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Gender Differences in Rheumatic Heart Disease: Data from a District Hospital in Cirebon, Indonesia

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Abstract
Rheumatic heart disease (RHD) has a high prevalence in low- and middle-income countries, including Indonesia. Gender is among the sociodemographic factors that can influence RHD prevention and management strategies. This study aims to describe the clinical profile of RHD patients, with a focus on gender differences. This cross-sectional study was conducted at Hasna Medika Cardiovascular Hospital in Cirebon, Indonesia. This study included RHD patients in the outpatient clinics, either who came for routine treatment or were newly diagnosed with RHD. Patients' demographic and clinical data were collected through medical records from January 2023 to December 2023. A total of 157 patients' data were analyzed. RHD was more common in women (70.7%) than men (29.3%). The incidence of RHD in women was higher (27.9%) in the age group 60 years old and above than in men (19.6%). The most common valve involved in RHD was the mitral valve, more frequently in women (100%) than men (97.8%), with severe mitral stenosis being the most prevalent valve abnormality in both genders (52.3% in women, 47.8% in men). Women have a higher prevalence of RHD than men. This study emphasises the importance of education and the needed improvement of RHD management strategies, specifically for women, as they have a higher burden of RHD.
Keywords : gender, rheumatic heart disease, RHD, women, heart valve diseases

Introduction

Rheumatic heart disease (RHD) remains a major burden in developing countries. Globally, there are more than 33 million cases of RHD, according to a recent survey. Nevertheless, these data may underestimate the disease burden, due to underreporting, limited healthcare resources, and a small number of systematic registry healthcare program in the low- and middle-income countries where the disease is becoming endemic.

For the Asian region, the age-standardized prevalence was lower than the global estimate (465.6 cases per 100,000 population vs. 513.7 cases per 100,000 population), according to a study conducted by C. Guan et al. As for Indonesia, it was one of the countries with the highest number of RHD cases in 2015. According to a study done by Muharram et al., women in Indonesia have a higher prevalence of RHD than men. It is in concordance with many previous studies. Aside from several possible hypotheses, such as females' innate immunological sensitivity, the need to have a better healthcare system, especially for women, is highlighted. Based on several studies, the prevalence of RHD is prominent in women of reproductive age. This has significant implications for maternal and perinatal health, as it can increase the burden of cardiovascular complications and death during pregnancy. Hence, this study aims to describe the clinical profile of RHD patients with a focus on gender differences, as it is an essential part of determining and improving prevention and management strategies for RHD patients.

Research Methods

Study design

This cross-sectional study was conducted at Hasna Medika Cardiovascular Hospital in Cirebon, Indonesia. A total of 157 patients' data were analyzed from January 2023 to December 2023 using a total sampling technique.

Study population and data collection

This study included RHD patients aged 19 and above who visited the outpatient clinic. The patients included were both patients who came for routine treatment and patients who were newly diagnosed with RHD. The demographic and clinical data were obtained from the hospital's medical records. The results of echocardiography examination were used to determine the characteristics of valve disorders and the severity of rheumatic valve disease.

Statistical analysis

The subject's data were described using descriptive statistics. Frequencies and percentages were available for categorical variables. The mean and standard deviation (SD) were shown for continuous variables. The statistical significance of gender-based differences in the distribution of categorical variables was tested using the chi square test and fisher's exact test. The p-value of <0.05 was taken as statistical significance. The statistical analysis was done using IBM SPSS Statistics version 27 statistical software.

Ethics

This study was conducted according to the principles of the Declaration of Helsinki and has been approved by the ethics committee of Gunung Jati Hospital Cirebon City No. 058/LAIKETIK/KEPPKRSGJ/IX/2024.

Results and Discussion

Population

A total of 157 patients' data were included in the study and analyzed. The results showed that majority of RHD patients were female (70.7%). The mean ± SD age of sample was 50.3 ± 12.2 years, with age range of 19-83 years. The highest proportion of RHD patients were aged 40-49 years (35%). In this study, we also found that 25.5% of RHD patients were elderly. Based on educational level, it was found that the majority of the sample had a low educational level, namely 1.3% had no formal education and 94.3% had elementary school graduates. Most of the samples were housewives (64,9%), followed by informal workers (33,1%). About 81.5% of the sample lives in Cirebon district and 5.7% in Cirebon city. All samples used national health insurance for payment of health services. Over a hundred patients had atrial fibrillation (AF) (78.3%) and pulmonary hypertension (PH) (73.2%) as complications. A total of 111 (70.7%) patients were indicated to have surgical procedure. Among them, 97 (87.4%) patients refused to have the surgery. (Table 1)

Table 1. Socio-demographics and clinical characteristics of study population (n=157)

Characteristics		Frequency	Percentage (%)
Sex	Male	46	29.3
	Female	111	70.7
Age group	19–29 years	4	2.5

Characteristics		Frequency	Percentage (%)
	30–39 years	23	14.6
	40–49 years	55	35
	50–59 years	35	22.3
	≥60 years	40	25.5
Level of education	No formal education	2	1.3
	Elementary school	148	94.3
	High school education	5	3.2
	University graduated	2	1.3
Occupational status	Unemployed	1	0.6
	Informal worker	52	33,1
	Civil servant	2	1.3
	Housewife	102	64.9
Living area	Cirebon regency	128	81.5
	Cirebon city	9	5.7
	Other area	20	12.7
Health service payment	National health insurance	157	100
	Private insurance	0	0
	Out of pocket	0	0
RHD complication	Atrial fibrillation	123	78.3
	Pulmonary hypertension	115	73.2
Indication for surgery	No	46	29.3
	Yes	111	70.7
	Agreed to	14	12.6
	Refused to	97	87.4

The most common valve affected was mitral valve (99.4%), with mitral stenosis (91.08%) as the most prevalent form of valvular disease. A total of 68 (43.31%) patients had both mitral and aortic valve lesions. (Figure 1)

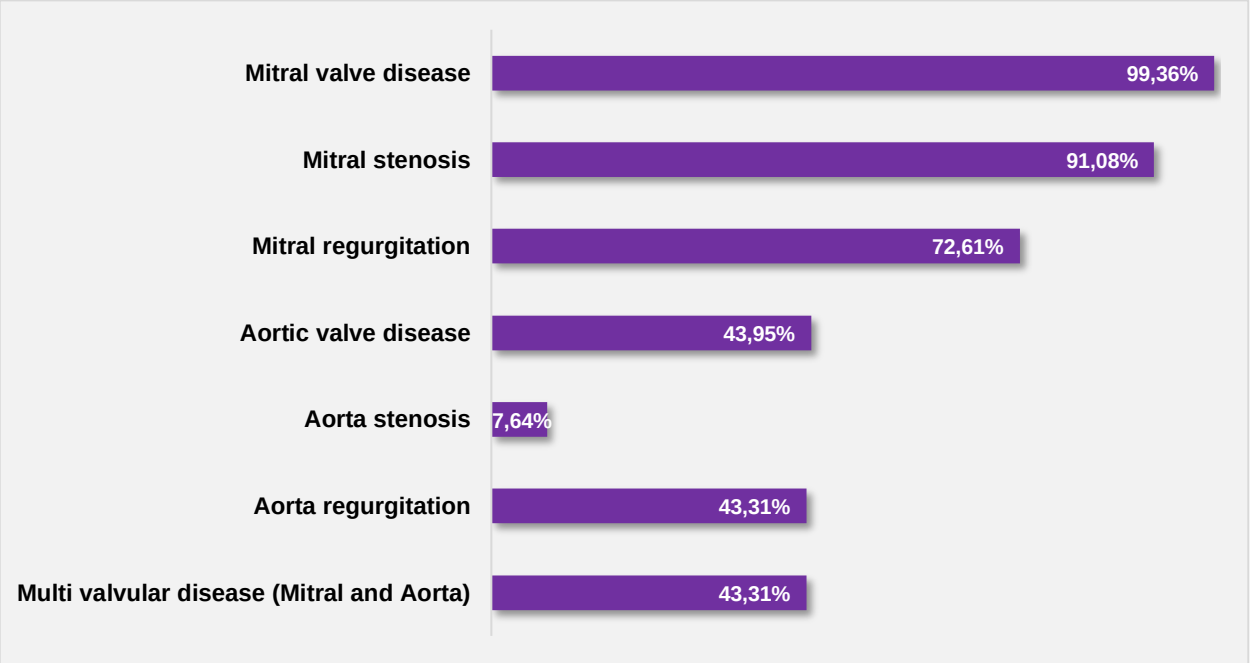
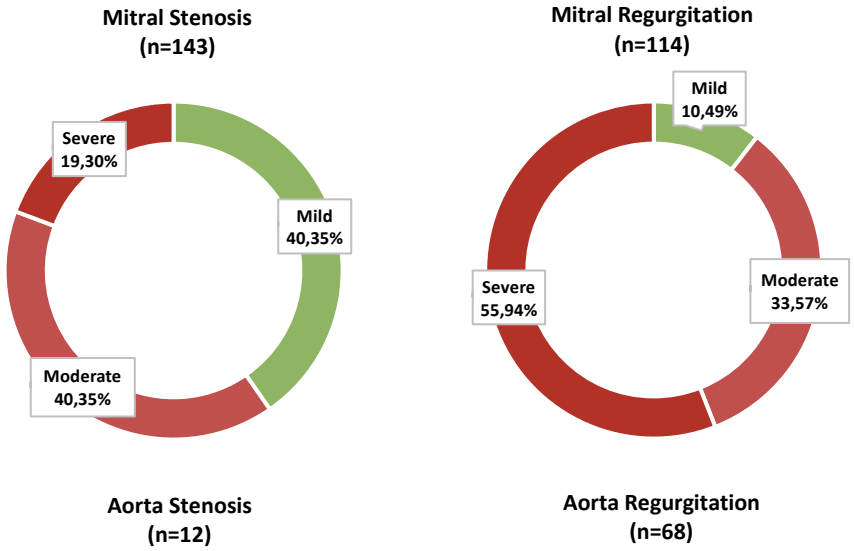


Figure 1. Rheumatic valve disease characteristics

Figure 2 shows the severity of rheumatic valve disease experienced by the sample. A total of 19.3% of samples with mitral stenosis experienced severe mitral stenosis. Of those who experienced mitral regurgitation, the majority experienced severe mitral regurgitation (55.94%). Samples with aortic stenosis experienced severe disorders as much as 41.67%. Of the 68 samples with aortic regurgitation, 4.41% experienced severe degrees.



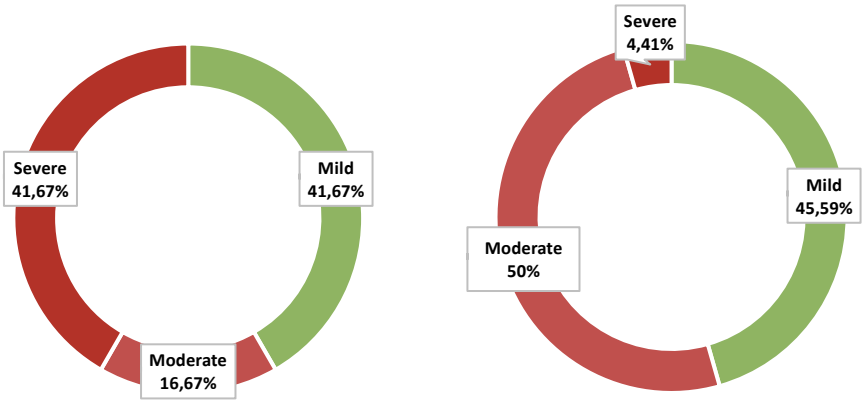


Figure 2. Severity of rheumatic valve disease in RHD patients

Characteristics based on gender differences

The prevalence of RHD was higher in female patients (70.7%) than in male patients (29.3%). Table 4 shows the distribution of characteristics based on gender differences. In the age group between 40 and 49 years, the prevalence of RHD was higher in males (39.1%) than females (33.3%), whereas older patients (≥60 years) were more dominated by females than males (27.9% vs 19.6%). All the female patients (100%) have mitral valve abnormalities, with severe mitral stenosis (52.3%) being the most common severity of valve lesion. The prevalence of multivalvular disease and complications in both genders was almost identical but higher in females. However, the differences related to valve lesions, the severity of the valve, and complications in both genders were statistically insignificant.

Table 2. Distribution of characteristics based on gender differences

Variables	Male (n = 46) n (%)	Female (n = 111) n (%)	P value
Age groups			
19–29 years	1 (2.2)	3 (2.7)	0.572
30–39 years	5 (10.9)	18 (16.2)	
40–49 years	18 (39.1)	37 (33.3)	
50–59 years	13 (28.3)	22 (19.8)	
≥60 years	9 (19.6)	31 (27.9)	
Age, in years (mean ± SD)	50.4 ± 11.1	50.3 ± 12.7	0.963
RHD complication			
Atrial fibrillation	36 (78.3)	87 (78.4)	0.571
Pulmonary hypertension	34 (73.9)	81 (73)	0.536
Surgery			
Indicated	31 (67.4)	80 (72.1)	
Refused	29 (93.5)	68 (85)	

As for surgical intervention, 67.4% of male patients and 72.1% of female patients were indicated to have surgery, but most of them (93.5% in males, 85% in females) refused the procedure.

Discussion

This study has two key results. First, mitral stenosis was the most common valve lesion. Second, based on gender differences, women were predominant in RHD. The mitral valve is the most common valve affected by RHD. Mitral valve lesions typically start as regurgitant lesions, and as the damage continues, stenosis develops.(Simpson et al., 2023) In this study, mitral stenosis was the most prevalent mitral valve lesion involved in RHD. This finding is in contrast with data from several previous studies, as they reported mitral regurgitation as the most common valve lesion found in RHD. A study conducted by (Rudiktyo et al.,2022) stated that this disparity of findings may be caused by the differences in the age group of study population. Studies that included patients younger than 18 years old found mitral regurgitation to be the most prevalent valve lesion, whereas several studies with subjects older than 18 years old reported mitral stenosis as the most common affected valve. One of the possible explanations is that mitral stenosis became more common in patients from the fourth to the sixth decade of life. This interpretation may represent the pathogenesis of RHD in that mitral stenosis usually develops later than mitral regurgitation following the first episode of acute rheumatic fever.

In this study, 43.3% of patients had aortic and mitral valve lesions. As stated in a study done by Owusu et al., the involvement of the aortic valve may be linked to the greater impact RHD has on the left-sided heart, with the mitral valve appearing to be the most affected.

Based on age group, the highest prevalence of RHD is between 40 and 49 years old. This finding is in line with a study done by (Shi et al., 2023), where it was found that RHD is more prevalent in people under 50 years old. (Lv et al., 2022) also found the prevalence of RHD to be higher in the age group of 15–49 years old. These results show the importance of early screening and a better management strategy for people under 50 years old to prevent the progression of RHD.

Most patients in this study were indicated to have surgical procedures as part of their treatment of RHD. However, most of them refused to comply. This refusal to undergo cardiac surgery may be caused by several factors, such as fear of the procedure and the fact that the patients felt that the symptoms were tolerable.

Gender-based differences

There was notable gender-based differences observed in this study. Female patients were found to have a higher prevalence of RHD compared with male patients. This finding was in accordance with many of the previous studies. The cause of this remains unclear. Studies hypothesize that this could be due to females' genetic immunological susceptibility, hemodynamic changes during pregnancy, the increased probability of acquiring Group A streptococcus (GAS) infection caused by women's involvement in childcare, or reduced access to medical care for girls and women.

This study also found that the number of mitral stenosis was higher in female than male patients. On the contrary, aortic regurgitation was higher in male patients. Although these results were statistically insignificant, a study done by (Negi *et al.,* 2020) revealed the significance of these results.(Negi et al., 2020) Both findings are also consistent with several previous studies.(Movahed et al., 2006; Ozer et al., 2009) The statistical insignificance may be related to the small sample size used in this study. These findings remain to be explored.

A study done by (Mutagaywa *et al.,* 2020) stated that mitral stenosis is frequently predominated by females, but there is a difference in the epidemiological presentation of mitral stenosis based on regions. In Africa, the prevalence of MS is higher in women with an early presentation in life (31 years), whereas in South Asia and western countries, the prevalence of

mitral stenosis is dominated by women with a higher mean age of 39 years.

In this study, compared with males, RHD in female patients was found to be higher in the age group of 60 years old and older. As observed in a study conducted by (Kislitsina *et al.*, 2019), the pathology of mitral valve is playing a significant role in gender-based differences. Compared to males, females with RHD are found to be older, have more symptoms, and have more comorbidities. There is postulation that females have a different presentation than males, such as a higher prevalence of preserved left ventricular function, less clear symptoms, and poor socioeconomic status, causing them to have late referrals for intervention and therefore frequently come in an already advanced state.

Rheumatic heart disease occurs as an autoimmune sequela of acute rheumatic fever (ARF). ARF primarily affects school-aged children, which is most likely caused by GAS transmission among students. In many populations and studies, the prevalence of ARF, as with RHD, is more common in females than males. Additionally, research has indicated that women of childbearing age are more prone to RHD, and this could have an effect on maternal health, increasing the risk of morbidity and mortality in pregnancy. These occurrences create a higher burden of RHD in girls and women, especially in developing countries where there are still many impoverished neighborhoods, socioeconomic constraints, limited awareness and education about RHD, a lack of prophylactic measures, and limited access to healthcare.

According to a study done by Hu *et al*., global prevalence, death, and HF burden related to RHD will remain higher in females than in males by 2030. The importance of improving the health system, including awareness and education about RHD, is vital to ensuring that patients receive adequate and reliable treatment, particularly young girls and women. Early detection and RHD prevention measures are immensely needed, as patients in this study most frequently come in an already advanced state. Additionally, there should be more attention given to women of childbearing age by implementing cardiac examination and treatment for high-risk women before and during pregnancy.

Limitations

This study has several limitations. First, it has selection bias because the study was conducted in a cardiovascular district hospital and involved only data from the outpatient clinic. Second, the patients in this hospital only come from the surrounding area of the hospital, resulting in the small sample size used in this study. Thus, this study may have low external validity as the sample is not representative of the population.

Conclusion

This study addresses the higher prevalence of rheumatic heart disease (RHD) in women compared to men, which is suspected to be influenced by genetic susceptibility. Despite this significant burden, current RHD management strategies may not adequately cater to the specific needs of women, potentially exacerbating disease outcomes. The lack of targeted educational initiatives and gender-sensitive healthcare interventions further highlights the need for improved approaches. Therefore, this study aims to investigate the role of genetic predisposition in RHD among women, assess the effectiveness of existing management strategies, and propose necessary improvements in education and healthcare interventions to reduce the burden of RHD in women.

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