic fever, improving early detection of rheumatic valve disease, ensuring regular follow-up and nutritional support, and expanding access to definitive cardiac interventions for children with advanced rheumatic MS. In settings where surgical care remains limited, early identification of high-risk patients and optimization of medical management are essential to reduce preventable morbidity and mortality.

Abbreviations

AF: Atrial fibrillation; AOR: Adjusted odds ratio; ARF: Acute rheumatic fever; CHF: Congestive heart failure; CI: Confidence interval; COR: Crude odds ratio; CXR: Chest radiograph; EF: Ejection fraction; IE: Infective endocarditis; IQR: Interquartile range; LA: Left atrium; MS: Mitral stenosis; MVA: Mitral valve area; PH: Pulmonary hypertension; RHD: Rheumatic heart disease; SD: Standard deviation; SPSS: Statistical Package for the Social Sciences; TR Vmax: Peak tricuspid regurgitation velocity.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Review Board of the College of Health Sciences, Mekelle University, Ethiopia (reference number: MU-IRB 2323/2024). Permission to access and review the relevant medical records was obtained from Ayder Comprehensive Specialized Hospital. As this was a retrospective medical-record-based study using routinely collected clinical data and no direct contact with participants, the requirement for individual informed consent was waived by the Institutional Review Board. All data were anonymized during data extraction and analysis, and confidentiality of patient information was maintained throughout the study.

Consent for publication

Not applicable. The manuscript does not contain identifiable individual patient information.

Availability of data and materials

The dataset used and/or analyzed during the current study is available from the corresponding author on reasonable request, subject to institutional and ethical restrictions concerning patient confidentiality.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ABT conceived the study, contributed to the research question and study design, supervised the research process, interpreted the findings, and prepared and finalized the manuscript. EFG contributed to study conception, proposal development, study implementation, data collection, data management, statistical analysis, and manuscript preparation. THA, MYH, ZWM, and MMM contributed to study design, proposal development, interpretation of findings, and critical revision of the manuscript. YML provided public-health and statistical expertise and critically reviewed the analysis and manuscript. DYA contributed to data collection, clinical record review, and critical revision of the manuscript. All authors reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Figures

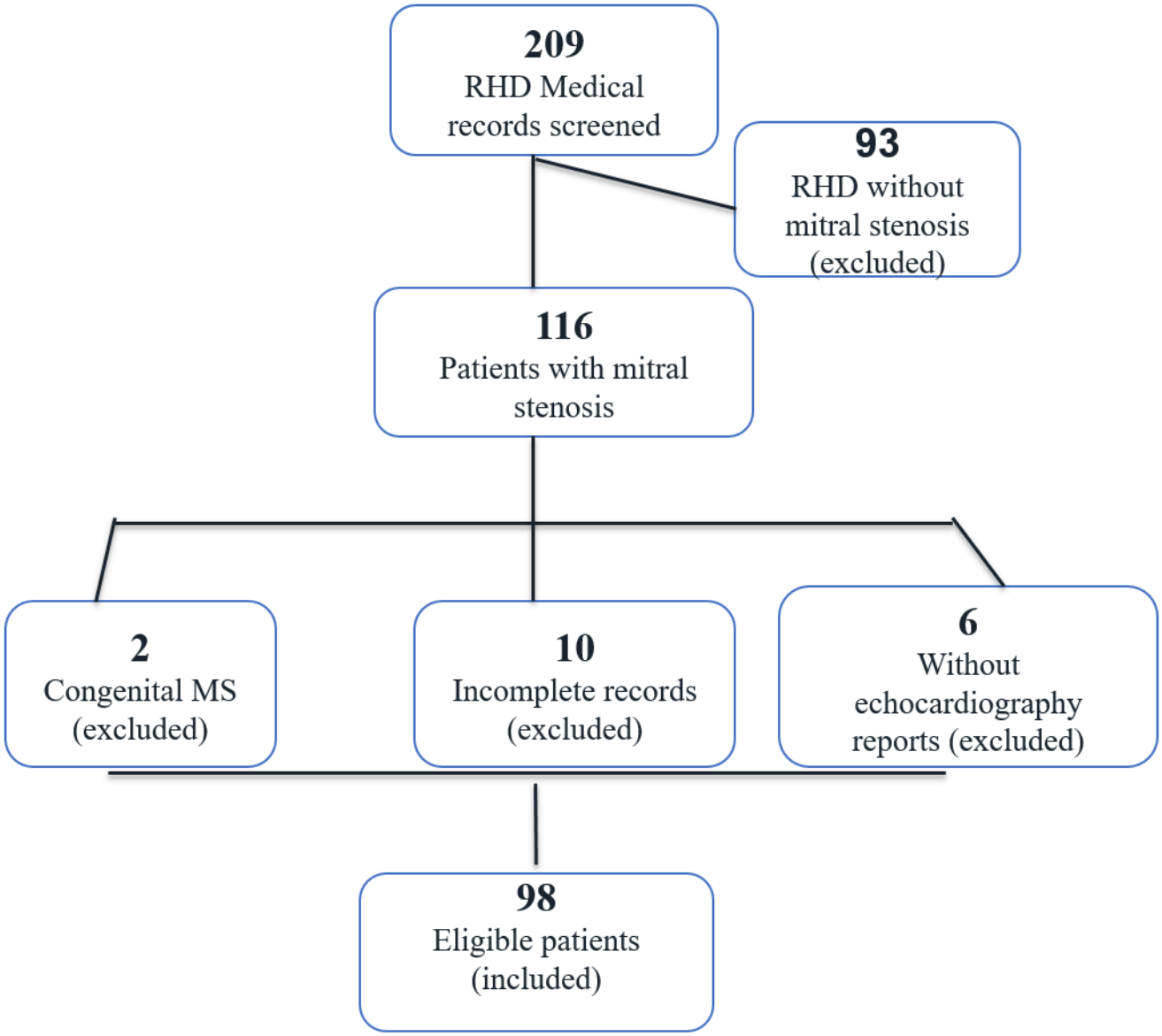


Figure 1

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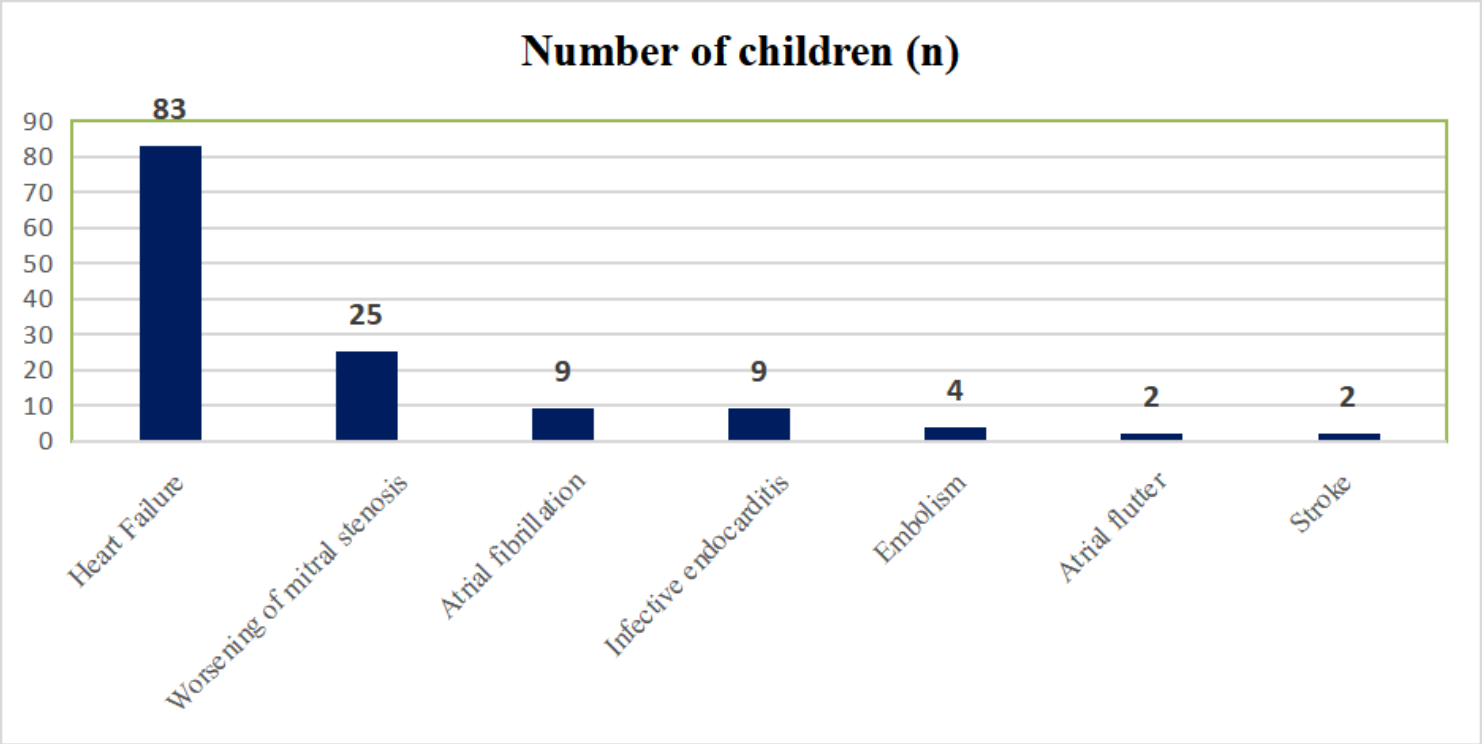


Figure 2

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