Original Article

Journal of Occupational Health and Epidemiology

Journal Homepage: https://johe.rums.ac.ir/

JOHE

Rafsanjan University of Medical Sciences

Epidemiological and Demographic Analysis of Rheumatic Heart Diseases in Northeastern Iran: A Cross-Sectional Study

Leila Bigdelu[1*], Mohammad Baradaran Firoozabadi[2], Yousef Dowlatabadi[3], Hedieh Alimi[1], Hourak Poorzand[4], Maryam Emadzadeh[5], Fereshteh Ghaderi[1]

1. Associate Prof., Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Neurological Surgery Resident, Dept. of Neurosurgery, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Medical Doctor, Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
4. Professor, Vascular and Endovascular Surgery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
5. Associate Prof., Mashhad University of Medical Sciences, Mashhad, Iran.

CrossMark

Citation: Bigdelu L, Baradaran Firoozabadi M, Dowlatabadi Y, Alimi H, Poorzand H, Emadzadeh M, et al. Epidemiological and Demographic Analysis of Rheumatic Heart Diseases in Northeastern Iran: A Cross-Sectional Study. J Occup Health Epidemiol. 2025;14(3):153-61.

Article Info

*** Corresponding author:**
Leila Bigdelu,
E-mail:
bigdelul9706@gmail.com

Article history
Received: Dec 2024
Accepted: May 2025

10.61882/johe.14.3.153

Print ISSN: 2251-8096
Online ISSN: 2252-0902

Peer review under responsibility of Journal of Occupational Health and Epidemiology

Abstract

Background: Rheumatic mitral stenosis (MS) remains a significant health concern in developing regions. This study aimed to determine the prevalence and characteristics of rheumatic MS in Northeastern Iran.

Material and Methods: In this cross-sectional study (2016-2020), we analyzed data from 1,035 rheumatic MS patients at two tertiary cardiology centers in Mashhad. Demographic, clinical, and echocardiographic parameters were extracted from the registered echocardiographic database at Mashhad University of Medical Sciences. Statistical analysis was undertaken using SPSSv22 with appropriate tests (Chi-square, ANOVA, Kruskal-Wallis; $p<0.05$).

Results: The study population (mean age 50.0±13.3 years) revealed 79.3% female predominance. Prevalence was 0.3 per 1,000 population. Concomitant valvular involvement was common: aortic regurgitation (60.4%), mitral regurgitation (43.8%), tricuspid regurgitation (38%), and aortic stenosis (25%). Males exhibited more severe MS ($p<0.05$) with greater pulmonary artery pressures and greater need for percutaneous transvenous mitral commissurotomy (PTMC).

Conclusion: While rheumatic MS prevalence in Northeastern Iran aligns with global declining trends, the significant female predominance contrasts with greater disease severity in males. These findings highlight the need for: 1) comprehensive echocardiographic evaluation, 2) gender-specific management approaches, and 3) strengthened prevention programs. The persistence of clinically significant MS burden underlines the importance of ameliorating primary and secondary prevention strategies in the region.

Keywords: Valvular Heart Disease, Mitral Valve Stenosis, Aortic Stenosis, Aortic Regurgitation, Prevalence

Introduction

Cardiovascular diseases remain a leading cause of mortality worldwide, accounting for over 18 million deaths in 2019 [1]. The epidemiology of valvular heart diseases has undergone significant changes in recent decades [2]. Nevertheless, global epidemiological data often lack reliability, as post-mortem evaluations indicate a higher prevalence of valvular heart disease than clinical reports suggest. This discrepancy is further aggevevated in underdeveloped countries, where access to advanced diagnostic equipment and tests is limited [3-5].

In Iran, the prevalence of rheumatic heart disease (RHD) has been estimated at 0.02%, corresponding to

20 cases per 100,000 individuals [6]. Among cardiovascular diseases, treating rheumatic heart disease incurred the highest cost, averaging around US $4,710.78 [7]. A recent Chinese study estimates that the prevalence of rheumatic heart disease will exceed 48 million cases by 2030, which is expected to impose a substantial economic burden [8].

Valvular heart disease remains a significant issue in developed countries. Although the prevalence of RHD has diminished over the past decade, the prevalence of degenerative valvular diseases has grown. In Europe, aortic stenosis and mitral regurgitation are currently the most common valvular diseases. The prevalence of mitral valve disease rises with age, affecting approximately 12% of individuals over the age of 75. The primary manifestations of mitral valve disease are regurgitation and stenosis, which can stem from various underlying conditions. These include degenerative changes, mitral annular calcification, both ischemic and nonischemic cardiomyopathies, and, less frequently, rheumatic fever. Congenital mitral valve pathologies can also contribute to these conditions [9, 10]. Mitral valve insufficiency accounts for only 15% of deaths due to valvular diseases, while aortic valve diseases are responsible for over 60% of such deaths. Aortic valve disorders often arise from chronic heart conditions and aging. In contrast, rheumatic heart disease is primarily caused by infections and limited access to healthcare [11, 12].

Although Asia's RHD prevalence remained 9% lower than the global average in 2019, the region witnessed mortality rates that were 41% greater [13]. In high-prevalence regions, RHD is the dominant cardiovascular disorder in young women and pregnant women, fuelling substantial maternal and perinatal complications and deaths [14]. Gedefaw, et al. (2023) reported that 56.5% (95% CI: 50.9–61.9) of RHD patients in Ethiopia had pulmonary hypertension, with 51% classified as severe cases [15]. Another study noted that patients with RHD face a 1–2.4% two-year cumulative risk of stroke, equating to an annual incidence of approximately 8 strokes per 1,000 patients [16]. RHD contributes to over 10 million disability-adjusted life-years (DALYs) annually and remains the leading cause of valvular heart disease-related deaths worldwide [2]. In spite of its preventable nature, RHD persists as a neglected global health challenge, disproportionately affecting low-income countries with limited healthcare access and delayed diagnosis [17]. Rheumatic disease is the most prevalent cause of mitral stenosis worldwide. Other contributing factors include a history of chest radiation, carcinoid heart disease, and rare hereditary metabolic disorders, accounting for around 3% of cases [18, 19]. If mitral valve stenosis (MS) is not properly diagnosed and treated, it can result in elevated pressure in the left atrium, leading to atrial enlargement. This can cause atrial tachyarrhythmia, atrial fibrillation (AF), or flutter, which may result in clot formation and, subsequently, ischemic stroke and severe neurological complications. Chronic MS elevates pressure in the left atrium, causing pulmonary congestion and elevated pulmonary blood pressure. This pressure can affect the right side of the heart, eventually causing right ventricular dysfunction and tricuspid valve failure. Over time, symptoms such as peripheral edema, ascites, and pleural effusion may develop [20].

Echocardiography is a crucial tool for evaluating the severity of mitral valve stenosis. By utilizing ultrasound waves, echocardiography can ascertain the heart's structure and calculate its cardiac function, enabling precise diagnosis and proper treatment strategies [17, 21].

Understanding regional epidemiology is essential for adopting effective treatment strategies. Recent studies in Iran have primarily been undertaken in a single center, limiting the generalizability of their results. Thus, this study examine the prevalence of MS and its relationship with patient demographics, as well as its association with other heart valve diseases. The study was performed over five years in two comprehensive cardiovascular centers in the northeast of Iran.

Materials and Methods

This cross-sectional study was undertaken in the cardiology departments of two prominent hospitals in northeastern Iran, Imam Reza and Ghaem Hospitals, from 2016 to 2020. Data were extracted from the registered echocardiographic database at Mashhad University of Medical Sciences. The checklist included the following variables:

- Demographic data (age, gender, residential location)
- Duke activity status index (DASI)
- Echocardiographic indices (valvular condition, stenosis, insufficiency, rheumatic involvement, area of the mitral and aortic valve (MVA, AVA), rhythm, heart rate, body surface area (BSA), left ventricle ejection fraction (LVEF), pulmonary artery pressure (PAP), Percutaneous Trans-Mitral Commissurotomy score (PTMC score), also known as the Wilkins score)

Patients diagnosed with rheumatic MS between 2016 and 2020 were eligible for inclusion. We excluded individuals with incomplete medical records or severe non-cardiac comorbidities—such as advanced chronic obstructive pulmonary disease or end-stage renal disease—which could adversely affect echocardiographic indices, DASI scores, or overall cardiovascular function. Further, patients whose echocardiographic images were of insufficient quality for accurate measurements (e.g., MVA, LVEF, PAP) were excluded, as consistent and reliable imaging is critical for robust analysis.

SPSS version 22 and Microsoft Excel were employed for data analysis and chart creation. Chi-square tests

were utilized for qualitative variables to ascertain associations, while one-way ANOVA or Kruskal-Wallis tests were applied for quantitative variables to compare means across groups. A p-value < 0.05 was considered statistically significant.

The study adhered to the Helsinki ethical guidelines and was approved by the Mashhad University Ethical Committee (Ethical number: 791157, Code: IR.MUMS.MEDICAL.REC.1399.114).

Results

Of the total 1,035 patients in the study, 821 (79.3%) were women, while the remaining were men. The mean age was 50.04 ± 13.32 years. A total of 321 (31%) patients underwent Percutaneous Transluminal Mitral Commissurotomy (PTMC). Further, 346 patients (33.4%) had AF; 281 patients (27.1%) had rheumatic involvement of the aortic valve; and 74 patients (7.1%) had rheumatic involvement of the tricuspid valve.

As displayed in Fig. 1, the percentages of valvular diseases were as follows: aortic regurgitation (AR) in 625 patients (60.4%), mitral regurgitation (MR) in 454 patients (43.8%), Tricuspid regurgitation (TR) in 395 patients (38%), and aortic stenosis (AS) in 259 patients (25%). These findings demonstrate that AR is the most common valvular disease, followed by MR, TR, and AS. None of our patients had severe pulmonary stenosis.

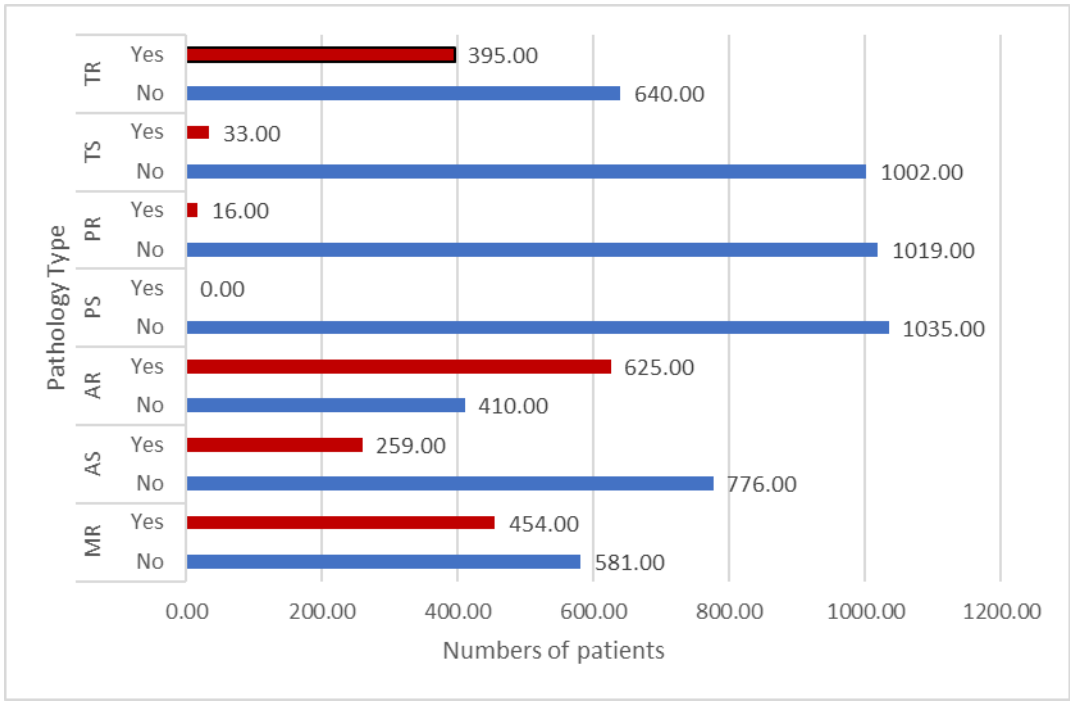

Fig. 1. Distribution of Patients by Type of Involvement.

The study included 1,035 patients, with a mean age at the time of diagnosis as 33.61 years. The average heart rate was 80.35 beats per minute, and the mean BSA was 1.69 m². The average LVEF was 53.06%, which indicates the heart's pumping efficiency. The mean PTMC score was 7.99. The MVA averaged 1.16 cm², while the AVA was 1.65 cm². PAP averaged 40.97 mmHg, reflecting the pressure in the pulmonary artery. The DASTI, measuring functional capacity, had a mean score of 17.44 (as detailed in Table 1).

According to Table 2, sinus rhythm, AS, aortic valve regurgitation, rheumatic AR, rheumatic tricuspid involvement, and MS were statistically significant and different between males and females. Nevertheless, we found no significant difference between males and females for mitral regurgitation (MR), pulmonary regurgitation (PR), TS, and TR.

Since the majority of participants in this study were women, the observed frequency of sinus rhythm and AF appears higher in women. Specifically, among the 821 women included in the study, 31.54% (259 women) had AF. On the contrary, among the 214 men studied, 40.65% (87 men) had AF. Thus, Atrial fibrillation is 9.11% more common in men.

We observed that the prevalence of AS is higher in men and tends to be more severe compared to women. Interestingly, while rheumatic tricuspid valve involvement was more common in females, AR was more prevalent in males compared to females (33% versus 25%).

Table 1. Indices Measured by Echocardiography and Standard Questionnaire

Variable	Mean± SD	Median (IQR)	Minimum	Maximum
Patient Age at the time of diagnosis (years)	33.61±11.16	35(23-47)	11	59
Heart rate/ minute	80.35±19.91	78(67-90)	45	200
BSA	1.69±0.17	1.70(1.59-1.80)	1.16	2.40
LVEF (%)	53.06±6.93	55(50-55)	15	70
PTMC Score	7.99±1.39	8(7-9)	1	13
MVA	1.16±0.42	1.1(0.9-1.3)	0.30	3.20
AVA	1.65±0.43	1.70(1.40-1.90)	0.50	3.20
PAP	40.97±15.33	38(30-45)	10	120
DASI	17.44±7.97	17.95(13.45-23.20)	1.75	50.20

Abbreviation: BSA= Body Surface Area, LVEF= Left Ventricle Ejection Fraction, MVA= Mitral Valve Area, AVA= Aortic Valve Area, PAP= Pulmonary Artery Pressure, DASI= Duke Activity Status Index, SD= Standard Deviation, IQR= Interquartile Range
PTMC Score: Percutaneous Trans-Mitral Commissurotomy score, also known as the Wilkins score

Table 2. Gender-Based Comparison of Heart Rhythm and Valve Conditions

Variable		Female	Male	*P-value
		Numbers (present %)	**Numbers (present %)**	
Rhythm	Sinus	562 (87.6)	127 (18.4)	**0.012**
	AF	259 (74.9)	87 (25.1)	
MR	Without MR	95 (74.2)	33 (25.8)	0.393
	Minimal involvement	188 (77)	56 (23)	
	Minimal to mild	172 (82.3)	37 (17.7)	
	Mild to moderate	231 (81.6)	52 (18.4)	
	Moderate to severe	71 (80.7)	17 (19.3)	
	Severe	64 (77.1)	19 (22.9)	
AS	Without AS	563 (82)	140 (18)	**<0.001**
	Minimal involvement	53 (70.7)	22 (29.3)	
	Minimal to mild	75 (75.8)	24 (24.2)	
	Mild to moderate	43 (75.4)	14 (24.6)	
	Moderate to severe	3 (42.9)	4 (57.1)	
	Severe	11 (52.4)	10 (47.6)	
AR	Without AR	360 (87.8)	50 (12.2)	**<0.001**
	Minimal involvement	164 (78.8)	44 (21.2)	
	Minimal to mild	152 (73.4)	55 (21.6)	
	Mild to moderate	119 (70.8)	49 (29.2)	
	Moderate to severe	21 (61.8)	13 (38.2)	
	Severe	5 (62.5)	3 (37.5)	
Rheumatic-AR	No	612 (81.2)	142 (18.8)	**0.016**
	Yes	209 (74.4)	72 (25.6)	
PR	Without PR	242 (77.1)	72 (22.9)	0.730
	Minimal involvement	550 (80.2)	136 (19.8)	
	Minimal to mild	15 (78.9)	4 (21.1)	
	Mild to moderate	13 (87.7)	2 (13.3)	
	Moderate to severe	1 (100)	0 (0.0)	
TS	Without TS	794 (79.2)	208 (20.8)	0.922
	Minimal involvement	9 (81.8)	2 (18.2)	
	Minimal to mild	12 (85.7)	2 (14.3)	
	Mild to moderate	6 (85.7)	2 (14.3)	
TR	Without TR	47 (70.1)	20 (29.9)	0.086
	Minimal involvement	283 (76.1)	89 (23.9)	
	Minimal to mild	163 (81.1)	38 (18.9)	
	Mild to moderate	175 (82.5)	37 (17.5)	
	Moderate to severe	59 (84.3)	11 (15.7)	
	Severe	94 (93.2)	19 (16.8)	
Rheumatic tricuspid involvement	No	755 (78.6)	206 (21.4)	**0.030**
	Yes	66 (89.2)	8 (10.8)	
MS	Mild	72 (84.7)	13 (15.3)	**0.003**
	Moderate	519 (81.7)	116 (18.3)	
	Severe	230 (73)	85 (27)	

*A chi-square test was conducted to compare the groups.
Abbreviation: AS= Aortic Stenosis, MR= Mitral Regurgitation, AR= Aortic Regurgitation, PR= Pulmonary Regurgitation, TS=Tricuspid Stenosis, TR= Tricuspid Regurgitation, MS= Mitral Stenosis

Table 3 compares the severity of MS in individuals with different rhythms and valvular disorders. The data are categorized into three groups depending on the severity of MS. MS is classified based on the MVA measured via echocardiography. An MVA between 1.0 cm² and 1.5 cm² indicates severe stenosis, an MVA larger than 1.5 cm² is considered mild stenosis, and an MVA smaller than 1 cm² is classified as very severe stenosis.

As the severity of MS grows from mild to very severe, there are significant increases in MR (P-value = 0.0002), TR (P-value < 0.001), TS (P-value = 0.027), as well as atrial fibrillation (AF) (P-value < 0.0001). These findings highlight the correlation between the severity of MS and the presence of other valvular disorders as well as rhythm abnormalities.

Table 3. Comparison of Mitral Stenosis Severity in Patients with Different Rhythms and Various Valvular Involvements

Variables		Mild mitral stenosis (>1.5 Cm)	Severe mitral stenosis (1-1.5 Cm)	Very Severe mitral stenosis (<1 Cm)	*P-Value
		Numbers (present)%	Numbers (present)%	Numbers (present)%	
Rhythm	**Sinus**	97 (65.5)	419 (73.3)	173 (54.9)	**<0.001**
	AFs	51 (34.5)	153 (26.7)	142 (45.1)	
AS	Without AS	112 (75.7)	441 (77.1)	223 (70.8)	0.130
	Minimal involvement	15 (10.1)	38 (6.6)	22 (7)	
	Minimal to mild	16 (10.8)	47 (8.2)	36 (11.4)	
	Mild to moderate	4 (2.7)	32 (5.6)	21 (6.7)	
	Moderate to severe	0 (0)	5 (0.9)	2 (0.6)	
	Severe	1 (0.7)	9 (1.6)	11 (3.5)	
AR	Without AR	60 (40.5)	237 (41.4)	113 (35.9)	0.333
	Minimal involvement	32 (21.6)	121 (21.2)	55 (17.5)	
	Minimal to mild	28 (18.9)	99 (17.3)	80 (25.4)	
	Mild to moderate	28 (14.2)	93 (16.3)	54 (17.1)	
	Moderate to severe	5 (3.4)	18 (3.1)	11 (3.5)	
	Severe	2 (1.4)	4 (0.7)	2 (0.6)	
Rheumatic-AR	NO	111 (75.0)	431 (141)	212 (103)	**0.017**
	Yes	37 (25.0)	75.3 (24.7)	67.3 (32.7)	
MR	Without MR	23 (15.5)	77 (13.5)	28 (8.9)	**0.002**
	Minimal involvement	23 (15.5)	127 (22.2)	94 (29.8)	
	Minimal to mild	25 (16.9)	115 (20.1)	69 (21.9)	
	Mild to moderate	40 (27.0)	158 (27.6)	85 (27.0)	
	Moderate to severe	22 (14.9)	46 (8.0)	20 (6.3)	
	Severe	15 (10.1)	49 (8.6)	19 (6.0)	
PR	Without PR	55 (37.2)	173 (30.2)	86 (27.3)	0.201
	Minimal involvement	89 (60.1)	385 (67.3)	212 (67.3)	
	Minimal to mild	2 (1.4)	8 (1.4)	9 (2.9)	
	Mild to moderate	2 (1.4)	6 (1.0)	7 (2.2)	
	Moderate to severe	0 (0)	0 (0)	1 (0.3)	
TR	Without TR	11 (7.4)	41 (7.2)	15 (4.8)	**<0.001**
	Minimal involvement	55 (37.2)	238 (41.6)	79 (25.1)	
	Minimal to mild	26 (17.6)	114 (19.9)	61 (19.4)	
	Mild to moderate	34 (23.0)	104 (18.2)	74 (23.5)	
	Moderate to severe	9 (6.1)	29 (5.1)	32 (10.2)	
	Severe	13 (8.8)	46 (8.0)	54 (17.1)	
Rheumatic tricuspid involvement	No	142 (95.9)	537 (93.9)	282 (89.5)	**0.016**
	Yes	6 (4.1)	35 (6.1)	33 (10.5)	
TS	Without TS	145 (98.0)	561 (98.1)	296 (94.0)	**0.027**
	Mild	1 (0.7)	5 (0.9)	5 (1.6)	
	Moderate	1 (0.7)	3 (0.5)	10 (3.2)	
	Severe	1 (0.7)	3 (0.5)	4 (1.3)	

*The groups were compared using a chi-square test.
Abbreviation: AS= Aortic Stenosis, AR= Aortic Regurgitation, MR= Mitral Regurgitation, PR= Pulmonary Regurgitation, TR= Tricuspid Regurgitation, TS= Tricuspid Stenosis

Table 4 compares various indicators such as age, heart rate, PTMC score, AVA, and PAP among patients with different degrees of mitral valve stenosis.

The findings indicate that:

PTMC scores (P-value < 0.001) and PAP (P-value < 0.001) are significantly higher in patients with very severe MS. These results highlight the significant differences in these parameters depending on the severity of MS.

Table 4. Comparison of Echocardiographic Indices and Standard Questionnaire Results in Patients with Different Severities of MS

Variable	mild mitral valve stenosis	Severe mitral valve stenosis	Very severe mitral valve stenosis	P-value
Age (years)	53.5±13.44	47.67±12.97	50.86±13.57	*<0.001
Median heart rate (IQR)	78 (16)	76 (25)	76 (21)	**0.585
PTMC score (Mean± SD)	7.45±1.51	7.54±1.17	8.65±1.32	*<0.001
Median AVA (IQR)	1.70 (0.41)	1.60 (2.28)	1.60 (0.40)	**0.80
Median PAP (IQR)	40 (11)	35 (15)	45 (20)	**<0.001

*The one-way ANOVA was employed to compare two groups,
**A Kruskal-Walli's test was conducted to assess the differences between the groups.
Abbreviation: AVA= Aortic Valve Area, PAP= Pulmonary Artery Pressure.

Discussion

In this cross-sectional study, we examined the prevalence of rheumatic MS in the city of Mashhad over five years. We identified 1,035 patients with MS between 2016 and 2020. Since the population of Mashhad is approximately 3 million, the prevalence of MS along this period was estimated to be 0.3 per 1,000 patients. Note that some patients may have come from other cities in Khorasan Razavi, which could influence this estimate [22]. Geographical conditions affect the prevalence of MS, with an estimated rate of 0.2-0.3 per 1000 in developed countries and 5.5-5.7 per 1000 in developing countries [23, 24]. Of the entire population studied, 21% were male and 79% were female, revealing that mitral stenosis is more prevalent among women. Similarly, a study conducted by Movahed et al. in 2006 on 24,265 patients found that MS was significantly more prevalent in females (1.6% vs. 0.4% in males). Nevertheless, the prevalence of mitral regurgitation (MR) was similar between both genders (24.4% in females vs. 25% in males) [25]. Based on our findings, we infer that females exhibit enhanced susceptibility to rheumatic mitral stenosis. This predisposition appears to emanate from a more robust autoimmune response, which accelerates valvular damage following infection. In the context of rheumatic heart disease, the autoimmune cascade is likely amplified in females owing to sex-specific differences in immune regulation, leading to a more rapid progression of valve fibrosis and stenosis. Moreover, inherent anatomical variations—such as thinner valve leaflets and a greater propensity for mitral annular calcification—may further promote their vulnerability. Collectively, these interrelated factors help explain the higher prevalence of rheumatic mitral stenosis in women compared to men.

The mean age of patients was 50 years, suggesting a middle-aged predominance. Notably, 67% of patients maintained normal sinus rhythm, while 33% exhibited AF, comparable to Stassen et al. (2023), who found 32.8% of MS patients developed new-onset AF [26]. It can be suggested that the link between AF and advanced MS, especially when the mitral valve area falls below 0.5 cm^2, is likely driven by increased left atrial strain. Nonetheless, widespread antibiotic use has contributed to reducing the occurrence of severe AF cases related to rheumatic heart disease.

Our study found that rheumatic aortic valve involvement in Mashhad is nearly four times more common than rheumatic tricuspid valve involvement. This finding contrasts with a 2019 study from Pakistan by Baqi et al., in which 7% of rheumatic heart patients had tricuspid stenosis and 93.9% manifested tricuspid regurgitation [27]. In our cohort, aortic regurgitation emerged as the most prevalent valvular abnormality, followed by mitral regurgitation, tricuspid regurgitation, and aortic stenosis. Several factors may account for this discrepancy. For instance, regional differences in the immunological and inflammatory response to group A streptococcal infections may predispose patients in Mashhad to aortic, rather than tricuspid, valve involvement. Furthermore, variations in genetic susceptibility, environmental influences, and healthcare access—including differences in the implementation of prophylactic antibiotic regimens—may contribute to distinct patterns of valve damage. Methodological factors, such as variations in diagnostic protocols and imaging techniques, could further affect the detection and classification of valve lesions.

Interestingly, sinus rhythm, AS, AR, rheumatic AR, rheumatic tricuspid involvement, and MS were statistically significantly different between males and females. We observed that AF is more prevalent among male patients with MS compared to their female counterparts. One potential explanation for this disparity is that men generally have a higher body mass index (BMI), a known risk factor for AF. Elevated BMI can contribute to structural and electrical remodeling of the

atria, increasing susceptibility to AF. Further, hormonal and metabolic differences between genders, together with lifestyle factors such as higher rates of smoking and alcohol consumption among men, may further exacerbate the risk [19].

Although AS and AR are more prevalent in men, tricuspid valve involvement is more common in women. Rheumatic stenosis of the mitral valve is three times more common in women than in men [25]. Degenerative stenosis of the mitral valve is also more prevalent in women, possibly due to higher rates of mitral annular calcification [28]. Moreover, rheumatic mitral insufficiency, tricuspid valve stenosis, and secondary tricuspid valve insufficiency are more common in women [29]. These differences may be assigned to changes in estrogen levels at various ages and their effects on heart valves.

Our findings demonstrate that while mild and moderate MS is more common in women, the severe form is more prevalent in men. This disparity may be attributed to higher rates of risky behaviors such as excessive alcohol consumption and smoking among men, which contribute to increased atherosclerosis and, hence, more severe mitral stenosis. Further, a traditional belief in male stubbornness often prevents men from seeking medical attention in the early stages of the disease, resulting in diagnoses at more advanced stages.

It appears that more severe MS is associated with a higher incidence of AF, as most cases of AF take place when the MVA is smaller than 0.5 cm^2. We found a statistically significant difference in the distribution of mitral stenosis severity between patients with and without rheumatic AR. Most patients, regardless of the presence of rheumatic AR, have also mild to moderate MS. it seems logical because the presence of rheumatic AR can impact the left atrium and mitral valve by enlarging the volume and pressure on the left ventricle, which might lead to MS.

We found that severe MS is more common among patients with comorbid mitral regurgitation. This indicates a relationship between the severity of mitral stenosis and the presence of mitral regurgitation. Although 22% of patients with severe MS do not have TR, more severe TR is often accompanied by more severe MS. This suggests a direct linear relationship between the severity of MS and TR. Both MS and TR can emanate from rheumatic heart disease, affecting multiple valves. Hence, the progression of rheumatic disease can lead to the simultaneous worsening of both MS and TR.

The data revealed a statistically significant difference in the prevalence of rheumatic tricuspid involvement and TS across different severities of MS. Patients with severe MS indicate higher rates of both rheumatic tricuspid involvement and TS compared to those with mild or moderate MS. Thus, severe mitral valve involvement is often linked to the involvement of multiple valves, irrespective of the underlying cause. We infer that as MS progresses, the heart's structural and functional integrity gradually deteriorates, elevating the risk of multiple valve involvement. Ultimately, altered hemodynamics-characterized by changes in blood flow dynamics and elevated pressures on adjacent structures, such as the tricuspid valve, would further contribute to the likelihood of multi-valvular damage.

We did not find any significant relationship between the severity of MS and age, heart rate, or aortic valve area. Nonetheless, a smaller body surface area was associated with more severe MS. Moreover, higher pulmonary artery pressure and PTMC scores were observed in patients with more severe MS. In severe MS, the obstruction of the valve results in increased pressure in the left atrium, which subsequently drains into the pulmonary veins. Over time, this culminates in changes to the pulmonary arteries and an increase in pulmonary pressure. Finally, rheumatic heart disease can independently cause valvular disease, leading to left ventricle dysfunction [30, 31].

In summary, our study is underpinned by several notable strengths. The robust sample size of above 1,000 patients collected over a five-year period from two major cardiology centers provided a solid foundation for reliable prevalence estimates and detailed clinical characterization. Further, the use of comprehensive echocardiographic evaluations along with standardized measurements boosted the accuracy of our findings. Nevertheless, certain limitations must be acknowledged. The hospital-based, cross-sectional design may restrict the generalizability of our results to the wider community of Mashhad, given the potential referral bias and the possibility that some patients originated from outside the city. In addition, the retrospective nature of the data collection and inherent variability in echocardiographic imaging, in spite of our strict exclusion criteria, could have introduced measurement inconsistencies. Unaccounted confounders, such as socioeconomic factors and differential access to healthcare, may have also influenced our observations. Future prospective and multicenter studies are warranted to further clarify the epidemiology of rheumatic heart disease and address these limitations.

Conclusion

This study of 1,035 rheumatic MS patients in northeastern Iran (prevalence: 0.3/1,000) found that while MS was more common in women, severe cases predominated in men, likely owing to delayed care and riskier behaviors. Severe MS often involved multiple valves, with higher pulmonary artery pressure and PTMC scores. Women indicated more tricuspid valve involvement, while 60.4% had concurrent aortic regurgitation, challenging the notion of isolated MS.

Despite downward prevalence aligning with global trends, the significant female predominance contrasts with greater male disease severity. These findings highlight the need for: 1) comprehensive echocardiographic evaluation to ascertain multivalvular involvement, 2) gender-specific management approaches addressing delayed male presentation and female susceptibility, as well as 3) strengthened primary and secondary prevention programs. The persistence of clinically significant MS burden underscores the significance of early detection, proactive care, and targeted interventions to lower complications, providing key insights for clinicians and policymakers in managing this pan-valvular disease.

Acknowledgments

The authors thank the Deputy of Research and Technology at Mashhad University of Medical Sciences for their support. This article is based on the doctoral thesis of Dr. Mohammad Baradaran Firoozabadi, completed as part of his medical degree requirements. We acknowledge his scholarly commitment and contribution to this work.

Conflict of interest

None declared.

Funding

We extend our sincere gratitude to the Mashhad Research Council for accrediting this research.

Ethical Considerations

The study adhered to the Helsinki ethical guidelines.

Code of Ethics

This study was approved by the Mashhad University Ethical Committee with Ethical Code: IR.MUMS.MEDICAL.REC.1399.114.

Authors' Contributions

Leila Bigdelu: study was conceived and designed, authored the final manuscript; Mohammad Baradaran Firoozabadi: study was conceived and designed, performed the data analysis, authored the final manuscript; Yousef Dowlatabadi: drafted the manuscript and contributed to its critical revision; Hedieh Alimi: drafted the manuscript and contributed to its critical revision; Hourak Poorzand: drafted the manuscript and contributed to its critical revision; Maryam Emadzadeh: provided language polishing and scientific editing; Fereshteh Ghaderi: provided language polishing and scientific editing.

References

1. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol. 2020;76(25):2982-3021.
2. Watkins DA, Johnson CO, Colquhoun SM, Karthikeyan G, Beaton A, Bukhman G, et al. Global, Regional, and National Burden of Rheumatic Heart Disease, 1990-2015. N Engl J Med. 2017;377(8):713-22.
3. Coffey S, Harper AR, Cairns BJ, Roberts IS, Prendergast BD. Clinical information has low sensitivity for postmortem diagnosis of heart valve disease. Heart. 2017;103(13):1031-5.
4. Marangou J, Beaton A, Aliku TO, Nunes MCP, Kangaharan N, Remenyi B. Echocardiography in Indigenous Populations and Resource Poor Settings. Heart Lung Circ. 2019;28(9):1427-35.
5. Aluru JS, Barsouk A, Saginala K, Rawla P, Barsouk A. Valvular Heart Disease Epidemiology. Med Sci (Basel). 2022;10(2):32.
6. Qazizadeh Z, Shahmoradi L, Moosazadeh M, Shahbaznejad L, Rezai MS. Prevalence of rheumatic heart disease in iran: A systematic review and meta-analysis. J Pediatr Rev. 2021;9(2):97-104.
7. Kumar A, Siddharth V, Singh SI, Narang R. Cost analysis of treating cardiovascular diseases in a super-specialty hospital. PLoS One. 2022;17(1):e0262190.
8. Hu Y, Tong Z, Huang X, Qin JJ, Lin L, Lei F, et al. The projections of global and regional rheumatic heart disease burden from 2020 to 2030. Front Cardiovasc Med. 2022;9:941917.
9. Tumenas A, Tamkeviciute L, Arzanauskiene R, Arzanauskaite M. Multimodality Imaging of the Mitral Valve: Morphology, Function, and Disease. Curr Probl Diagn Radiol. 2021;50(6):905-24.
10. Kawel-Boehm N, Maceira A, Valsangiacomo-Buechel ER, Vogel-Claussen J, Turkbey EB, Williams R, et al. Normal values for cardiovascular magnetic resonance in adults and children. J Cardiovasc Magn Reson. 2015;17(1):29.
11. Roth GA, Mensah GA, Fuster V. The global burden of cardiovascular diseases and risks: a compass for global action. Am Coll Cardiol. 2020;76(25):2980-1.
12. Mensah GA, Roth GA, Fuster V. The global burden of cardiovascular diseases and risk factors: 2020 and beyond. J Am Coll Cardiol. 2019;74(20):2529-32.
13. Guan C, Xu W, Wu S, Zhang J. Rheumatic heart disease burden, trends, and inequalities in Asia, 1990-2019. Glob Health Action. 2023;16(1):2215011.
14. Abdu SM, Kassaw AB, Tareke AA, Mankelkl G, Belete M, Bihonegn MD, et al. Prevalence and pattern of rheumatic valvular heart disease in Africa: Systematic review and meta-analysis, 2015–2023, population based studies. PLoS One. 2024;19(7):e0302636.
15. Gedefaw A, Yabebal YY, Wudie G, Tefera A, Kassa AK, Demilew T. Prevalence of pulmonary

hypertension and associated factors among rheumatic heart disease patients in Ethiopia. BMC Cardiovasc Disord. 2025;25(1):20.
16. Zuhlke L, Karthikeyan G, Engel ME, Rangarajan S, Mackie P, Cupido-Katya Mauff B, et al. Clinical Outcomes in 3343 Children and Adults With Rheumatic Heart Disease From 14 Low- and Middle-Income Countries: Two-Year Follow-Up of the Global Rheumatic Heart Disease Registry (the REMEDY Study). Circulation. 2016;134(19):1456-66.
17. Kumar RK, Antunes MJ, Beaton A, Mirabel M, Nkomo VT, Okello E, et al. Contemporary Diagnosis and Management of Rheumatic Heart Disease: Implications for Closing the Gap: A Scientific Statement From the American Heart Association. Circulation. 2020;142(20):e337-57.
18. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol. 2020;76(25):2982-3021.
19. Napoli F, Vella C, Ferri L, Ancona MB, Bellini B, Russo F, et al. Rheumatic and Degenerative Mitral Stenosis: From an Iconic Clinical Case to the Literature Review. J Cardiovasc Dev Dis. 2024;11(5):153.
20. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. Eur J Echocardiogr. 2009;10(1):1-25.
21. Dwigustiningrum NK, Rahimah AF, Karolina W, Martini H. Echocardiography Features in Patient Rheumatic Mitral Stenosis. Heart Sci J. 2024;5(2):23-30.
22. Mansouritorghabeh H, Bagherimoghaddam A, Eslami S, Raouf-Rahmati A, Hamer DH, Kiani B, et al. Spatial epidemiology of COVID-19 infection through the first outbreak in the city of Mashhad, Iran. Spat Inf Res. 2022;30(5):585-95.
23. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. Lancet Infect Dis. 2005;5(11):685-94.
24. Ginting Munte FA, Ahmadi AP, Fauziah M, Hasanah DY. Mitral facies-a classic feature of chronic mitral stenosis: A case report. SAGE Open Med Case Rep. 2023;11:2050313X231200965.
25. Movahed MR, Ahmadi-Kashani M, Kasravi B, Saito Y. Increased prevalence of mitral stenosis in women. J Am Soc Echocardiogr. 2006;19(7):911-3.
26. Stassen J, Butcher SC, Namazi F, Ajmone Marsan N, Bax JJ, Delgado V. Left Atrial Deformation Imaging and Atrial Fibrillation in Patients with Rheumatic Mitral Stenosis. J Am Soc Echocardiogr. 2022;35(5):486-94.e2.
27. Baqai L, Rasheed S, Nasim N, Balouch IJ, Gurmani S, Kubra G. Tricupsid valve involvement in chronic rheumatic mitral stenosis: An observational study. Prof Med J. 2021;28(09):1315-21.
28. Pasca I, Dang P, Tyagi G, Pai RG. Survival in Patients with Degenerative Mitral Stenosis: Results from a Large Retrospective Cohort Study. J Am Soc Echocardiogr. 2016;29(5):461-9.
29. Youssef G. Valvular heart diseases in women. Egypt Heart J. 2021;73(1):58.
30. Maeder MT, Weber L, Buser M, Gerhard M, Haager PK, Maisano F, et al. Pulmonary Hypertension in Aortic and Mitral Valve Disease. Front Cardiovasc Med. 2018;5:40.
31. Magne J, Pibarot P, Sengupta PP, Donal E, Rosenhek R, Lancellotti P. Pulmonary hypertension in valvular disease: a comprehensive review on pathophysiology to therapy from the HAVEC Group. JACC Cardiovasc Imaging. 2015;8(1):83-99.