Clinical Research

Characteristics of patients with rheumatic heart disease in a national referral hospital in Indonesia

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pISSN: 0853-1773 • eISSN: 2252-8083
https://doi.org/10.13181/mji.oa.226150
Med J Indones. 2022;31:178–85

Received: March 16, 2022
Accepted: December 01, 2022

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ABSTRACT

BACKGROUND Rheumatic heart disease (RHD) is one of the most common cardiovascular problems in Indonesia. Comprehensive data regarding patient characteristics are critical in planning optimal treatment strategies to relieve the burden of RHD. This study aimed to describe the clinical and echocardiographic characteristics of patients across several types of valvular lesions in RHD in the Indonesian population.

METHODS This retrospective study was performed between January 2016 and June 2019 at the National Cardiovascular Center Harapan Kita, Jakarta, Indonesia. The study population comprised all patients with significant valve disease aged ≥18 years. Patient characteristics and echocardiographic parameters were collected retrospectively from medical records and hospital information systems. Patients were classified into several groups based on etiologies of valve disease.

RESULTS Of 5,482 patients with significant valve lesions**,** 2,333 (42.6%) were RHD patients. They were predominantly female (64.1%) and younger (mean [standard deviation] age 42.61 [12.01] years). Atrial fibrillation (AF) was the most frequent rhythm disorder observed in RHD (65.4%). Isolated mitral stenosis was the most common valve lesion in RHD patients (46.5%). Most patients with RHD had preserved left ventricular (LV) ejection fraction. Half of the patients with mitral stenosis had reduced right ventricular (RV) contractility (tricuspid annular plane systolic excursion <17 mm).

CONCLUSIONS Isolated mitral stenosis was the most observed condition of valve lesions in RHD. Characteristics of RHD patients in this study were predominantly female, younger age, had preserved LV function, reduced RV function, and high prevalence of AF.

KEYWORDS echocardiography, pathology, rheumatic heart disease, right ventricular dysfunction

Rheumatic heart disease (RHD) and its complications are significant healthcare problems in the middle- and low-income countries due to its very high prevalence and tendency to affect patients at a productive age. According to the data published by the Global Burden of Disease in 2015, at least 33.4 million people worldwide had RHD.[1] This is significantly higher than the global prevalence of tuberculosis in 2018, accounting for approximately 10 million people.[2] Unfortunately, no contemporary national data on the characteristics of RHD are available in Indonesia despite the high predictive prevalence of the disease. The characteristics of RHD patients, including clinical and echocardiographic characteristics, can be crucial for optimizing patient treatment. Currently, only a few published studies have reported clinical and echocardiographic parameters in patients with RHD.

In developing countries, many patients with RHD will deteriorate into a state of clinical heart failure signified by dyspnea and evidence of pulmonary edema with or without embolic events. Although the rate of clinical heart failure depends on the stage of valve disease at diagnosis, data showed that there are still many patients with advanced clinical cases in endemic areas.[3–5] Therefore, the complications such as heart failure, atrial fibrillation (AF), pulmonary hypertension, and cardioembolic stroke are still commonly found.[4,6,7] In developing countries, this becomes a challenge with an increased rate of exacerbation caused by these complication. Moreover, the resources to deal with the preventive or early diagnostic stage are also limited. This study aimed to describe the contemporary clinical and echocardiographic characteristics of patients across several types of valvular lesions in RHD in the Indonesian population.

METHODS

Study design

This was a retrospective study of demography, clinical, and echocardiographic data from all patients with valvular heart disease between January 2016 and June 2019 (42 months) at National Cardiovascular Center Harapan Kita, Jakarta, Indonesia.

Study site

National Cardiovascular Center Harapan Kita is a national referral hospital for cardiovascular disease located in the capital city of Indonesia, Jakarta. It is a teaching hospital for the Faculty of Medicine, Universitas Indonesia. The echocardiography laboratory provides cardiac examinations for at least 12,000 adults and children anually, with 10 echocardiography machines from various manufacturers.

Study population and data collection

The study population comprised 5,482 patients with significant valve disease, aged 18 years or older, and had undergone transthoracic echocardiography at National Cardiovascular Center Harapan Kita during the study period with at least moderate mitral or aortic valve lesions (regurgitation or stenosis) with or without right-sided valve lesions. Patient characteristics and echocardiographic parameters were collected retrospectively from medical records and hospital information systems. Ethical approval was obtained from the Institutional Review Board of National Cardiovascular Center Harapan Kita, Jakarta, Indonesia (No: LB.02.01/VII/469/KEP070/2020).

Demographic and clinical parameters

Demographic parameters included in this study were age and sex. AF was defined as documented AF, paroxysmal, or persistent on electrocardiogram (ECG) (at outpatient, inpatient, or during echocardiographic examination).

Echocardiography parameters

Echocardiography was performed by echocardiography consultants, echocardiography fellows, cardiology residents, and sonographers. All reports were reviewed by echocardiography consultants, and all examiners were certified by the European Association of Cardiovascular Imaging (EACVI). General echocardiographic parameters obtained were left ventricular (LV) end-diastolic diameter, LV end-systolic diameter, LV ejection fraction (EF), tricuspid annular plane systolic excursion (TAPSE), and peak tricuspid regurgitation velocity (TR Vmax). Cut-off values for cardiac chamber dimension, LV, and right ventricular (RV) contractility were based on American Society of Echocardiography/EACVI recommendations for cardiac chamber quantification by echocardiography,[8] while diagnosis and grading severities of valve abnormality were performed according to the 2012 and 2017 European Society of Cardiology (ESC) guidelines for the management of valvular heart disease.[9,10] In patients with mitral stenosis, the valve morphology was evaluated using the Wilkins score, consisted of four echocardiographic parameters: leaflet mobility, leaflet thickness, leaflet calcification, and subvalvular thickening.[11] The 2015 ESC/European Respiratory Society guidelines for the diagnosis and treatment of pulmonary hypertension were used to decide the TR Vmax cut-off value.[12]

Data management

Data management was performed using the SPSS software version 23 (IBM Corp., USA). Descriptive statistics were used to describe and summarize the data. Patients were classified into several groups based on the etiology of valve disease. Patients with RHD were then grouped based on left-sided valve(s) involvement, classified into isolated mitral valve lesions, isolated aortic valve lesions, and mixed

aortic and mitral valve lesions groups. Between these groups, categorical variables were expressed as percentages, and continuous data were expressed as mean (standard deviation [SD]).

RESULTS

RHD was the most common etiology of valve lesions observed (42.6%, n = 2,333) (Figure 1). Patients with RHD were predominantly female (64.1%) and younger (mean [SD] age 42.61 [12.01] years) than patients with other etiologies. These patients mostly had AF, and only 29.1% had sinus rhythm on ECG.

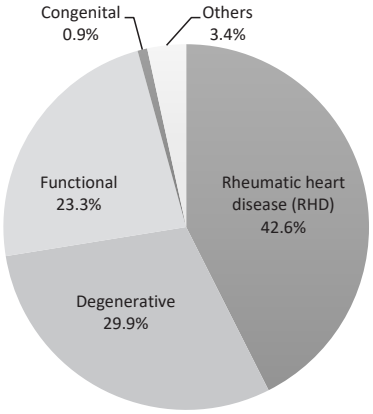

Figure 1. Causes of valvular heart disease

Isolated mitral stenosis was the most common valve lesion observed in this study (46.5%), followed by multiple valve lesions (aortic and mitral) (18.3%) and mixed mitral stenosis and regurgitation (17.7%). Tricuspid valve regurgitation in conjunction with left-sided valvular lesion was found in almost half of the patients (48.4%). Primary right-sided involvement of RHD was rarely seen, with only 19 patients having rheumatic tricuspid valve stenosis secondary to RHD. No cases of rheumatic pulmonary valve lesions were observed.

Among all patients with RHD, patients with isolated mitral regurgitation and isolated aortic valve regurgitation tended to be younger than other groups (mean age 36.84 and 38.46 years, respectively). AF was predominantly found in groups with mitral valve involvement (isolated mitral stenosis, isolated mitral regurgitation, mixed mitral stenosis and regurgitation,

Table 1. Characteristics classified by the pattern of valvular involvement in RHD

Parameters	Isolated mitral stenosis, n (%) (N = 1,085)	Isolated mitral regurgitation, n (%) (N = 276)	Mitral stenosis and regurgitation, n (%) (N = 414)	Isolated aortic stenosis, n (%) (N = 25)	Isolated aortic regurgitation, n (%) (N = 85)	Aortic stenosis and regurgitation, n (%) (N = 21)	Mixed valve (aortic and mitral), n (%) (N = 427)
Male sex	365 (33.7)	64 (23.2)	131 (31.6)	13 (52.0)	52 (61.2)	12 (57.1)	200 (46.8)
Age (years), mean (SD)	44.61 (10.46)	36.84 (14.03)	41.72 (11.69)	54.40 (12.96)	38.46 (12.99)	50.33 (9.78)	41.89 (12.53)
ECG							
AF	788 (72.6)	145 (52.5)	336 (81.2)	1 (4.0)	7 (8.2)	1 (4.8)	248 (58.1)
LVEF <50%	149 (13.7)	32 (11.6)	57 (13.8)	4 (16.0)	22 (25.9)	4 (19.0)	84 (19.7)
EDD, mean (SD)	43.3 (6.8)	57.7 (10.0)	50.8 (9.4)	49.9 (5.5)	64.5 (12.5)	55.2 (9.8)	54.6 (21.2)
ESD, mean (SD)	29.3 (6.1)	38.6 (8.4)	34.8 (8.7)	29.6 (7.3)	45.5 (13.6)	38.3 (12.7)	36.9 (12.1)
LAVi, mean (SD)	110 (90)	193 (307)	195 (168)	42 (15)	51 (33)	71 (35)	125 (86)
>34 ml/m²	985 (90.8)	242 (87.7)	384 (92.8)	16 (64.0)	57 (67.1)	19 (90.5)	375 (87.8)
TAPSE <17 mm	500 (46.1)	68 (24.6)	198 (47.8)	1 (4.0)	5 (5.9)	3 (14.3)	160 (37.5)
TR Vmax							
<2.8 m/s	222 (20.5)	77 (27.9)	90 (21.7)	9 (36.0)	21 (24.7)	6 (28.6)	82 (19.2)
2.8–3.4 m/s	223 (20.6)	58 (21.0)	102 (24.6)	2 (8.0)	9 (10.6)	3 (14.3)	109 (25.5)
>3.4 m/s	535 (49.3)	97 (35.1)	187 (45.2)	2 (8.0)	5 (5.9)	5 (23.8)	168 (39.3)
No TR	105 (9.7)	44 (15.9)	35 (8.5)	12 (48.0)	50 (58.8)	7 (33.3)	68 (15.9)
Presence of at least moderate TR	511 (47.1)	144 (52.2)	237 (57.2)	1 (4.0)	2 (2.4)	3 (14.3)	231 (54.1)

AF=atrial fibrillation; ECG=electrocardiogram; EDD=end-diastolic diameter; ESD=end-systolic diameter; LAVi=left atrium volume index; LVEF=left ventricular ejection fraction; RHD=rheumatic heart disease; SD=standard deviation; SR=sinus rhythm; TAPSE=tricuspid annular plane systolic excursion; TR=tricuspid regurgitation; TR Vmax=peak TR velocity

Table 2. Comparison between groups classified by left-sided valve(s) lesions

Variables	Isolated mitral valve lesions group (%)	Isolated aortic valve lesions group (%)	Mitral and aortic valve lesions group (%)
Female sex	68.4	41.2	53.2
Age (years), mean (SD)	42.73 (11.70)	43.45 (14.21)	41.89 (12.53)
AF	74.9	8	62.2
LVEF <50%	13.6	23.3	20
EDD (mm), mean (SD)	47.19 (9.67)	60.86 (12.62)	54.56 (21.17)
LAVi >34 ml/m²	98.7	74.8	99.2
TAPSE <17 mm	44.4	6.9	38.7
TR Vmax >3.4 m/s	51.5	19.4	46.8
At least moderate TR	52	8.5	58

AF=atrial fibrillation; EDD=end-diastolic diameter; LAVi=left atrium volume index; LVEF=left ventricular ejection fraction; SD=standard deviation; TAPSE=tricuspid annular plane systolic excursion; TR=tricuspid regurgitation; TR Vmax=peak TR velocity

and multiple valve pattern). Most patients with RHD had preserved left LVEF (>50%). However, a higher proportion of patients with reduced EF was observed in patients with isolated aortic regurgitation and multiple valve lesion (aortic and mitral).

Patients with regurgitant lesions had larger LV dimensions than patients with isolated stenotic valves, whereas significant dilatation of the left atrium (LA) was found in all groups, especially when mitral involvement occurred. In this group, approximately 90% of patients had an LA volume index (LAVi) of >34 ml/m². Table 1 summarizes the clinical and echocardiographic characteristics of RHD patients classified by the pattern of valvular involvement.

The data were available in 1,665 patients, with 8 as the most frequent score observed, followed by scores 7 and 9. Almost half of the patients with mitral stenosis (isolated or with mitral regurgitation) had reduced RV contractility (TAPSE <17 mm). High tricuspid regurgitation maximum velocity was mainly seen in groups with mitral valve disease, signifying possible underlying pulmonary hypertension. Significant tricuspid regurgitation was only found in a minority of patients with isolated aortic valve lesions.

Further analysis between three larger groups based on left-sided valve involvement showed a higher proportion of females and AF in the isolated mitral valve lesions group compared with other groups. A higher proportion of decreased RV contractility was also found in this group compared with other groups of valvular involvement (Table 2).

DISCUSSION

This study found isolated mitral stenosis as the most common pattern in RHD patients, followed by multiple valve lesions (aortic and mitral) and mixed mitral stenosis and regurgitation. This finding differs from several studies that reported mitral regurgitation as the most common RHD pattern.[6,13–16] This may be because the subjects were younger in the previous studies, whereas this study only included patients older than 18 years. However, a study in Tunisia that included patients over 18 years reported similar findings as this study,[17] while a prospective study in North India described mitral regurgitation as the most common form of valve lesion in children and young adults.[18] In contrast, mitral stenosis was increasingly frequent in patients from the fourth to the sixth decade of life.[18] This finding reflects the pathogenesis of RHD that mitral stenosis usually develops later than mitral regurgitation after the first episode of acute rheumatic fever.

In this study, females were predominant in all spectra of valve involvement in RHD. Similar findings were observed in almost all studies (Table 3).[6,14,15,19–21] Whether this was caused by the sexual disparity of proper healthcare access during childhood or a specific pathogenesis mechanism of RHD is unknown. The female sex was also more predominant in the rheumatic mitral disease group compared with the aortic valve involvement-only group. There is no clear explanation for this finding, and no other studies have reported this difference. Moreover, RHD patients were also younger than non-RHD patients. This finding reflects the pathogenesis process of RHD that occurs earlier in life than other etiologies such as degenerative or functional disease secondary to ischemia. The proportion of AF in patients with RHD was also higher than in other groups. A plausible explanation of this finding is that the rheumatic process affects not only leaflet tissue but also all layers of the heart, which is termed as pancarditis, whereas remodeling of the atrial wall is responsible for the development of AF. However, further study is needed to prove the hypothesis.

Table 3. Summary of findings of studies examining the characteristics of RHD patients

First author, year	Study location	Sample characteristics and sizes	Age inclusion criteria	Findings
Rwebembera,[13] 2018	Uganda (tertiary hospital)	Patient underwent echocardiographic examination Total: 15,009 cases RHD: 709 cases	≥13 years	28 patients at stage A VHD and 681 patients at stage B to D VHD*; RHD disproportionately affected the young under 40 years age group; isolated MR was the most lesion observed, followed by isolated MS.
Sani,[14] 2007	Nigeria (hospital-based)	Patient underwent echocardiographic examination Total: 1,499 cases RHD: 129 cases	≥5 years	Mean age 24.02 (12.75) years; predominantly females (82:47); isolated MR was the most commonly observed lesion, followed by combined MR and MS.
Butt,[16] 2019	Pakistan (hospital-based)	Patient underwent surgery RHD: 87 cases	NA	Mean (SD) age 32.79 (13.06) years; male predominance (52.9%); isolated MR was the most commonly observed lesion.
Triki,[17] 2017	Tunisia (hospital-based)	Patient underwent echocardiographic examination Total: 589 cases RHD: 355 cases	≥18 years	Isolated MS was the most commonly observed lesion.
Kingué,[15] 2016	Western and Central Africa (multi-center) (hospital based)	Patient underwent echocardiographic examination RHD: 3,441 cases	≥3 years	Female predominance; mean age 29.1 years for men and 31.1 for women; AF was observed in 129 cases; isolated MR was the most commonly observed lesion (52.8%); pulmonary hypertension was found in 28.7% of patients; LA dilatation was found in 13.8% of patients.
Laudari,[6] 2017	Nepal (tertiary hospital)	Patient underwent echocardiographic examination RHD: 235 cases	≥7 years	Mean age 39.82 (4.2) years; female predominance (2.1:1); AF was observed in 29.78% of cases; isolated MR was the most commonly observed lesion; PASP >30 mmHg was detected In 51.06% of cases.
Chockalingam,[7] 2003	India (tertiary hospital)	Patient underwent echocardiographic examination RHD: 10,000 cases	NA	Divided into 2 groups: group I, aged ≤18 years (n = 2,910); and group II, aged >18 years (n = 7,090); isolated MR was the most commonly observed lesion in group I, while isolated MS was the most frequent in group II; pulmonary hypertension was present in 42.4% and 80.8% in groups I and II, respectively; functional TR in 38.9% and 77.2%, respectively; 5.9% of patients had AF.
Shaikh,[19] 2006	Pakistan (hospital-based)	Patient underwent echocardiographic examination RHD: 100 cases	≥12 years	Female predominance (51%); isolated MS was the most commonly observed lesion.
Faheem,[20] 2007	Pakistan (hospital-based)	Patient underwent echocardiographic examination RHD: 3,060 cases	≥5 years	Mean age 22 (6) years; female predominance (52.83%); mixed valve disease was the most commonly observed lesion (56.3%), followed by isolated MS.
Manjunath,[21] 2014	India (tertiary hospital)	Patient underwent echocardiographic examination Total: 13,289 cases RHD: NA	NA	Female predominance; isolated MS was the most commonly observed lesion.
Aurakzai,[38] 2009	Pakistan (tertiary hospital)	Patient underwent echocardiographic examination RHD: 13,414 cases	≥11 years	Male predominance (53.8%); mean age 42.33 (18.976) years; isolated MR was the most commonly observed lesion.

AF=atrial fibrillation; LA=left atrium; MR=mitral regurgitation; MS=mitral stenosis; NA=not available; PASP=pulmonary artery systolic pressure; RHD=rheumatic heart disease; SD=standard deviation; TR=tricuspid regurgitation; VHD=valvular heart disease
*Stages A to D VHD according to the 2014 American College of Cardiology and American Heart Association guideline for the management of patients with VHD

RHD patients with mitral valve involvement showed higher rates of AF compared with the aortic valve involvement-only group. This finding reflects the differences in hemodynamic changes between those groups. In the former group, increased LA pressure occurred with subsequent dilatation and remodeling that eventually triggered AF. In contrast, in the latter group, the LV was affected earlier than the LA. In association with this finding, we also found increased LA size (represented with LAVi) in both the aortic and mitral valve lesions groups. However, in the mitral valve lesions group, the LAVi was significantly larger than in the aortic valve group. Mean LAVi values for isolated mitral regurgitation and isolated mitral stenosis were 193 and 110 ml/m^2, respectively, whereas only a mild increase of LAVi (51 and 42 ml/m^2, respectively) was found in isolated aortic regurgitation and isolated aortic stenosis. Butt et al[16] reported that only 36% of patients with significant aortic regurgitation or stenosis who underwent surgery were observed with LA enlargement. Increased LV end-diastolic pressure in these patients may be responsible for the increased LA size.[22]

A significant proportion of RHD patients had also reduced RV contractility, especially in patients with mitral valve involvement (isolated mitral lesion or combined with aortic valve lesions compared with aortic valve lesion only, $p<0.001$). This is unfortunate because most patients require surgical intervention. Decreased RV function (RV fractional area change <32% or RV myocardial performance index >0.50) before surgery is associated with a poor postoperative prognosis in high-risk valvular surgery.[23] Preoperative RV dysfunction in patients with valvular heart disease mostly occurs because of long-standing pulmonary hypertension, secondary to left-sided valve lesions, or significant tricuspid valve regurgitation.[24] In mitral valve lesions, either stenosis or regurgitation LA is directly affected by increased pressure or volume that is subsequently transmitted to the pulmonary circulation and, ultimately, the RV and RA. The chronically increased volume and pressure trigger maladaptive remodeling and dilatation of RV, leading to decreased contractility.[25–27] A higher proportion of significant tricuspid regurgitation and a high probability of pulmonary hypertension in the mitral valve lesions group can also be explained with this mechanism.[24,25]

This study also highlighted the different characteristics between isolated mitral valve lesions, aortic valve lesions, and mixed valve lesions (Table 2). Patients with RHD and mitral valve lesions tended to have AF, dilated LA, lower RV contractility, higher pulmonary pressure, and more significant TR compared with the isolated aortic lesions group. Hence, these parameters should be identified as they are associated with a worse prognosis.[28–31] Early accurate diagnostic and timely referral (as indicated) to the secondary or tertiary hospital is essential to reduce RHD morbidity and mortality. In addition, referral hospitals must be ready to manage those high-risk patients.

Another interesting result in this study is related to ventricular systolic function. Most RHD patients had preserved LVEF, except in patients with isolated aortic regurgitation and multiple valve lesions (aortic and mitral) with a higher proportion of patients with reduced LV contractility. This finding may be caused by a higher hemodynamic burden (volume overload) to the ventricle in multiple valve lesions or volume overload in isolated aortic regurgitation.[22,32,33] Other studies suggested that, apart from hemodynamic changes due to valvular lesions, intrinsic processes also occurred in the myocardium in RHD that might cause decreased LV contractility.[34,35] Myocardial involvement is confirmed by the finding of Aschoff nodules through histology, which is also found in cardiac valve tissue.[36] Aschoff nodules are a pathognomonic finding in RHD. Another study using magnetic resonance imaging with late gadolinium enhancement showed myocardial fibrosis in 91.5% of patients with rheumatic mitral stenosis who did not have ischemic heart disease.[35]

Our data showed that most patients with mitral stenosis had favorable valve morphology to the percutaneous transvenous mitral commissurotomy (PTMC) procedure (Wilkins score 8 or less). This is favorable because the non-surgical intervention of mitral stenosis is less expensive and less complex than surgical procedures with similar efficacy and lower peri-procedural morbidity.[37] Hence, this procedure is more feasible to perform in developing countries. However, other parameters such as the presence of intracardiac thrombus, more severe mitral regurgitation, and other significant valve lesions must be evaluated before performing PTMC.[10]

In conclusion, isolated mitral stenosis was the most common pattern of valve lesions in RHD. Patients with RHD were predominantly female and younger. Meanwhile, AF, reduced RV contractility, elevated

pulmonary pressure, and preserved LVEF were common findings in this population.

Conflict of Interest

Bambang Budi Siswanto is the editorial board member but was not involved in the review or decision process of the article.

Acknowledgment

We gratefully acknowledge the support of Ms. Fadhilla Azzahra for the data collection and dr. Emir Yonas for the statistical analysis.

Funding Sources

None.

REFERENCES

1. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1459–544.
2. Harding E. WHO global progress report on tuberculosis elimination. Lancet Respir Med. 2020;8(1):19.
3. 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.
4. Okello E, Longenecker CT, Beaton A, Kamya MR, Lwabi P. Rheumatic heart disease in Uganda: predictors of morbidity and mortality one year after presentation. BMC Cardiovasc Disord. 2017;17(20).
5. Ghamari SH, Abbasi-Kangevari M, Moghaddam SS, Aminorroaya A, Rezaei N, Shobeiri P, et al. Rheumatic heart disease is a neglected disease relative to its burden worldwide: findings from global burden of disease 2019. J Am Heart Assoc. 2022;11(13):e025284.
6. Laudari S, Subramanyam G. A study of spectrum of rheumatic heart disease in a tertiary care hospital in Central Nepal. Int J Cardiol Heart Vasc. 2017;15:26–30.
7. Chockalingam A, Gnanavelu G, Elangovan S, Chockalingam V. Clinical spectrum of chronic rheumatic heart disease in India. J Heart Valve Dis. 2003;12(5):577–81.
8. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1–39. e14.
9. Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H, et al. [Guidelines on the management of valvular heart disease (version 2012). The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)]. G Ital Cardiol (Rome). 2013;14(3):167–214. Italian.
10. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J. 2017;38(36):2739–91.
11. Wilkins GT, Weyman AE, Abascal VM, Block PC, Palacios IF. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. Br Heart J. 1988;60(4):299–308.
12. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, et al. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J. 2016;37(1):67–119.
13. Rwebembera J, Manyilirah W, Zhu ZW, Nabbaale J, Namuyonga J, Ssinabulya I, et al. Prevalence and characteristics of primary left-sided valve disease in a cohort of 15,000 patients undergoing echocardiography studies in a tertiary hospital in Uganda. BMC Cardiovasc Disord. 2018;18(1):82.
14. Sani MU, Karaye KM, Borodo MM. Prevalence and pattern of rheumatic heart disease in the Nigerian savannah: an echocardiographic study. Cardiovasc J Afr. 2007;18(5):295–9.
15. Kingué S, Ba SA, Balde D, Diarra MB, Anzouan-Kacou JB, Anisubia B, et al. The VALVAFRIC study: a registry of rheumatic heart disease in Western and Central Africa. Arch Cardiovasc Dis. 2016;109(5):321–9.
16. Butt HI, Shahbaz A, Nawaz H, Butt K. Comparative clinical characteristics of rheumatic heart disease patients undergoing surgical valve replacement. Cureus. 2019;11(6):e4889.
17. Triki F, Jdidi J, Abid D, Tabbabi N, Charfeddine S, Ben Kahla S, et al. Characteristics, aetiological spectrum and management of valvular heart disease in a Tunisian cardiovascular centre. Arch Cardiovasc Dis. 2017;110(8–9):439–46.
18. Sanyal SK, Berry AM, Duggal S, Hooja V, Ghosh S. Sequelae of the initial attack of acute rheumatic fever in children from north India. A prospective 5-year follow-up study. Circulation. 1982;65(2):375–9.
19. Shaikh MA, Ghori RA, Devrajani BR. Sequelae of chronic rheumatic heart disease among patients at two teaching hospitals in Sindh, Pakistan. J Liaquat Univ Med Heal Sci. 2006;5(3):114–8.
20. Faheem M, Hafizullah M, Gul A, Jan HU, Khan MA. Pattern of valvular lesions in rheumatic heart disease. J Postgrad Med Inst. 2007;21(2):99–103.
21. Manjunath CN, Srinivas P, Ravindranath KS, Dhanalakshmi C. Incidence and patterns of valvular heart disease in a tertiary care high-volume cardiac center: a single center experience. Indian Heart J. 2014;66(3):320–6.
22. Maurer G. Aortic regurgitation. Heart. 2006;92(7):994–1000.
23. Haddad F, Denault AY, Couture P, Cartier R, Pellerin M, Levesque S, et al. Right ventricular myocardial performance index predicts perioperative mortality or circulatory failure in high-risk valvular surgery. J Am Soc Echocardiogr. 2007;20(9):1065–72.
24. Haddad F, Couture P, Tousignant C, Denault AY. The right ventricle in cardiac surgery, a perioperative perspective: II. Pathophysiology, clinical importance, and management. Anesth Analg. 2009;108(2):422–33.
25. Del Rio JM, Grecu L, Nicoara A. Right ventricular function in left heart disease. Semin Cardiothorac Vasc Anesth. 2019;23(1):88–107.
26. Nagel E, Stuber M, Hess OM. Importance of the right ventricle in valvular heart disease. Eur Heart J. 1996;17(6):829–36.
27. Ahmed MK, Reda AA, Ibrahim MH. Right ventricular function and symptomatology in patients with isolated mitral stenosis: a Doppler tissue imaging study. Egyptian Heart J. 2015;67(1):41–6.
28. Tsang TS, Abhayaratna WP, Barnes ME, Miyasaka Y, Gersh BJ, Bailey KR, et al. Prediction of cardiovascular outcomes with left atrial size: is volume superior to area or diameter? J Am Coll Cardiol. 2006;47(5):1018–23.
29. Gupta A, Bhatia R, Sharma G, Prasad K, Singh MB, Vibha D. Predictors of ischemic stroke in rheumatic heart disease. J Stroke Cerebrovasc Dis. 2015;24(12):2810–5.
30. Pande S, Agarwal SK, Dhir U, Chaudhary A, Kumar S, Agarwal V. Pulmonary arterial hypertension in rheumatic mitral stenosis: does it affect right ventricular function and outcome after mitral valve replacement? Interact Cardiovasc Thorac Surg. 2009;9(3):421–5.
31. Shiran A, Sagie A. Tricuspid regurgitation in mitral valve disease incidence, prognostic implications, mechanism, and

management. J Am Coll Cardiol. 2009;53(5):401–8.
32. Unger P, Clavel MA, Lindman BR, Mathieu P, Pibarot P. Pathophysiology and management of multivalvular disease. Nat Rev Cardiol. 2016;13(7):429–40.
33. Galli E, Lancellotti P, Sengupta PP, Donal E. LV mechanics in mitral and aortic valve diseases: value of functional assessment beyond ejection fraction. JACC Cardiovasc Imaging. 2014;7(11):1151–66.
34. Fraser AG. Inge Edler and the origins of clinical echocardiography. Eur J Echocardiogr. 2001;2(1):3–5.
35. Putra TMH, Sukmawan R, Elen E, Atmadikoesoemah CA, Desandri DR, Kasim M. Prognostic value of late gadolinium enhancement in postoperative morbidity following mitral valve surgery in rheumatic mitral stenosis. Int J Angiol. 2019;28(4):237–44.
36. Fraser WJ, Haffejee Z, Cooper K. Rheumatic Aschoff nodules revisited: an immunohistological reappraisal of the cellular component. Histopathology. 1995;27(5):457–61.
37. Singh AD, Mian A, Devasenapathy N, Guyatt G, Karthikeyan G. Percutaneous mitral commissurotomy versus surgical commissurotomy for rheumatic mitral stenosis: a systematic review and meta-analysis of randomised controlled trials. Heart. 2020;106(14):1094–101.
38. Aurakzai HA, Hameed S, Shahbaz A, Gohar S, Qureshi M, Khan H, et al. Echocardiographic profile of rheumatic heart disease at a tertiary cardiac centre. J Ayub Med Coll Abbottabad. 2009;21(3):122–6.