JACC: ASIA VOL. 5, NO. 9, 2025
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ORIGINAL RESEARCH

Characteristics and Problems of Rheumatic Heart Disease in Indonesia

The Ina-RHD Multicenter Study

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ABSTRACT

BACKGROUND Rheumatic heart disease (RHD) presents a significant public health challenge. Unfortunately, there is a lack of national data regarding the incidence and prevalence of RHD in Indonesia.

OBJECTIVES The purpose of this study was to evaluate the characteristics, burdens, and problems of RHD in Indonesia.

METHODS We collected medical reports of RHD patients over 18 years of age from 21 hospitals. Secondary data about clinical and echocardiography was collected to describe the characteristics, disease conditions, and complications of the disease.

RESULTS We recruited 3,431 patients, average age was 44 years, and 64.4% (2,209 of 3,431) were women. Dyspnea was found in 85.7% (2,939 of 3,431), and 25% (862 of 3,431) of patients with NYHA functional class III to IV. Isolated mitral stenosis was the most prevalent valve lesion in 1,357 of 3,431 patients (39.6%). A total of 62.5 % (2,146 of 3,431) of patients had atrial fibrillation (AF), with the highest prevalence being in MV lesions. Vitamin K antagonist was prescribed in 2,411 of 3,431 (70.3%) of patients. A history of stroke was reported in 227 of 3,431 (6.6%) of patients and most frequently happened in isolated mitral stenosis patients 128 of 1,357 (9.4%). Finally, secondary prophylaxis was only administered in 1,279 of 3,431 (37.3%) of patients, and only 23.2% (796 of 3,431) had it regularly.

CONCLUSIONS Our patients were predominantly women and had isolated mitral stenosis. Many patients came at a later stage of the disease, with older average age, a high prevalence of AF, pulmonary hypertension, and right heart involvement. The challenges were suboptimal use of anticoagulation despite the high prevalence of AF and underused secondary prophylaxis. (JACC Asia. 2025;5:1171–1183) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ISSN 2772-3747 https://doi.org/10.1016/j.jacasi.2025.03.010

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

BPG = benzathine penicillin G

INR = International Normalized Ratio

MR = mitral regurgitation

MS = mitral stenosis

MV = mitral valve

OAC = oral anticoagulant

PVR = pulmonary vascular resistance

VKA = vitamin K antagonist

Rheumatic heart disease (RHD) presents a significant public health challenge. A report showed a global increase in the incidence and prevalence rates of RHD, with an estimated 40.5 million people worldwide, although declining in death rates of approximately 305,000 deaths per year. The burden mainly affects lower-income countries.[1] A newer report analyzed the trend of RHD in high-income countries in Europe, America, Canada, and Australia and demonstrated an overall decline in 2019 from 1990 in RHD incidence and mortality. However, more than one-half of those countries showed a recent increase in RHD incidence rate.[2] Another newer report showed that the age-standardized incidence rate and age-standardized prevalence rate in Asian countries vary widely. However, the South Asia super region had the highest age-standardized disability-adjusted life years and deaths among all countries, globally.[1]

Despite the profound impact of this health crisis, there is a lack of systematically collected contemporary data on the disease characteristics, treatment, complications, and long-term outcomes of patients with RHD. This condition is particularly evident in the need for adequate data collection systems in developing countries, including Indonesia. Therefore, it is imperative to collect more comprehensive and up-to-date data on RHD to develop targeted strategies to alleviate the burden of this disease.[3] Several studies have been conducted to collect data on patient characteristics and treatment patterns in RHD patients and the projected global and regional burden of RHD from 2020 to 2030.[4-6] The acquisition of more comprehensive and up-to-date data is anticipated to aid in developing more effective strategies to reduce the disease burden of RHD.

Indonesia is considered one of the significant contributors to RHD cases worldwide. A report on the global, regional, and national burden of RHD reported that more than 73% of the cases came from India, China, Pakistan, Indonesia, and the Republic of Congo, where most of those countries are in Asia.[7] However, the data was derived from some algorithms and extrapolation of the studies reported from 1990 to 2015. Several recent studies from Indonesia showed variations in RHD prevalence and RHD cases in several hospitals. Those studies are relatively small and originated in just a few areas of Indonesia,[8-12] Unfortunately, the national data to understand the disease burden is lacking. We initiated a multicenter study—Ina-RHD (the Indonesia Rheumatic Heart Disease Study)—to gain an essential insight into the current state of RHD in Indonesia, including the baseline of patient characteristics, and address important issues in managing RHD. Our study will provide additional perspectives on national and local challenges. It may further facilitate the development of a targeted strategy for RHD control in Indonesia and other Asian countries with similar problems, potentially making a significant impact on the global fight against RHD.[7]

METHODS

STUDY DESIGN, STUDY POPULATION, AND STUDY ELIGIBILITY. This is the first phase of a prospective, national, multicenter, hospital-based study known as Ina-RHD. The study was conducted in 21 hospitals in 14 provinces of Indonesia, which were regional reference hospitals placed in several big islands, with

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received November 6, 2024; revised manuscript received March 11, 2025, accepted March 11, 2025.

TABLE 1 Baseline Demographic Characteristics of 3,431 Subjects With Rheumatic Heart Disease (N = 3,431)

Age, y	44 (18-82)
Gender	
Female	2,209 (64.4)
Male	1,222 (35.6)
Body surface area, m^2	1.55 (1.08-2.52)
Medical coverage	
Class III	2,216 (64.6)
Class II	395 (11.5)
Class I/VIP/insurance/private	820 (23.9)

Values are median (minimum-maximum) or n (%) as appropriate. Medical coverage indirectly showed the economic level of the subjects based on the health insurance premium payment. Class III is the lowest level, class II is intermediate level, and class I/VIP/insurance/private is the highest level.

echocardiologist consultants to ensure the validity of echocardiography data. Operational definition and universal case report forms were applied to avoid bias that might influence results. We collected data from the medical records of patients over 18 years of age with a clinical and echocardiographic diagnosis of RHD from the outpatient, inpatient, or emergency department from January 2020 to June 2023. Patients are dropped from analysis if they have any missing data. The severity of the valve lesion was evaluated based on the American Heart Association/American College of Cardiology guidelines for managing valvular heart disease.[13]

Compliance with secondary prophylaxis was based on how routinely the subject received the regiments for the last 12 months. It could be a benzathine penicillin G (BPG) injection every 3 to 4 weeks or oral regimens twice a day. Evaluation of the INR was considered routine if checked every month, not routine if checked within 1 to 6 months, and seldom/never if checked more than 6 months ago. The right heart involvement was positive when echocardiography detected at least 1 of these conditions: dilated right atrium (area >18 cm^2), dilated right ventricle (RV) (basal RV diameter >41 mm or mid RV >35 mm or RV > left ventricle [LV] dimension), and plethora of inferior cava veins (diameter >21 mm with collapsibility <50%).[14]

Demographic data, clinical findings, and details of electrocardiographic and echocardiographic findings were recorded in case report forms at the research centers and sent to the National Cardiovascular Centre Harapan Kita as the research coordinator's office. The data was processed for verification, ensuring data quality and storage. This study protocol and approval were reviewed and obtained from the ethical boards of each of the 21 hospitals in 14 provinces in Indonesia.

STATISTICAL ANALYSIS. A manual data verification method was applied to ensure the data was correctly entered. Baseline characteristics and clinical data were presented using descriptive statistics. Numeric variables were displayed as or mean ± SD as median (minimum-maximal ranges) as appropriate, whereas categorical variables were displayed as absolute numbers (percentages). For the bivariate model, a comparison between 2 variables was analyzed using an unpaired Student's *t*-test for continuous variables and chi-square test for categorical variables. A statistically significant value is when $P < 0.05$. Data analysis was performed using SPSS version 25.0 (SPSS, IBM).

RESULTS

BASELINE, CLINICAL, AND ECHOCARDIOGRAPHIC CHARACTERISTICS. This study included 3,431 patients who met the inclusion criteria. Baseline demographic characteristics are shown in Table 1. The median age of subjects was 44 years, and 2,209 of 3,431 (64.4%) of subjects were women. The mean body surface area was 1.55 m^2. Most subjects (64.6%, 2,216 of 3,431) had access to government health insurance at its lowest level (class III), which corresponds to a low economic level.

Clinical presentations are shown in Table 2. Dyspnea (85.7%, 2,939 of 3,431), palpitations (24.2%, 829 of 3,431), edema (15.3%, 526 of 3,431), chest pain (13.5%, 463 of 3,431), and fatigue (12.5%, 430 of 3,431) were the most prevalent symptoms. Among the patients, 862 of 3,431 (25.1%) were in NYHA functional class III to IV. Only 231 of 3,431 subjects (6.7%) reported having a history of rheumatic fever. Several comorbidities were identified in a small percentage of patients. The most common comorbidity was hypertension (9.6%, 329 of 3,431), and atrial fibrillation (AF) was found in 2,146 of 3,431 (62.5%) patients. There were 86 of 3,431 (2.5%) patients with a stroke at admission, whereas only 11.6% (10 of 86) of them had the first stroke attack. Further, 227 of 3,431 (6.6%) had a history of stroke.

Medication data showed that only 1,279 of 3,431 (37%) of the patients received secondary prophylaxis, whereas 796 of 1,279 (62%) of them took it regularly, and only 147 of 1,279 (11.5%) used BPG. Other medications commonly used were diuretic agents in 2,741 of 3,431 (79.9%) patients, beta-blockers in 2,555 of 3,431 (74.5%), vitamin K antagonist (VKA) in 2,411 of 3,431 (70.3%), mineralocorticoid receptor antagonist in 2,202 of 3,431 (64.2%), angiotensin-converting enzyme inhibitor/angiotensin receptor blocker in 1,418 of 3,431 (41.3%), and digitalis in 1,005 of 3,431

TABLE 2 Clinical Presentations of 3,431 Subjects With Rheumatic Heart Disease (N = 3,431)

Symptoms	
Dyspnea	2,939 (85.7)
Palpitations	829 (24.2)
Ankle edema	526 (15.3)
Chest pain	463 (13.5)
Fatigue	430 (12.5)
Ascites	115 (3.4)
Stroke	86 (2.5)
Syncope	49 (1.4)
Hemoptysis	29 (0.8)
Bleeding	7 (0.2)
NYHA functional class	
I-II	2,569 (74.9)
III-IV	862 (25.1)
Known history of rheumatic fever	
Yes	231 (6.7)
No	3,200 (93.3)
Comorbidities	
Hypertension	329 (9.6)
Diabetes mellitus	141 (4.1)
Chronic lung disease	133 (3.9)
Coronary heart disease	117 (3.4)
Dyslipidemia	99 (2.9)
Infection	93 (2.7)
Renal failure	81 (2.4)
Malignancy	17 (0.5)
Chronic liver disease	17 (0.5)
Thyroid	17 (0.5)
Reactivation rheumatic fever	13 (0.4)
Congenital heart disease	10 (0.3)
Peripheral arterial disease	9 (0.3)
Autoimmune	8 (0.2)
Anemia	2 (0.1)
Others	38 (1.1)
ECG	
Sinus	1,277 (37.2)
AF	2,146 (62.5)
Others[a]	8 (0.2)
Secondary prophylaxis	
Yes, regularly	796 (23.2)
Yes, not regularly	483 (14.1)
No	2,152 (62.7)
Secondary prophylaxis drugs (n = 1,279)	
BPG	147 (11.5)
Oral penicillin	1,023 (80)
Oral erythromycin	109 (8.5)
Medications	
Diuretic agent	2,741 (79.9)
Beta-blockers	2,555 (74.5)
VKA	2,411 (70.3)
MRA	2,202 (64.2)
ACEI/ARB	1,418 (41.3)
Digitalis	1,005 (29.3)
Antiplatelet	127 (3.7)
DOAC	16 (0.5)
Amiodarone	8 (0.2)
Others	104 (3)
History of IE	
Yes	22 (0.6)
No	3,409 (99.4)
History of stroke	
Once	210 (6.1)
More than once	17 (0.5)
Never	3,204 (93.4)
Prior HF admission	
Once	808 (23.5)
More than once	376 (11)
Never	2,247 (65.5)
Echocardiography data	
LVEF, %	59 (10-90)
TAPSE, mm	19 (2-45)
Probability of PH	
Low	1,107 (32.3)
Intermediate	800 (23.3)
High	1,524 (44.4)
Significant functional TR	1,009 (29.4)
Right heart involvement	
No	1,715 (50)
Yes	1,716 (50)

Values are n (%) or median, as appropriate. [a]Others include pacing rhythm (n = 4), junctional rhythm (n = 3), and total AV block (n = 1).

ACEI = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin receptor blocker; BPG = benzathine penicillin G; ECG = electrocardiography; HF = heart failure; IE = infective endocarditis; LVEF = left ventricular ejection; MRA = mineralocorticoid receptor antagonist; DOAC = direct oral anticoagulant; PH = pulmonary hypertension; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation; VKA = vitamin K antagonist.

Continued in the next column

(29.3%) patients. A history of stroke or recurrent stroke was seen in 227 of 3,431 (6.6%) patients. A history of hospitalization caused by heart failure was observed in 1,184 of 3,341 (34.5%) patients.

The echocardiographic data showed that isolated mitral stenosis (MS) with or without concomitant tricuspid regurgitation (TR) was the most common valve lesion observed in 1,357 of 3,431 patients (39.6%). It was followed by multiple mitral valve (MV) and aortic valve (AV) lesions with or without TR in 828 of 3,431 (24.1%) patients and mixed MV lesions in 560 of 3,431 (16.3%) patients. Triple valve diseases involving the aortic, mitral, and tricuspid valve lesions were present in 437 of 3,431 (12.7%) patients. The mixed MV lesions group had the highest prevalence of AF and tricuspid annular plane excursion (TAPSE) <16 mm, which was found in 433 of 560 (77.3%) and 181 of 560 (32.3%) patients, respectively. A high probability of pulmonary hypertension (PH) and clinical signs of right heart involvement was found in 669 of 1,357 (49.3%) and 746 of 1,357 (55%) patients, respectively, in the isolated MS group.

TABLE 3 Clinical Presentations Based on Specific Valve Lesions

	Isolated MS (± TR) (n = 1,357)	Isolated MR (± TR) (n = 510)	Mixed MV (± TR) (n = 560)	Isolated AS (± TR) (n = 35)	Isolated AR (± TR) (n = 102)	Mixed AV (± TR) (n = 39)	Multiple AV and MV (± TR) (n = 828)
Female	941 (69.3)	341 (66.9)	396 (70.7)	13 (37.1)	46 (45.1)	14 (35.9)	458 (55.3)
Age, y	45 (18-82)	42 (18-82)	45 (19-78)	54.69 ± 11.4	41.53 ± 13.1)	49.08 ± 11.3)	43 (18-80)
AF	955 (70.4)	237 (46.5)	433 (77.3)	9 (25.7)	21 (20.6)	7 (17.9)	484 (58.5)
LVEF <50%	220 (16.2)	96 (18.8)	87 (15.5)	7 (20)	35 (34.3)	17 (43.6)	189 (22.8)
TAPSE <16 mm	409 (30.1)	87 (17.1)	181 (32.3)	8 (22.9)	10 (9.8)	4 (10.3)	218 (26.3)
Probability of PH							
Low	391 (28.8)	216 (42.4)	135 (24.1)	30 (85.7)	75 (73.5)	23 (59)	237 (28.6)
Intermediate	297 (21.9)	127 (24.9)	154 (27.5)	3 (8.6)	17 (16.7)	8 (20.5)	194 (23.4)
High	669 (49.3)	167 (32.7)	271 (48.4)	2 (5.7)	10 (9.8)	8 (20.5)	397 (47.9)
Significant functional TR	417 (30.7)	148 (29)	183 (32.7)	2 (5.7)	10 (9.8)	6 (15.4)	243 (29.3)
Right heart involvement	746 (55)	206 (40.4)	291 (52)	5 (14.3)	19 (18.6)	6 (15.4)	443 (53.5)
Intracardiac thrombus	205 (15.1)	8 (1.6)	18 (3.2)	1 (2.9)	1 (1)	0	56 (6.8)
History/current stroke	128 (9.4)	21 (4.1)	43 (7.7)	2 (5.7)	8 (7.8)	0	35 (4.2)

Values are n (%), or median (minimum-maximum), or mean ± SD.

AR = aortic regurgitation; AS = aortic stenosis; AV = aortic valve; MR = mitral regurgitation; MS = mitral stenosis; MV = mitral valve; other abbreviations as in Table 2.

Intracardiac thrombi and a history of stroke were also found most frequently in the isolated MS group, with a prevalence of 205 of 1,357 (15.1%) patients and 128 of 1,357 (9.4%), respectively. The complete comparison of demography, clinical, and echocardiography variables among each type of valve lesion is shown in Table 3.

We performed a subgroup analysis based on electrocardiographic rhythm, as shown in Table 4. A significantly higher prevalence of intracardiac thrombus was observed in patients with AF than those in sinus rhythm (11.8%, 254 of 2,146 vs 2.7%, 35 of 1,277; 95% CI: 0.15-0.30; $P < 0.001$). History of stroke was also more common in the AF group than in the sinus rhythm group (7.6%, 164 of 2,146 vs 5.6%, 72 of 1,277; 95% CI: 0.54-0.96; $P = 0.030$). One stroke patient who had pacemaker rhythm was excluded from the statistical calculation. Although anticoagulant use was considerably higher in the AF group compared with the SR group (85.6%, 1,837 of 2,146 vs 44.6%, 570 of 1,277; 95% CI: 0.12-0.16; $P < 0.001$), the adequate international normalized ratio (INR) level was only achieved in 34.9% (203 of 581) of routinely INR-tested patients (Table 4). However, there was no significant association found between the INR level and history of stroke ($P = 0.349$), as seen in Table 5. Based on the valve lesions, the most frequent AF was found in mixed MV disease (77.3%, 433 of 560), followed by MS (70.4%, 955 of 1,357), multiple AV and MV diseases (58.5%, 484 of 828), and mitral regurgitation (MR) (46.5%, 237 of 510) as shown in Figure 1.

We found that 33.4% (1,147 of 3,431) of our patients were over 50 years of age. A subgroup analysis was performed based on age ≤50 years and more than 50 years. As shown in Table 6, dyspnea (87%, 1,987 of 2,284 vs 83%, 952 of 1,147; 95% CI: 0.60-0.88; $P = 0.002$) and palpitations (25.3%,577 of 2,284 vs 22%, 252 of 1,147; 95% CI: 0.70-0.99; $P = 0.037$) were significantly more frequent in patients ≤50 years of age, although the frequency of chest pain (12.6%,288 of 2,284 vs 15.3%, 175 of 1,147; 95% CI: 1.02-1.53; $P = 0.037$), NYHA functional class III to IV (24%, 549 of 2,284 vs 27.3%, 313 of 1,147; 95% CI: 1.01-1.39; $P = 0.042$), the presence of cardiovascular

TABLE 4 Comparison of Thromboembolic Events and Anticoagulant Use Based on ECG

	ECG (N = 3,423)			
	SR (n = 1,277)	AF (n = 2,146)	95% CI	*P* Value
Intracardiac thrombus	35 (2.7)	254 (11.8)	0.15-0.30	**<0.001**
Stroke/history of stroke	72 (5.6)	164 (7.6)	0.54-0.96	**0.030**[a]
Anticoagulation (n = 2,407)	570 (44.6)	1,837 (85.6)	0.12-0.16	**<0.001**
Routinely tested	151 (26.5)	581 (31.6)	0.63-0.96	**0.023**
INR level <1.5	58 (38.4)	165 (28.4)	1.08-2.29	**0.022**
INR level 1.5-2.0	60 (39.7)	213 (36.7)	0.79-1.64	0.548
INR level >2.0	33 (21.9)	203 (34.9)	0.34-0.79	**0.003**
Not routinely tested	227 (39.8)	761 (41.4)	0.77-1.13	0.528
Never tested	192 (33.7)	495 (26.9)	1.13-1.69	**0.002**
Not on anticoagulation	707 (55.4)	309 (14.4)	0.12-0.16	**<0.001**

Values are n (%) unless otherwise indicated. 8 patients were excluded because of other electrocardiography (ECG) rhythm (pacing rhythm 4 patients, junctional rhythm 3 patients, total AV block 1 patient). **Bold** *P* values indicate statistical significance.

AF = atrial fibrillation; INR = International Normalized Ratio; SR = sinus rhythm.

TABLE 5 Comparison of History of Stroke in AF Based on the INR Levels

	Routine INR Examination (AF) (N = 581)			
	INR Level <1.5 (n = 165)	INR Level 1.5-2.0 (n = 213)	INR Level >2.0 (n = 203)	*P* Value
History of stroke	15 (9.1)	12 (5.6)	18 (8.9)	0.349

Values are n (%).
Abbreviations as in Table 4.

comorbidities (10.3%, 236 of 2,284 vs 27.6%, 316 of 1,147; 95% CI: 2.74-3.98; $P < 0.001$), stroke (6.2%,142 of 2,284 vs 8.3%, 95 of 1,147; 95% CI: 1.04-1.79; $P = 0.029$), and AF (58.8%, 1,344 of 2,284 vs 69.9%, 802 of 1,147; 95% CI: 1.39-1.89; $P < 0.001$) were significantly higher in the older group. Echocardiographic parameters also showed that LV ejection fraction <50% was found in 651 of 3,431 (19%) patients, and TAPSE <16 mm was found in 917 of 3,431 (26.7%) patients. Further, LV ejection fraction <50%, TAPSE <16 mm, and a moderate to high probability of PH were significantly more common in the older ages.

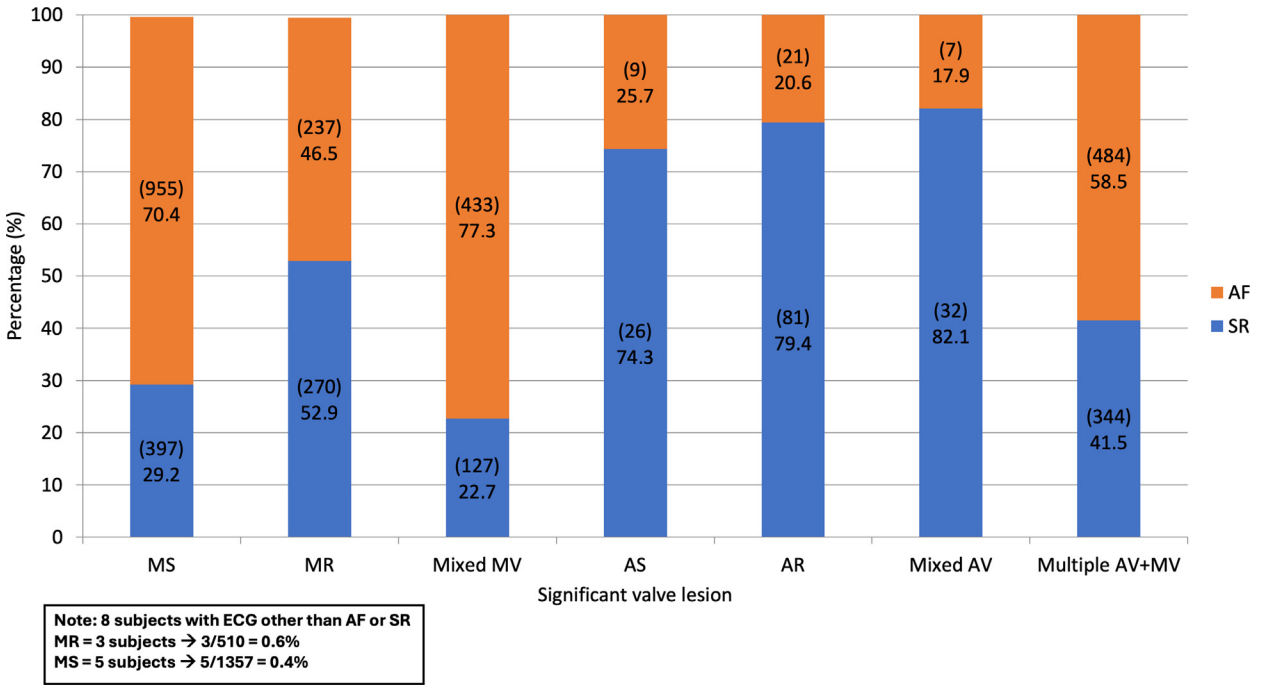
Then, we compared the proportion of valve lesions among patients aged 50 years or less with a group older than 50, as shown in Table 7. The proportion of isolated aortic stenosis was higher in individuals aged >50 years compared with their younger counterparts (2.1%, 24 of 1,147 vs 0.5%, 11 of 2,284; 95% CI: 2.16-9.05; $P < 0.001$). A similar finding was also seen in the multiple AV and MV lesions (25.7%, 587 of 2,284 vs 21%, 241 of 1,147; 95% CI: 0.65-0.91; $P < 0.003$).

Further, of all patients with isolated aortic stenosis, 68.6% (24 of 35) of them are older than 50 years of age. In the mixed AV lesions group, 48.7% (19 of 39) of the cases were patients older than 50 years of age. Other age groups within each valve lesion are depicted in Figure 2.

DISCUSSION

This is the largest multicenter study conducted in Indonesia, evaluating 3,431 subjects. We found that the most frequent valve lesion was mitral stenosis, followed by multiple mitral and aortic valve lesions. Aortic stenosis was the least common lesion. Our main findings were as follows: 1) female gender predominated; 2) the prevalence of AF was high, especially in lesions involving the mitral valve; 3) most subjects were under 50 years of age, but there was a

FIGURE 1 Comparison of ECG Findings for Each Type of Valvular Lesion



The proportion of atrial fibrillation (AF) and sinus rhythm (SR) among each valve lesion shows that AF is more prevalent in any involvement of mitral valve (MV) lesion.
AR = aortic regurgitation; AS = aortic stenosis; AV = aortic valve; MR = mitral regurgitation; MS = mitral stenosis.

significant proportion of patients older than 50 years of age, especially those with aortic stenosis; and 4) there was a lack of adequate secondary prophylaxis (**Central Illustration**). Other important findings were that our subjects had a low socioeconomic status and presented with moderate-severe heart failure with NYHA functional class III to IV. Pulmonary hypertension and right heart problems were found more frequently in patients with mitral valve involvement.

Similar to our findings, female predominance is also reported in most studies. The cause of this gender difference and the specific pathogenesis of RHD remain unclear. Comparing the characteristics between genders, we found that AF was higher in female subjects (Supplemental Table 1), suggesting a later stage of the disease. More commonly, women—especially women with children—tend to put their families' needs above their own. In certain circumstances, this practice may cause a delay in health care for women. The female predominance within their reproductive period in RHD may cause potential problems, such as pregnancy with RHD, which may increase the morbidity and mortality of mother and baby. Further, our subjects were older than those reported from some low-middle-income countries.[4] A registry of black African women showed an early peak of all cases in the third decade of life, followed by a plateau of cases in the 40 to 49 years (17%) and 50 to 59 years (19%) age groups.[15] These reports showed a much lower proportion of older RHD patients than ours. Congestive heart failure was the most reported symptom of our patients, and 25.1% of the patients had low functional capacity (NYHA functional class III or IV); a multicenter study reported that NYHA functional class III or IV classifications were present in between 13.9% and 29.1% of patients.[4] We also found that 34.5% of our patients had prior heart failure admissions, and 11% had multiple rehospitalizations. These findings may suggest that our patients were presented at a later stage because of cultural problems, economic constraints, and geographic challenges, because it is known that our country is one of the biggest archipelagos in the world. The older age of our study subjects may have contributed to the development of some degenerative diseases, such as hypertension, type 2 diabetes mellitus, coronary artery disease, and chronic lung disease, which need to be considered when managing their conditions. Investigators from Australia found higher comorbidity and mortality in older patients, possibly

TABLE 6 Comparison of Clinical and Echocardiographic Variables Based on Age

	Age, (N = 3,431)			
	≤50 y (n = 2,284)	>50 y (n = 1,147)	95% CI	*P* Value
Female	1,491 (65.3)	718 (62.6)	0.77-1.03	0.131
BSA	1.54 (1.08-2.52)	1.56 (1.08-2.30)	1.55-1.57	0.168
Clinical presentations				
Symptoms				
Dyspnea	1,987 (87)	952 (83)	0.60-0.88	**0.002**
Palpitations	577 (25.3)	252 (22)	0.70-0.99	**0.037**
Ankle edema	370 (16.2)	156 (13.6)	0.67-0.99	0.052
Chest pain	288 (12.6)	175 (15.3)	1.02-1.53	**0.037**
Fatigue	276 (12.1)	154 (13.4)	0.91-1.39	0.287
Ascites	81 (3.5)	34 (3)	0.55-1.25	0.428
Syncope	33 (1.4)	16 (1.4)	0.53-1.76	1
Hemoptysis	22 (1)	7 (0.6)	0.27-1.48	0.386
Bleeding	4 (0.2)	3 (0.3)	0.33-6.69	0.693
NYHA functional class III-IV	549 (24)	313 (27.3)	1.01-1.39	**0.042**
Comorbidities				
CV comorbidities[a]	236 (10.3)	316 (27.6)	2.74-3.98	**<0.001**
Chronic lung disease	84 (3.7)	49 (4.3)	0.82-1.68	0.449
Renal failure	32 (1.4)	49 (4.3)	2.00-4.93	**<0.001**
Chronic liver disease	10 (0.4)	7 (0.6)	0.53-3.68	0.674
Atrial fibrillation/atrial flutter	1,344 (58.8)	802 (69.9)	1.39-1.89	**<0.001**
History of IE	20 (0.9)	2 (0.2)	1.18-21.68	**0.028**
Stroke/history of stroke	142 (6.2)	95 (8.3)	1.04-1.79	**0.029**
Prior HF admission	754 (33)	430 (37.5)	1.05-1.41	**0.010**
Echocardiography data				
LVEF <50%	387 (16.9)	264 (23)	0.57-0.81	**<0.001**
TAPSE <16 mm	579 (25.4)	338 (29.5)	0.69-0.95	**0.011**
Probability of PH				
Intermediate + high	1,616 (70.8)	708 (61.7)	0.57-0.77	**<0.001**
Significant functional TR	679 (29.7)	330 (28.8)	0.82-1.12	0.588

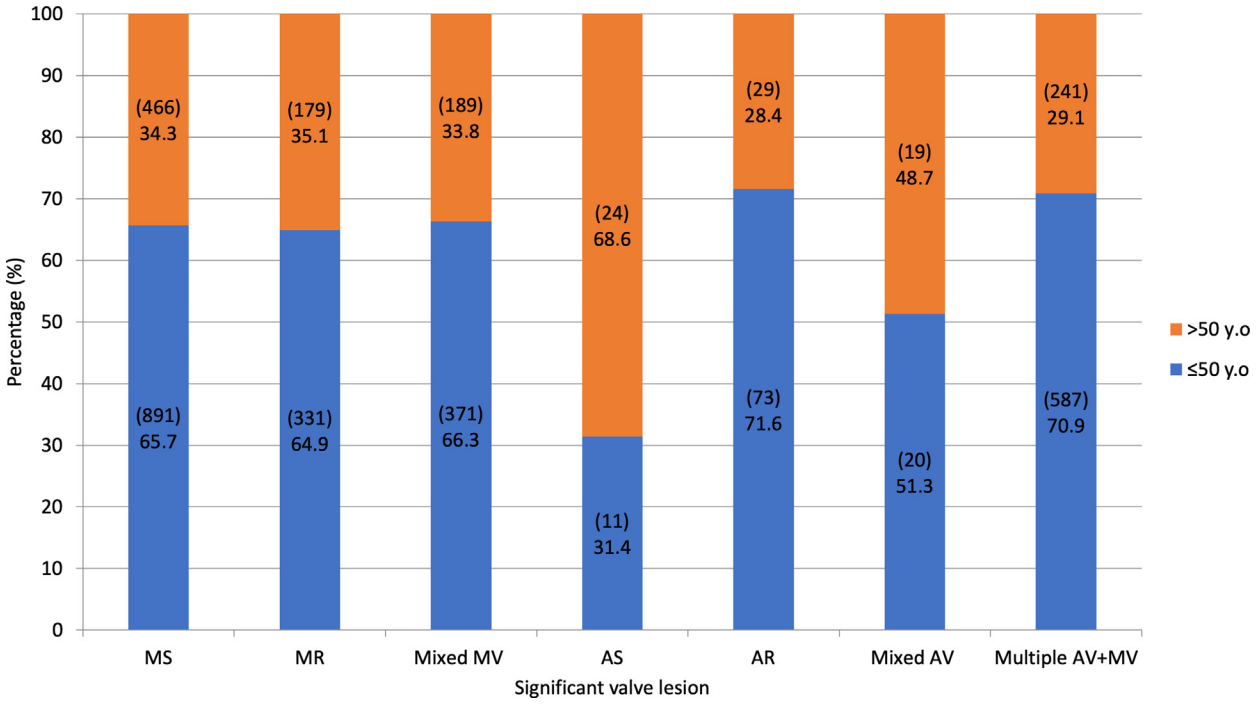
Values are n (%) or median **Bold** *P* values indicate statistical significance. [a]Cardiovascular (CV) comorbidities included hypertension, diabetes mellitus, coronary artery disease, and dyslipidemia.
BSA = body surface area, other abbreviations as in Table 2.

TABLE 7 The Distribution of Valve Lesions Based on Patient Age

	Age, (N = 3,431)			
Valve Lesions	≤50 y (n = 2,284)	>50 y (n = 1,147)	95% CI	*P* Value
Isolated MS (± TR)	891 (39)	466 (40.6)	0.93-1.24	0.381
Isolated MR (± TR)	331 (14.5)	179 (15.6)	0.89-1.33	0.415
Mixed MV disease (± TR)	371 (16.2)	189 (16.5)	0.84-1.23	0.900
Isolated AS (± TR)	11 (0.5)	24 (2.1)	2.16-9.05	**<0.001**
Isolated AR (± TR)	73 (3.2)	29 (2.5)	0.51-1.22	0.327
Mixed AV disease (± TR)	20 (0.9)	19 (1.7)	1.01-3.59	0.062
Multiple AV and MV (± TR)	587 (25.7)	241 (21)	0.65-0.91	**0.003**

Values are n (%) unless otherwise indicated. **Bold** *P* values indicate statistical significance.
Abbreviations as in Table 3.

FIGURE 2 Distribution of Valve Lesion Type by Age Group



Most subjects are under 50 years of age. However, there is a significant proportion of patients older than 50 years of age, especially those with AS. >50 = older than 50 years of age; ≤50 = equal or younger than 50 years of age; other abbreviations as in Figure 1.

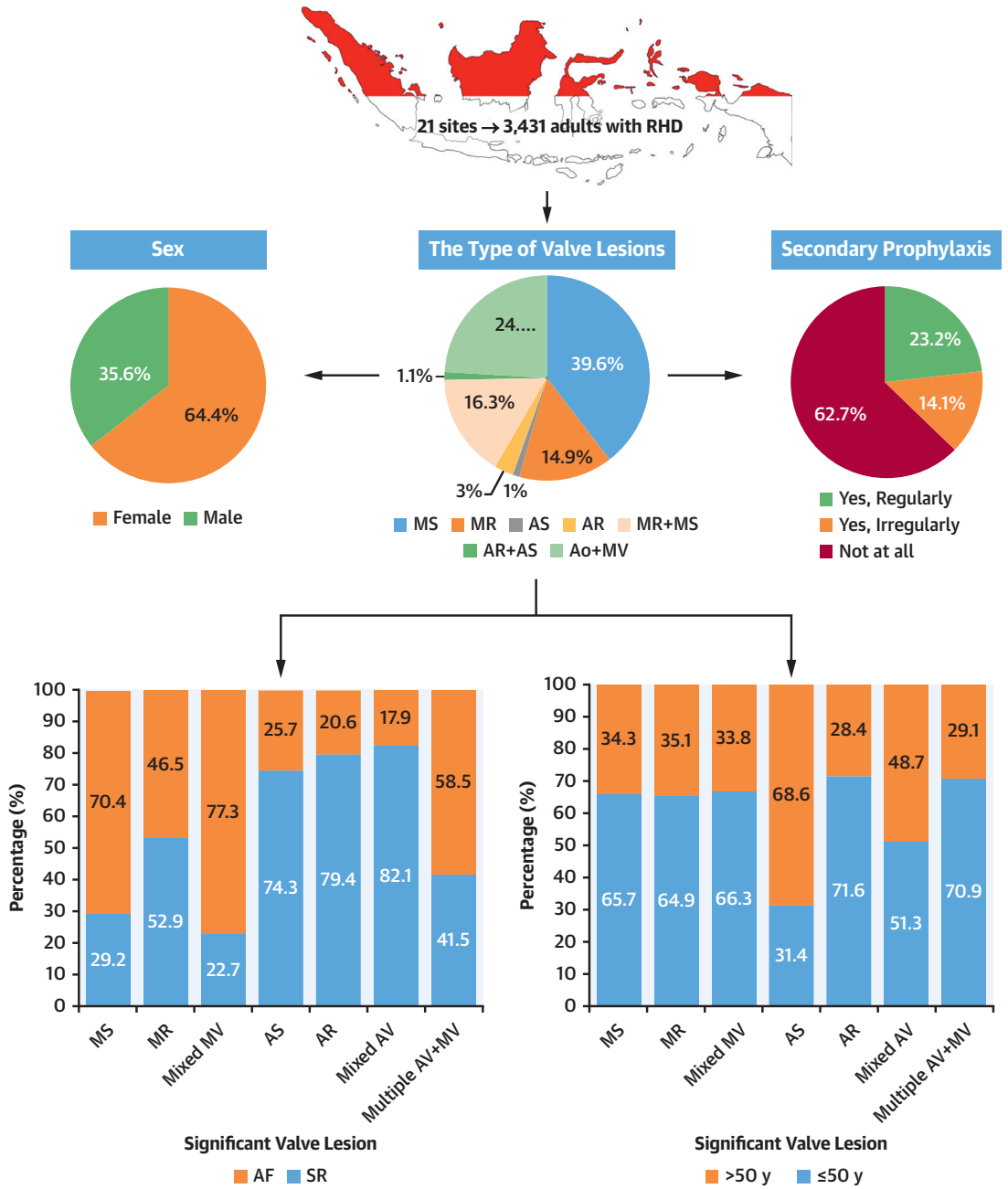
experiencing renal failure caused by the presence of hypertension, coronary artery disease, type 2 diabetes mellitus, or dyslipidemia.[16] These findings highlight the importance of early diagnosis and treatment of RF to reduce chronic complications.

In this study, rheumatic mitral valve diseases were predominant. Isolated MS had the highest frequency, followed by mixed MV disease. Those groups were associated with female predominance, higher prevalence of AF, and right heart problems, including lower TAPSE, higher probability of PH, more frequent significant secondary TR, and clinical right heart failure. These findings were also reported in a single-center study by our national referral hospital.[17] On the contrary, our patients with rheumatic aortic valve diseases showed male predominance, much older ages (except in isolated AR), and more frequent LV dysfunction. This interesting phenomenon needs to be elaborated further. The distribution of valve lesions in our study differed from reports from another large study, which found that MR was the most common lesion.[4]

As mentioned in the previous text, our patients mostly had mitral valve lesions, and they were associated with a high prevalence of AF. In this study, 62.5% of all patients had AF, including 77.3% of mixed MV patients and 70.4% of isolated MS patients. The prevalence of AF is higher in our study than in several other studies. The global prevalence of AF in RHD reported in a meta-analysis was 32.8% (range, 4.3%-79.9%).[18] The higher prevalence of AF may suggest that our patients presented later in the disease stage. AF is more common in severe RHD and, consequently, in patients who had a valvular intervention, because these patients had more severe diseases. The explanation for the higher prevalence of AF in mitral valve disease was that mitral valve lesions directly increase left atrial (LA) pressure, leading to LA enlargement, and there is a strong correlation between LA size and new-onset AF.[19-22] In patients with RHD and AF, amiodarone, cardioversion, or even catheter ablation may be useful to restore sinus rhythm and prevent the AF's complication.[13]

We identified the presence of a history or current stroke in 237 of 3,431 (6.9%) of all patients. Stroke was reported in 128 of 1,357 (9.4%) of isolated MS patients. This data may be related to the high incidence of intracardiac thrombi (15.1%, 205 of 1,357 patients) and

CENTRAL ILLUSTRATION **The Pattern of Rheumatic Valvular Lesions Distribution**



Note: 8 subjects with ECG other than AF or SR
MR = 5 subjects = 0.6%
MS = 3 subjects = 0.4%

Soesanto AM, et al. JACC Asia. 2025;5(9):1171-1183.

The Ina-RHD (Indonesia Rheumatic Heart Disease Study) recruited 3,431 adults from 21 sites in Indonesia. From the recruitment, the valve lesions' distribution showed that mitral stenosis (MS) was the most frequent lesion, followed by multiple aortic and mitral lesions (Ao+MV). Several important findings and issues include: 1) female gender predominated; 2) the prevalence of atrial fibrillation (AF) was high, especially in lesions involving the mitral valve; 3) most subjects are under 50 years of age, but there was a significant proportion of patients older than 50 years of age, especially those with aortic stenosis (AS); and 4) the concerning issue was the lack of adequate secondary prophylaxis. AR = aortic regurgitation; AV = aortic valve; MR = mitral regurgitation; MV = mitral valve; SR = sinus rhythm.

AF (70.4%), 955 of 1,357 patients) in isolated MS. Wang et al[23] reported that the prevalence of stroke in RHD patients in Asia over the past 30 years ranged from 0.37% to 12.6%. Approximately 80% of strokes in RHD patients occur in those with MS and AF. The annual risk of stroke and systemic embolism estimated from the 2 largest retrospective studies of MS and AF was 5.2% per year in one study and 2.4% per year in the other.[23]

Oral anticoagulants (OACs) have proven effective in reducing thromboembolic complications in patients with rheumatic AF, providing a valuable tool for managing this condition.[4,24] In our study, 2,407 of 3,431 (70.3%) patients were prescribed anticoagulants. Unfortunately, of all patients who were anticoagulated. only 732 of 2,407 (30.4%) routinely checked their INR level, and only 236 of 732 (32.2%) of them had an INR >2. Another large study also reported poor anticoagulation control in RHD patients with appropriate indications.[4] The use of OACs is recommended for stroke prevention in RHD patients, especially those with valvular heart disease associated with AF or MS in sinus rhythm associated with thrombus risk or dilated left atrium.[25] A national strategy is needed to provide an accessible nationwide laboratory facility for INR testing and to increase awareness of the use of OACs among health care providers and patients. Interestingly, we did not find any association between INR level and stroke. This lack of association may suggest that our subjects had a lower risk of stroke, regardless of the inadequate control of OACs and INR levels. Previous studies reported the INR target in the Asian population with AF and after-mechanical prosthetic valve surgery.[26-28] We can speculate that racial factors play a role in this phenomenon. Further studies are needed to confirm this hypothesis. Recently, the use of direct anticoagulants in patients with RHD and AF has been proposed. However, INVICTUS (Investigation of Rheumatic AF Treatment Using VKA, Rivaroxaban or Aspirin Studies) showed that compared with VKA, rivaroxaban was associated with an increased risk of ischemic stroke and vascular death. This trial further supports the use of VKA in RHD and AF as recommended by some guidelines.[29]

We observed a higher proportion of reduced EF in those with aortic valve involvement, especially in AR. This finding was also reported by Rudiktyo et al.[17] Aortic regurgitation causes chronic LV volume overload, leading to progressive LV enlargement and LV dysfunction. Another explanation for this reduced LV systolic dysfunction could be a higher hemodynamic burden (volume overload) of the ventricle in multiple valve disease or volume overload in isolated AR.[30,31] Studies have suggested that the intrinsic myocardial process in RHD may play a role in the mechanism of this impaired clinical or subclinical LV contractility.[32,33] Studies using cardiac magnetic resonance with late gadolinium enhancement showed myocardial fibrosis in patients with rheumatic valve disease.[32-34]

Our study found significant RV dysfunction, covering 26.7% (917 of 3,431) of all patients. Several studies also reported a proportion between 20.5% and 28.5%.[35,36] The highest prevalence of RV dysfunction was found in mixed MV disease and older age groups. Several studies suggested that the RV myocardium may be less affected by the rheumatic inflammatory process than the LV myocardium.[37-39] On the contrary, Rudiktyo et al[37] suggested that RV dysfunction might independently associated with more impaired LV systolic function. Meanwhile, a study by Pande et al showed evidence of apoptosis in the RV of patients with rheumatic MS that occurred early in rheumatic valve disease, even at low RV systolic pressure.[40] However, whether this apoptosis was significant enough to cause RV dysfunction was not addressed.

A high prevalence of PH and right heart involvement were detected in our study. A high prevalence of probability of PH was found in mitral valve involvements. Further, MS showed the highest prevalence of PH, right heart involvement, and RV dysfunction. Moderate to severe MS is generally associated with a variable degree of PH. The exact prevalence of intermediate-high probability PH varies widely between studies, the spectrum of MS severity, and symptomatic status.[41-43] Mitral stenosis directly causes an increase in LA pressure, chronically leads to increased pulmonary artery pressure, and causes pathological changes in the pulmonary veins and arteries, leading to increased pulmonary vascular resistance. An increase in pulmonary vascular resistance and systolic pulmonary artery pressure leads to RV dilation and hypertrophy. RV failure is associated with tricuspid annular dilation and an increase in the severity of tricuspid regurgitation, which further exacerbates RV dysfunction.[43,44] Elevated LA pressure creates heart failure symptoms. Because of its strong association with symptoms, the presence of PH in MS patients is associated with significantly worse functional class and worse outcomes.[43,45] RV failure is a major cause of morbidity and mortality in patients with PH. Very few studies have investigated the prevalence and impact of RV dysfunction on outcomes in patients with VHD.

It is well established that a significant proportion of the morbidity and mortality associated with RHD can

be prevented through existing therapies. The efficacy of secondary prophylaxis with long-acting penicillin in reducing the recurrence of acute rheumatic fever episodes is supported by compelling evidence, with studies demonstrating its efficacy in preventing recurrences.[46-51] Unfortunately, the coverage of secondary prevention in our patients was low. Although intramuscular BPG is more effective than oral antibiotics, most of our patients used oral antibiotics. Similarly, noncompliance with secondary antibiotic prophylaxis has been observed in other countries, but using BPG injections is predominant.[4,52,53] As also observed in our study, the most common reasons for missing prophylaxis were out of supply, lost follow-up, and poor adherence. Challenges to adherence include fear of injection pain, poor patient-provider communication, and cultural factors. The unknown history of acute rheumatic fever, as detected in our study, also becomes the reason for the low coverage of secondary prophylaxis.

Screening for latent RHD is one strategy to increase coverage of secondary prophylaxis,[54] along with community education to increase awareness of this disease and the use of oral penicillin as another option. Further, access to BPG remains limited in many settings, and effective administration and delivery are our national and global challenges. As is also relevant for Indonesia, global institutional leadership is essential to address priority issues and improve access. Strengthening long-term primary care strategies is crucial for enhancing adherence to secondary prophylaxis for rheumatic heart disease.[48,55-57]

STUDY LIMITATIONS. This study had some limitations that correlate with the nature of retrospective studies, because some information was taken from patient histories without objective records. We carefully included only reliable data from sites where cardiology consultants and echocardiography data were available, but the risk of incomplete and inaccurate data remains. Although 21 sites all over Indonesia participated in this study, the result was not enough to truly reflect all RHD problems countrywide. Nevertheless, the result can highlight the problems of RHD in Indonesia and serve as a reference for the RHD control strategy in our country. Population studies are needed to determine the incidence and prevalence of ARF and RHD and show the real burden of RHD in Indonesia.

CONCLUSIONS

Our patients were predominantly women and were older than reported in other studies, and MS was the most common lesion. AF was very common; however, the use of adequate anticoagulation was suboptimal. Underuse of secondary prophylaxis and late-stage disease marked by high prevalence of PH and right heart involvement showed the lack of awareness of RHD in the population. These challenges should be considered when we create a national RHD controlling program strategy.

ACKNOWLEDGMENT The authors would like to express their gratitude to the President of the Indonesian Heart Association, Radityo Prakoso, MD, for supporting this study.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

All authors are members of the Indonesian Society of Echocardiography. The study is under the Indonesian Society of Echocardiography and self-funded. The authors have reported that they have no relationships relevant to the contents of this paper to disclose

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KEY WORDS atrial fibrillation, echocardiography, mitral stenosis, rheumatic heart disease, valvular heart disease

APPENDIX For a supplemental table, please see the online version of this paper.