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A cross-sectional study of the spectrum, aetiology and clinical characteristics of adult mitral valve disease at Chris Hani Baragwanath Academic Hospital

Ebrahim Banderker, Geert Roozen, Merika Tsitsi, Ruchika Meel

Abstract

Background: Valvular heart disease constitutes a considerable amount of cardiovascular morbidity and mortality worldwide. There is a scarcity of data from Africa.

Methods: In this descriptive, cross-sectional study, we documented the demographic, clinical and echocardiographic features of current patients with adult mitral valve disease (MVD) at Chris Hani Baragwanath Academic Hospital from December 2018 to March 2019.

Results: The study included 134 patients (mean age 50 ± 13.3 years) and 77% were female. The majority were of African ethnicity (96%). Mitral regurgitation (39%), followed by mixed MVD (38%) were the dominant lesions. Mitral stenosis was found in 23% of the patients. The main aetiologies were rheumatic heart disease (80%), mitral valve prolapse (11%), myxomatous degeneration (6%) and infective endocarditis (3%). Hypertension (30%) and HIV (12%) were the main co-morbidities. Heart failure was present in 78% of the patients at index hospitalisation. The main complications were pulmonary hypertension (28%) and atrial fibrillation (14%).

Conclusion: The patients with MVD tended to be older African females with co-morbidities who had predominant rheumatic mitral regurgitation.

Keywords: mitral valve disease, echocardiography, Africa, rheumatic heart disease

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Valvular heart disease (VHD) remains a frequent aetiology of heart failure (HF).[1] It constitutes a considerable cause of cardiovascular morbidity and mortality worldwide.[2] In developed countries, degenerative valve disease is the most common aetiology of VHD.[3] Rheumatic heart disease (RHD) is responsible for the majority of VHD in developing countries, with mitral valve disease (MVD) being a common lesion.[3]

There is a scarcity of data in developing countries with regard to demographic information such as age and gender; symptoms and functional class; co-morbidities; aetiology of the valve lesion(s); and severity and complications of adult MVD. A study done by Sliwa *et al*. at Chris Hani Baragwanath Academic Hospital (CHBAH) in a similar setting focused on newly diagnosed RHD patients.[1]

From the available literature from developing countries, the mean/median age for patients with adult MVD was between 20 and 39 years.[4,5] Females were found to have a greater prevalence of adult MVD than males.[6] The most common symptoms included dyspnoea, decline in effort tolerance, palpitations and chest pains. Hypertension, diabetes mellitus, strokes and thyroid disease were common co-morbidities. Patients with adult MVD were reported to have New York Heart Association (NYHA) class III/IV symptoms.[1]

Mitral regurgitation (MR) was documented as the most common isolated adult valve lesion.[4,7] The predominance of mitral stenosis (MS) in female patients was almost exclusively related to RHD in all the previous literature.[7] RHD was the commonest aetiology in developing countries as opposed to degenerative calcific disease in developed countries. This was followed by mitral valve prolapse (MVP), myxomatous MVD, and ischaemic, infective and auto-immune disease. Most of the patients had moderate to severe valve dysfunction. The general complications of adult MVD patients included atrial fibrillation (AF) and pulmonary hypertension.[5,7]

No recent study has explored the clinical and socio-demographic profile of patients with MVD at CHBAH. We suspect that there has been a change in the clinical and demographic characteristics of these patients compared to the past, due to an aging population with better healthcare access,[8] and a decline in acute rheumatic fever (ARF).[9] Therefore the objective of this study was to describe the demographics, spectrum, aetiology, clinical and echocardiographic characteristics, and management of current adult MVD patients at CHBAH.

Methods

This was a descriptive, cross-sectional analysis and review of 134 patients with MVD conducted between December 2018 and March 2019. The study was performed in accordance with guidelines set out in the World Medical Association Declaration of Helsinki –

Ethical Principles for Medical Research Involving Human Subjects (http://www.wma.net/en/30publications/10policies/b3/index.html.pdf Accessed 08/02/2014) (revised October 2013). Ethics approval and clearance was obtained from the University of the Witwatersrand human research ethics committee, clearance certificate number: M180811.

All patients above 18 years of age with native MVD formed part of the study. Patients with previous mitral valve (MV) repair were included. Patients with prosthetic mitral valves, congenital VHD, non-dominant MVD and functional lesions were excluded.

Demographic information, co-morbidities and relevant past cardiovascular symptoms and systemic enquiries for all enrolled patients were retrieved from the patient file records on the day of their routine clinic visit, as the files are kept with the patients and not at the cardiac clinic. Echocardiographic and electrocardiographic (ECG) data were also collected from patient files. In cases where information was insufficient, patients were interviewed prospectively. Examination not done routinely in the clinic, such as weight and height, were done prospectively after obtaining the patient's consent.

Transthoracic echocardiography was performed on all patients in the left lateral position by trained technicians using a S5-1 transducer on a Philips iE33 system (Amsterdam, The Netherlands) during routine clinic visits. All images and echocardiographic measurements were interpreted and reported by the attending cardiologist as per standardised guidelines on chamber quantification and VHD assessment and quantification of severity.[10-12]

As per the current heart failure (HF) guidelines, preserved left ventricular ejection fraction (LVEF) was described as an EF above 50%. Severe LV systolic dysfunction was stipulated as an EF below 40%. An EF between 40 and 49% was defined as mid-range.[13] For MR, a LVEF of ≤ 60% was considered significant as per VHD guidelines.[14]

Pulmonary artery systolic pressure (PASP) was estimated from the peak velocity of the tricuspid regurgitation jet plus the estimated right atrial pressure. Patients with PASP ≥ 30 mmHg were classified as mild (< 50 mmHg), moderate was 50–79 mmHg and severe was ≥ 80 mmHg pulmonary hypertension.[15]

The MV was considered of rheumatic aetiology when there was a previous history of ARF and echocardiographic evidence of chordal thickening, thickened anterior mitral leaflet, calcification and excessive leaflet motion in systole as per the World Heart Federation criteria.[10]

ARF was diagnosed on the basis of clinical manifestations (carditis, arthritis, chorea, erythaema marginatum, subcutaneous nodules) supported by laboratory tests (for a preceding group A streptococcal infection) and echocardiography as per the revised Duckett Jones 2015 recommendations for a moderate- to high-risk population.[16]

A standard 12-lead ECG recording or a single-lead ECG tracing of ≥ 30 seconds showing heart rhythm with no discernible repeating P waves and irregular RR intervals (when atrioventricular conduction is not impaired) is diagnostic of clinical AF. ECG documentation is required to establish the diagnosis of AF.[17]

Surgical intervention included previous percutaneous mitral balloon valvotomy patients (where the Wilkins score was favourable). Patients with previous MV repair were also included. Prosthetic MV patients were excluded from this study.

Statistical analyses

Statistical analyses were performed with Statistica version 13 series 0414 for Windows. Descriptive statistics were used in the data analysis. Continuous variables are shown as mean ± standard deviation for data that was normally distributed. The median analyses were used for non-parametric distributions. Categorical variables are demonstrated as frequencies and percentages.

Results

Ninety-six per cent of the patients were of African ancestry. The group of patients with MVD were older and had numerous co-morbidities. The majority of patients were overweight and 36% were obese with a body mass index > 30 kg/m^2. All retroviral disease (RVD)-positive patients were on appropriate antiretroviral treatment regimens. Only 11% of patients were on penicillin prophylaxis for rheumatic fever. Most patients were on medical therapy for HF and heart rate control. Thirty-one per cent of patients were on an anticoagulation for AF (Table 1).

Table 1. Demographic and clinical characteristics of patients with MVD

Characteristics	*Study patients (n = 134)*
Age (years), mean ± SD	50 ± 13.3
Gender, *n* (%)	
Female	103 (77)
Male	31 (23)
Body mass index (kg/m^2), mean ± SD	29 ± 3
Heart rate (bpm), mean ± SD	75 ± 17
Systolic blood pressure (mmHg), mean ± SD	127 ± 21
Diastolic blood pressure (mmHg), mean ± SD	77 ± 12
Race, *n* (%)	
African	128 (96)
Mixed ancestry	3 (2)
Indian	3 (2)
Clinical indices	
NYHA functional class, *n* (%)	
I	58 (43)
II	71 (54)
III	5 (3)
IV	0 (0)
Heart failure hospitalisation, *n* (%)	
1 admission	104 (78)
2 admissions	17 (12)
3 or more admissions	13 (10)
Co-morbidities, *n* (%)	
Hypertension	40 (30)
Type 2 diabetes mellitus	6 (4)
Graves/hyper-/hypothyroidism	6 (4)
HIV	16 (12)
Cerebrovascular accident/TIA	10 (7)
Arrhythmias	3 (2)
Medication, *n* (%)	
HAART	16 (12)
Penicillin prophylaxis	14 (11)
Furosemide	126 (94)
Aldosterone receptor antagonist	64 (47)
Angiotensin converting enzyme inhibitor	85 (63)
Carvedilol or atenolol	75 (55)
Amlodipine	51 (38)
Warfarin	41 (31)
Digoxin	55 (41)

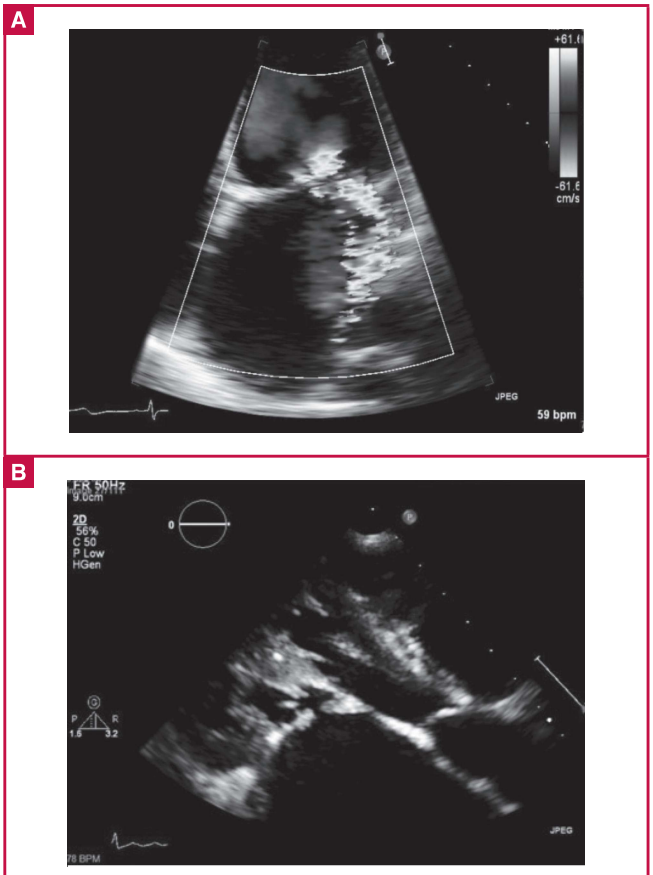


Fig. 1. Two-dimensional modified long-axis view depicting chronic RHD of the MV with thickening of the sub-valvar apparatus and the MV leaflets (A), and severe rheumatic mitral regurgitation (B) in a 50-year-old female.

Table 2. Echocardiographic findings of patients with MVD in absolute numbers and percentages

Echocardiography	*Study group (n = 134)*
Type of valve lesion, *n* (%)	
Isolated mitral stenosis	31 (23)
Isolated mitral regurgitation	52 (39)
Mixed mitral valve disease	51 (38)
Mitral valve disease severity, *n* (%)	
Mild	24 (18)
Moderate	41 (31)
Severe	69 (51)
Aetiology, *n* (%)	
Rheumatic heart disease	107 (80)
Mitral valve prolapse	15 (11)
Myxomatous degenerative disease	8 (6)
Infective endocarditis	4 (3)
Concomitant valve disease, *n* (%)	
Aortic regurgitation	23 (17)
Aortic stenosis	3 (2)
Mixed aortic valve disease	8 (4)
Tricuspid regurgitation	9 (6)
LV function, mean ± SD	
LV ejection fraction (%)	57.5 ± 11.5
LV end-diastolic diameter (mm)	50.7 ± 7.2
LV end-systolic diameter (mm)	34.6 ± 7.3
LV systolic function according to valve lesion and LVEF, *n* (%)	
LVEF < 40%	9 (7)
Mitral regurgitation	5 (4)
Mitral stenosis	2 (1.5)
Mixed mitral valve disease	2 (1.5)
LVEF 40–50%	17 (13)
Mitral regurgitation	5 (4)
Mitral stenosis	4 (3)
Mixed mitral valve disease	8 (6)
LVEF > 50%	108 (80)
Mitral regurgitation	42 (31)
Mitral stenosis	25 (19)
Mixed mitral valve disease	41 (30)
Mitral valve disease-related complications, *n* (%)	
Pulmonary hypertension	38 (28)
Arrhythmia (AF and flutter)	35 (26)
LV dysfunction	26 (19)
Left atrial clot	1 (0.7)

TIA, transient ischaemic attach; LV, left ventricular; LVEF, left ventricular ejection fraction.

The echocardiographic characteristics of the study patients are summarised in Table 2. RHD was the commonest aetiology (80%) of adult MVD in this study group. Infective endocarditis (IE) was diagnosed in four study participants. MR (39%) was closely followed by mixed mitral valve disease (MMVD) (38%) as the dominant lesions found in this study group and MS was found in 23% of patients (Fig. 1). Rheumatic MS was seen more frequently in younger females with 64% being under 50 years of age. Rheumatic MR was more prevalent in older females with 60% being more than 50 years of age.

Myxomatous MVD was noted in eight patients with an average age of 52 years (Fig. 2). Eighty-two per cent of patients in this research group suffered with moderate to severe MVD. Fifty-one per cent of the study population was found to have severe MVD with severe MR being the predominant pathology (20%) (Fig. 3).

Concomitant valve lesions were frequently noted with MVD. Aortic regurgitation (AR) co-existed in 17% of patients with MVD. The overall mean LVEF was 57.5 ± 11.5%. The majority had preserved LV systolic function (80%). Out of the nine patients with severe LV systolic dysfunction, five had severe MR, two had severe MMVD and two had severe MS (Fig. 4). Forty-eight per cent of MR patients had a LVEF of less than 60%. LV function according to MR severity is presented in Fig. 5.

HIV and hypertension were the main co-morbidities. The mean LVEF was 55 ± 13.3% in the isolated HIV MVD group and 58 ± 11.9 % in the isolated hypertensive MVD group. No significant LVEF changes were noted in patients with these co-morbidities compared to the rest of the study group. However, there were two patients who suffered from both HIV and hypertension concurrently. The mean LVEF dropped significantly to 32 ± 11.3% albeit a very small sample size.

One hundred and seven patients had RHD with a mean age of 51 ± 12.6 years and 78% were female. The majority were of African ethnicity (95%) and 55% of the RHD participants were in NYHA class II. The commonest lesion was MMVD (44%), followed by MS (29%) and MR (27%). Eighty-three per cent of the RHD patients had moderate to severe MVD. Thirty-five per cent of the patients had concomitant involvement of other valves. Hypertension (19%), RVD (14%) and cerebrovascular incidents (9%) were the main co-morbidities. HF was present in 75% of the RHD patients at initial hospitalisation. MVD was complicated with pulmonary hypertension (34%) and AF in 30% of patients. Eight patients had a reduced LVEF

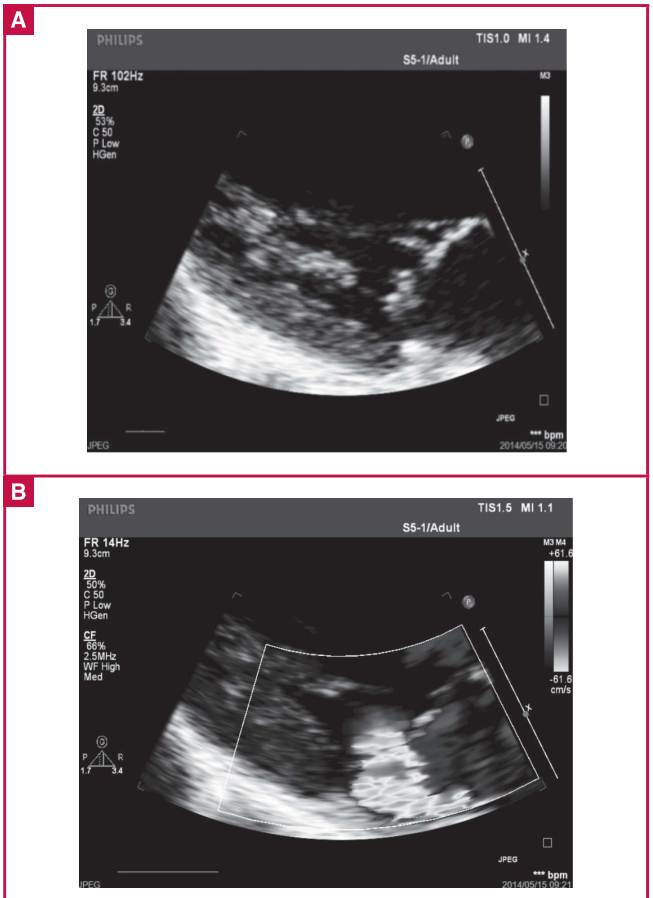


Fig. 2. Two-dimensional long-axis view depicting myxomatous degenerative disease in a 52-year-old female with multiple scallop involvement and predominant prolapse of the anterior mitral leaflet (A) with eccentric mitral regurgitation (B).

of < 40%. Fourteen patients were on rheumatic fever prophylaxis. All patients were on medication for HF or their co-morbidities.

The majority of the patients were on medical therapy (94%) for the management of MVD. Fifty-one per cent of these patients

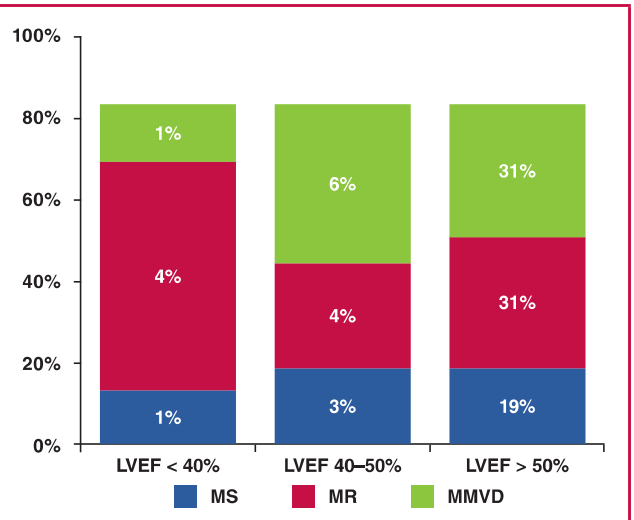


Fig. 4. LVEF according to valve lesion.

were awaiting surgery and suffered with severe isolated MVD or MMVD and required definitive surgical management. Twelve per cent of patients underwent previous MV repair surgery and 13% had had previous percutaneous MV procedures successfully performed. No reported cases of concomitant ischaemic heart disease (IHD) were noted among the patients who underwent previous surgical or percutaneous intervention.

Discussion

This is the first study documenting the characteristics of patients with adult MVD in the current era. Our study patients were older compared to previous studies by Negi *et al.*[6] and Sliwa *et al.*[1] Better accessibility to healthcare,[8] less overcrowding and improved socio-economic status are likely reasons for this finding of an older study population suffering with MVD.

Female gender predominated in this study, comprising 77% of the sample. This concurs with findings from previous studies by Sliwa *et al.*[1] and Zhang *et al.*[5] The possible reasons include health-seeking behaviour among females[18] and it has been

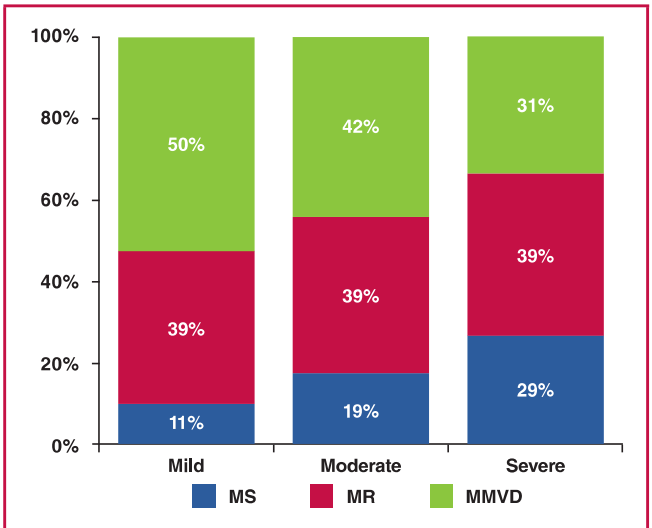


Fig. 3. Severity of adult MVD.

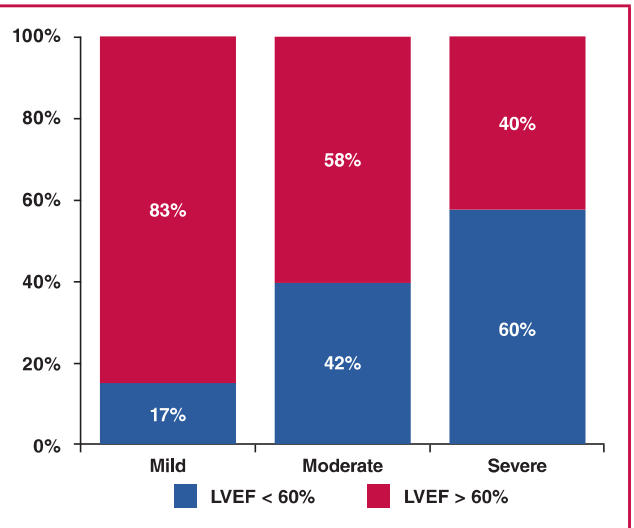


Fig. 5. LVEF according to severity of mitral regurgitation.

shown that rheumatic MVD inherently has a predilection for females.[1,18]

It is uncertain whether RHD prevalence is due to more vulnerability to developing an auto-immune response after *Streptococcus pyogenes* infection or whether social factors, such as involvement in parenting, leads to an increased susceptibility.[9] RHD often becomes apparent during pregnancy, especially with stenotic lesions, because of its associated higher cardiac output.[9] This may explain the younger age of patients with MS in the current study.

Risk factors for RHD include age, gender and numerous environmental factors, as reported by Carapetis *et al.*[9] With regard to age, the peak prevalence of RHD occurs in the second and third decades of life.[19] This is in contrast to the findings of this study, where the peak prevalence ranged between 30 and 70 years of age. The aforementioned findings can be attributed to the decline in cases of acute rheumatic carditis, which has a predilection for younger patients, as opposed to chronic rheumatic MR, which is now commonly seen in older RHD patients due to a decline in ARF.

MR is generally well tolerated with fewer complications than in MS patients and therefore patients can live longer with MR and are likely to have delayed presentation. Furthermore, better access to healthcare and advances in medical therapy for HF serves to stabilise the disease process, therefore prolonging the time to decompensated HF.[20]

In this study, severe LV systolic dysfunction (LVEF < 40%) occurred in very few MR patients, however 48% of the MR patients had LVEF < 60%, which heralds the onset of LV systolic dysfunction in this subgroup.[21] Eighty-two per cent of patients in this research group suffered with moderate to severe MVD. These findings were consistent with studies from developing countries.[5,6]

In the current African population, MVD was complicated by multiple co-morbidities such as older age, being overweight, RVD reactive and hypertensive, which makes it challenging to assess severity of MVD and aetiology of LV dysfunction in these patients. This is exemplified by cases where a high afterload from hypertensive heart disease results in overestimation of MR severity. In patients with co-existing RVD and chronic severe MR, it can be difficult to elucidate the predominant aetiology of LV systolic dysfunction. Therefore, a careful assessment is required that considers the confounding effects of these co-morbidities on LV function in patients with MVD.

The current study had a higher prevalence of myxomatous degenerative MVD (6%). This was greater than previously reported by Sliwa *et al.*,[1] where myxomatous disease of the MV was noted in three cases only. This is likely due to more accurate diagnosis of this condition as a result of evolution in echocardiographic imaging with better image resolution. Furthermore, the older age of the current study patients may partly explain the increase in degenerative myxomatous disease.[22] In contrast to the study by Sliwa *et al.*,[1] we did not observe any cases of calcific degenerative disease.

In this study, none of the patients who underwent a diagnostic coronary angiography had coronary artery disease (CAD). This is in line with the findings from a recent study by Meel *et al.*[23] In that study, a low prevalence of CAD was reported among patients undergoing valve replacement,[23] and the value of routine coronary angiography prior to surgery in VHD patients was also questioned.

IE (3%) was rare in this study group. This is likely an under-representation as the majority of these patients are sick and undergo emergency or urgent surgery soon after admission and therefore are not seen in an out-patients clinic setting.

Most of the patients were in the NYHA II functional class (54%). Patients suffering with chronic HF and NYHA III and IV functional class have poorer outcomes.[24,25] Eighty-one per cent of patients in this research group had a preserved LVEF and all were on HF therapy. The majority of patients with MVD were on loop diuretics (95%), beta-blockers (76%) and angiotensin converting enzyme (ACE) inhibitors (43%) compared to the findings of Sliwa *et al.*[1] Cardiac-specific treatment was better prescribed compared to the findings of the aforementioned study,[1] where loop diuretics, ACE inhibitors, beta-blockers and aldosterone inhibitors were prescribed in 57, 26, 22 and 14% of cases.

Despite being on medical therapy, a large proportion of patients in this study were symptomatic. This brings to the fore the advanced nature of disease in this population, likely a result of delayed medical attention, delayed diagnosis and limited resources. Twenty-two per cent of the patients had more than one HF-related admission. This translates into increased morbidity and mortality rates associated with HF secondary to VHD.[26] There is also an associated economic burden with repeated HF admissions to CHBAH. Facility fees for a patient at CHBAH, besides all other costs related to the HF admission, can range anywhere between ZAR135 and ZAR733 per night.[27] In a study by Ogah *et al.*,[28] the total cost for one HF patient per year equated to US$1 260.

Interestingly, despite a large burden of RHD, no cases of ARF were reported in this study. Only 11% of patients took penicillin prophylaxis. This is likely due to their older age and patients were therefore past the window period for ARF prophylaxis.[14] The decline in ARF is largely related to the general epidemiological transition to more degenerative diseases in our society and improved socio-economic status with better access to healthcare.[29] The other possible explanation of this perceived decline in rates of rheumatic fever may be due to under-reporting of rheumatic fever in South Africa.[30]

In this study group there was a significant time delay prior to surgical intervention. Currently, all state patients are being operated on at a single tertiary hospital in Gauteng with limited resources. This results in delayed definitive surgical management of these patients, with the resultant increase in morbidity and mortality rates, and further burdening of an under-resourced healthcare system. This highlights the dire need for an on-site cardiothoracic surgery service at CHBAH, the largest healthcare facility in the southern hemisphere.[1]

Study limitations

The main limitation of this study was its short duration and, in part, reliance on collection of data from patient files. Some patients were excluded from the study due to missing information or incomplete data-collection sheets. It was not possible at times to get the missing patient information as the files are kept with the patients themselves. In severe MR, a LVEF < 60% is an indication for surgery in symptomatic patients. Therefore, the EF classification used in this study is a limitation as some MR patients, classified as a preserved LVEF of > 50%, actually qualified for surgery. Few patients had systematically documented coronary angiography findings. The

level of education was poorly documented in patient records. IE patients were under-represented in this study as the majority of these patients do not present to an out-patient clinic. The echocardiographic technicians had varying levels of expertise and experience. Due to the lack of an existing database, we did not have access to information on mortality and hence were unable to report on this finding.

Conclusions

We noted a high burden of chronic RHD in the current population with MVD at our peri-urban institution. These patients were older with multiple co-morbidities and the majority presented in HF at the index admission. Delay to definitive surgical treatment remains an important concern and was responsible for considerable morbidity in this study.

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