Incidence, clinical outcomes and associated factors among valvular heart disease patients admitted to medical ward of Jimma Medical Center

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Abstract

Background: In Ethiopia, it was reported that valvular heart disease is the most prevalent diagnosis among cardiac cases admitted to hospitals. However, the existing studies did not assessed the risk factors and outcomes of this disease.

Objective: The aim of this study was to assess the incidence, clinical outcomes and associated factors of valvular heart disease patients admitted to the medical ward of Jimma Medical Center.

Methods: Hospital based prospective cohort study was used. A total of 156 moderate to severe valvular heart disease patients were followed for consecutive 90 days. Descriptive statistics was presented in frequency tables and figures. Chi-square ($\chi 2$) test was used to assess the associations between categorical variables. Independent student t-test and Mann whitney U test was used to compare the mean/median difference of continuous variables. Kaplan Meier with logrank test was used to describe and compare the survival status of the patients. Multivariate cox regression with hazard ratio (HR) was used to identify predictors of mortality. Finally, variables with a P value <0.05 was considered statistically significant.

Result: Female accounted for 79 (50.64%) of the study participants. The mean (SD) age of the paricipants was 45.62±19.126 years. Hypertension 36(23.1%) was the most common co-morbid disease. Cardiomyopathy 56 (35.90%) and rheumatic heart disease 48 (30.77%) was the two most common etiologies. Mitral regurgitation (84.0%) was the most frequent valvular disease. Majority 130 (83.33%) of the patients were presented with congestive heart failure and prescribed diuretics 145 (92.9%). The incidence of death was 2.38 cases per 1000 person days. The overall mean (SD) survival time was 80.80±1.84 (SE) days. Presence of chronic kidney disease (AHR=2.56, 95% confidence interval (CI) [1.62-4.06]), urban residence (AHR=1.598, 95%CI [1.11-2.305]), severe pulmonary stenosis (AHR=3.34, 95%CI [1.19-9.34]), and atrial fibrilation (AHR=1.52, 95%CI [1.05-2.19]) increased the risk of death. While admission with congestive heart failure (AHR=0.61, 95% CI [0.41-0.912]) and use of angiotensin converting enzyme inhibitors (AHR=0.36, 95%CI [0.135-0.96]) reduced the risk of death.

Conclusion: The all-cause mortality of valvualr heart disease patients was high. Etiologies of valvular heart disease patients were diverse, with high burden of mitral regurgitation. Presence of chronic kidney disease, urban residence, severe pulmonary stenosis and atrial fibrilation increased the risk of death. However, presence of admission congestive heart failure and use of angiotensin converting enzyme inhibitors decreased the risk of death. Thus, attention should be given to the care of valvular heart disease patients.

Key words: valvular heart disease, incidence, risk factors, clinical outcomes, Jimma medical center

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Abbreviations and Acronyms

ACEIs: Angiotensin Converting Enzyme Inhibitors

ARBs: Angiotensin-II Receptor Blockers

AF: Atrial Fibrillation

AV: Aortic Valve

AS: aortic stenosis

AR: Aortic Regurgitation

AHA/ACC: American Heart Association/American College of Cardiology

BBs: Beta-Blockers

CAD: Coronary Heart Disease

CW: Continuous-Wave

CHD: Congenital Heart Disease

CHF: Congestive Heart Failure

CAVD: Calcific Aortic Valve Disease

CKD: Chronic Kidney Disease

COPD: Chronic Obstructive Pulmonary Disease

CVD: Cardiovascular Disease

DIVHD: Drug-Induced Valvular Heart Disease

ECHO: Echocardiography

ESC/EACTS: Europian society of Cardiology/ European Association for Cardio-Thoracic Surgery

HVD: Heart Valve Disease

IE: Infective Endocarditis

IHD: Ischemic Heart Disease

JMC: Jimma Medical Center

LV: Left Ventricle

LoHS: Length of Hospital Stay

LVIDs: LV Internal Diameter End systole

LVIDd: LV Internal Diameter End diastole

MV: Mitral Valve

MS: Mitral Stenosis

MR: Mitral Regurgitation

PW: Pulsed-Wave

PAH: Pulmonary Arterial Hypertension

PR: Pulmonic Regurgitation

RHD: Rheumatic Heart Disease

RV: Right Ventricle

PS: Pulmonic Stenosis

PV: Pulmonic Valve

TV: Tricuspid Valve

TR: Tricuspid Regurgitation

TS: Tricuspid Stenosis

VHD: Valvular Heart Disease

1. Background

1.1. Introduction

Valvular heart disease (VHD) can be defined as a structural or functional abnormality of a cardiac valve (1). Normal cardiac valves permit unidirectional flow of blood. Abnormalities of one or more of the valve cusps/leaflets, their supporting structures, or both result in two major functional valvular abnormalities stenosis and regurgitation. A combination of the two is often a late occurrence (2, 3). Valvular heart disease can be categorized as congenital or acquired, and primary or secondary. It is a primary valve diseases if alteration arises on the valve apparatus or secondary if alteration is due to lesions in other structures (4). A heart murmur may have no pathological significance or may be an important clue to the presence of valvular, congenital, or other structural abnormalities of the heart. A comprehensive transthoracic echocardiogram (TTE) with 2-dimensional imaging and Doppler interrogation should then be performed to correlate findings with initial impressions based on the initial clinical evaluation (5). The work-up of VHD mainly include echocardiography, which is able to diagnose and quantitate both the valvular dysfunction and its impact on the myocardial and pulmonary vascular function (6).

According to 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease, there are four (A to D) staging of progression of VHD. Stage A (at risk) are those patients with risk factors for development of VHD. Stage B (progressive) are those patients with progressive VHD (mild-to-moderate severity and asymptomatic). Stage C (asymptomatic severe): Can be subdivided in to (C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated. C2: Asymptomatic patients with severe VHD, with decompensation of the left or right ventricle). Finally stage D is symptomatic severe patients who have developed symptoms as a result of VHD (5). Periodic monitoring with transthoracic echocardiogram (TTE) is recommended in asymptomatic patients with known VHD at intervals depending on valve lesion, severity, ventricular size, and ventricular function (5).

1.2. Principles of medical therapy of valvular heart disease

Treatment depends on VHD type and severity but when severe and symptomatic, usually involves mechanical intervention (7). Medical therapy in adults with valvular heart disease focuses on prevention and treatment of complications because there are no specific therapies to prevent progression of the valve disease itself (8). In most cases, medical therapy may be appropriate in acute valvular diseases or serves as a bridge to definitive mechanical or surgical therapy (9). The importance of drug therapy lies in stabilizing the patient's condition when the disease is due to abnormal valve structure and in treating the underlying condition when the condition is due to a functional abnormality. Drug therapy also lowers the risk of bacterial endocarditis and rheumatic fever (10).

Patients with mitral stenosis (MS) should receive drugs for heart rate control and anticoagulation if they have atrial fibrillation. Anticoagulation should also be used among patients with atrial fibrillation and a CHA_2DS_2-VASc score ≥ 2 in the setting of native aortic valve disease, tricuspid valve disease, or mitral regurgitation (MR) (11).

In acute mitral regurgitation, nitrates and diuretics are used to reduce filling pressures. Sodium nitroprusside reduces afterload and regurgitant fraction. Inotropic agents and an intra-aortic balloon pump are of use in hypotension and haemodynamic instability (12). The use of vasodilator therapy in chronic aortic regurgitation (AR) and MR may be beneficial in selected patients and harmful in others. In AR, vasodilators reduce afterload mismatch and can preserve LV function and delay the need for surgery. However, if the patient has severely reduced diastolic blood pressure, vasodilators could potentially impair coronary perfusion. In other primary causes of MR, vasodilators could potentially mask the development of LV dysfunction and lead to unnecessary and harmful delays in surgery (13). However, in mitral valve prolapse or hypertrophic cardiomyopathy, vasodilators may worsen the MR and should be avoided. In patients with MR caused by dilated cardiomyopathy, vasodilators reduce symptoms, and improve functional class (13). The 2017 ESC/EACTS Guidelines recommends, optimal medical therapy in line with the guidelines for the management of heart failure should be the first step in the management of all patients with secondary mitral regurgitation (12).

Tricuspid regurgitation (TR) is a complex condition of the right ventricle (RV) and tricuspid valve apparatus. Left heart pathologies can lead to chronic pressure overload of the RV, eventually

causing progressive RV dilatation and functional TR. Therefore, TR cannot be considered as isolated heart valve disease pathology and treated as one component of a complex structural RV pathology. Medical treatment is considered a symptomatic therapy limited to diuretics. Surgical repair or replacement is associated with a significant mortality and is therefore restricted to a selected group of patients with a suitable risk profile (14).

Calcific aortic valve disease (CAVD) is a common valvular heart disease in the elderly that increases with age and is characterized by intravascular calcium deposition and process with similarities to atherosclerosis. Clinical trials of statins, renin-angiotensin inhibitors and anti-osteoporosis drugs are well studied. However, the studies were inconclusive to allow recommendations (15). Medical treatment for aortic stenosis (AS) should be carefully titrated to avoid hypotension and patients should be re-evaluated frequently (12). Diuretics may be useful when symptoms of heart failure have developed, although should be used cautiously as hypovolemia may lower cardiac output and LV end-diastolic pressure and cause orthostatic hypotension. Beta-adrenergic blockers can depress myocardial function and should be avoided in patients with severe AS (16).

In patients with Marfan syndrome, beta-blockers and/or losartan may slow aortic root dilatation and reduce the risk of aortic complications and should be considered before and after surgery. By analogy, while there are no studies that provide evidence, it is common clinical practice to advise beta-blocker or losartan therapy in patients with bicuspid aortic valve if the aortic root and/or ascending aorta is dilated (12).

Patients with valvular heart disease (VHD) should also be treated for diabetes, hypertension, and hyperlipidemia. They also should receive therapy for left ventricular dysfunction, undergo interval echocardiography, and participate in aerobic exercise (17).

1.3. Preventive Therapies

1.3.1. Prevention of rheumatic fever

Rheumatic heart disease (RHD) is a chronic valvular disease resulting after severe or repetitive episodes of acute rheumatic fever (ARF) (18). In patients with rheumatic heart disease, prevention of recurrent episodes of rheumatic fever is critical for preventing further valve damage and progressive disease. Long-term penicillin-based treatment and surgery remain the backbone of a RHD control program in the absence of an effective vaccine. The duration of therapy is dependent on patient's age, severity of valvular disease, and last recurrence of ARF (8,18).

1.3.2. Prevention of infective endocarditis

In Africa, the high prevalence of largely RHD, combined with inadequate antibiotic prophylaxis, results in an unusually high incidence of infective endocarditis (19). Prophylaxis against IE is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa in patients with the following: Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts; Prosthetic material used for cardiac valve repair, such as annuloplasty rings and chords; Previous IE; Unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of or adjacent to the site of a prosthetic patch or prosthetic device; Cardiac transplant with valve regurgitation due to a structurally abnormal valve (11).

2. Statement of the problems

Valve disease is the third leading cause of cardiovascular disease and its incidence is increasing with increasing longevity. Valvular heart diseases (VHD) constitute an important subset of cardiovascular diseases and are responsible for significant morbidity and mortality at all ages (3). Valvular heart disease is present in ≈2.5% of the general US population, with prevalence increasing to 11.7% to 13.3% in those aged >75 years. Valve-disease related deaths account for 1.9% of total US mortality (20). There are large differences in heart valve disease (HVD) epidemiology between high-income and low-income countries and across different forms of HVD. The majority of morbidity and mortality attributable to HVD worldwide is due to rheumatic heart disease (RHD), which is most commonly seen in low-income countries. In high-income countries, the greatest burden of HVD referred to hospital is due to calcific aortic valve disease (CAVD) (21).

In Africa, the prevalence of RHD in school age children was estimated to be 2.7–14.3 per 1,000. For sub-Saharan Africa, the mean prevalence was estimated at 5.7 per 1,000. Besides recurrences of streptococcal infections, which have a major role in the development of RHD, individual host susceptibility and associated infections are likely to contribute to RHD. In addition, RHD is favored by overcrowding, malnutrition, and limited access to health care (22). In most sub-Saharan countries, socioeconomic factors strongly limit access to health services and to cardiac surgery in particular (23). There was also a report that, the use of secondary penicillin prophylaxis was suboptimal from low and Middle-income countries, which may also be a risk for recurrence of ARF (24).

Valvular heart disease often requires surgery particularly if severe and the patient is symptomatic (25). An interventional treatment was required in 55% of the patients (mostly surgical valve procedures) (26). However, surgery may not always go as planned, and frail patients or those whose symptoms are caused by other comorbidities may not benefit from valve intervention at all (27). Many African communities are not equipped with the resources and medical or surgical expertise to manage valvular diseases (32). In ethiopia, access to surgical intervention of valve disease is problematic (28).

Domenech et al (US), revealed VHD represented up to 24.2% of the in-hospital admissions (26). In US, the costs of valvular heart disorders are substantial, particularly in patients with symptomatic mitral valve disease (MVD). Medical Expenditure Panel Survey (MEPS) data (1996–

2011) evaluated annual direct healthcare costs of different symptomatic and asymptomatic VHD and compared with costs in patients without VHD. The incremental cost of VHD was $23.4 billion per year overall (27). The other study from Northern India, data on all resources utilized for the delivery of cardiac care services for valvular heart disease for 1 year (2016–2017) showed that, the health system cost of an outpatient cardiac consultation was estimated as US$2.8 and US$5.2 in the cardiology, and cardio-thoracic and vascular surgery (CTVS) departments, respectively. The cost of hospitalization per bed-day in cardiology, CTVS and the intensive care unit (ICU) was US$16, US$60 and US$197, respectively (29).

In Ethiopia, Abdissa et al, revealed, among 3,282 patients confirmed cardiovascular disorders, valvular heart disease (VHD) was identified in 2,036 (62.0%) with significantly higher proportion in the 3rd decade of life (30). Similarly, a multicenter study done by Yadeta et al reported, VHD accounted 40.5% of the cardiovascular diseases. Eighty six percent (86%) of VHD were caused by rheumatic heart disease. More than two-thirds of the patients (68.9%) were adults (age >18 years) (28). Another, six year retrospective study revealed, among a total of 457 cardiovascular deaths, including cerebrovascular accidents, 121 (26.5%) were due to rheumatic heart disease (RHD). About 70% of RHD patients died from congestive heart failure and 11% each died from systemic embolism and co-morbid conditions (31). However, most of the existing studies from Ethiopia suffers from methodological reliability i.e. retrospective, screening survey and focused only on rheumatic cause of valvular heart disease (28, 30, 32). Therefore, this study was aimed to assess the burden, clinical outcomes and associated factors of valvular heart disease.

3. Significance of the study

With an increasing of prevalence of patients with valvular heart disease, it is important to have an understanding of the different types of and its etiologies. Limited information is available on the incidence, non-rheumatic etiologies, clinical outcomes of valvular heart disease in developing countries. Therefore, this study will help clinicians to increase an awareness on current disease burden, etiologies, improve the care of patients with available supportive and preventing therapies. This study might also be an input for health policy makers to implement invasive treatment in the area. It may also support in educational purpose and as a baseline for further research.

4. Literature review

4.1. Burden of the disease

Valvular heart disease (VHD) is present in ≈2.5% of the general US population, with prevalence increasing to 11.7% to 13.3% in those aged >75 years. Valve-disease related deaths account for 1.9% of total US mortality. Of these, aortic and mitral valvular disease represent 99% of identified pathology and mortality (20). Another study reported, VHD account for 10% to 20% of all cardiac surgical procedures in the United States (33). Study done in 25 European countries: The Euro Heart Survey (EHS) on Valvular Heart Disease reported, of 5001 adults with moderate to severe native VHD, infective endocarditis, or previous valve intervention included, VHD was native in 71.9% of patients and 28.1% had a previous intervention (34). In the Swedish population (n=10, 164, 211) between 2003 and 2010, the incidence of VHD was 63.9 per 100,000 person-years, with aortic stenosis (AS; 47.2%), mitral regurgitation (MR; 24.2%) and aortic regurgitation (AR; 18.0%) contributing most of the VHD diagnoses. The majority of VHDs were diagnosed in the elderly (68.9% in subjects aged ≥65 years), but pulmonary valve disease incidence peaked in newborns. Rheumatic fever was rare (35). Study conducted in China (Cardiovascular Risk Survey (CRS) study) indicated, in the total study group (14,618 participants), VHD was observed in 1397 (9.65%) individuals. The prevalence rates of VHD in Han, Uygur and Kazak group are 13.51%, 2.71% and 12.29% respectively (36).

Unlike the western world, valvular disease ranks among the major cardiovascular afflictions in Africa. Acute rheumatic fever and chronic rheumatic valvular disease commonly encountered and impose a huge burden on limited healthcare resources (9). The 2015 Global Burden of Disease study (from 1990 through 2015), estimated that there were 319,400 deaths due to rheumatic heart disease. The highest age-standardized mortality due to and prevalence of rheumatic heart disease were observed in Oceania, South Asia, and central sub-Saharan Africa. The global rate of disability-adjusted life-years due to rheumatic heart disease in 2015 was 142.6 per 100,000 population (37). A retrospective study of over 4-year study period (between January 2010 and December 2013) from Tunisia, at Hédi Chaker University Hospital reported, 959 patients with a significant VHD were identified from a total of 24,422 echocardiographic examinations performed (38).

Yadeta D et al studied patterns of cardioscular disease from six referral hospitals of Ethiopia from January 1 to June 30, 2015 and concluded valvular heart disease (2,541 patients) was the most

common among patients (6,275) i.e 40.5% of the cases seen at cardiology clinics in the country. Among cases of VHD, chronic rheumatic heart disease accounted 2,184 (86%) (28). The other study done in Jimma University Specialized Hospital (JUSH) reported, rheumatic, hypertensive and cardiomyopathic heart diseases accounted for more than three-quarters of cardiac diseases in the study population. Among rheumatic heart disease patients; male to female ratio was 0.86:1 and the mean age was 31.4 years (32). Another retrospective study (September 2011 to June 2013) from North Ethiopia, Ayder referral Hospital reported, among a total of 1028 echocardiograms reviewed, the commonest echocardiographic abnormality was valvular heart disease (44.6%), with rheumatic (20.9%) in younger (mean age 33.01±11.6 years) and degenerative etiologies (20.2%) in older age with mean age of 67.4±11.4 years (39).

4.2. Etiologies and associated co-morbidities

Valve disease often is secondary to a systemic or inherited condition so it is important to inquire about diseases such as rheumatic fever, connective tissue disorders, rheumatologic diseases, or a family history of valve disease (6). In the 1950s, virtually all patients with clinically significant valvular disease had complications of acute rheumatic fever or syphilis, or congenital heart disease. Since then, the pattern of disease responsible for valvular dysfunction in adults has changed dramatically (40). A retrospective study done between January and June 2014 by Domenech et al, among a total of 1,935 adult patients, 453 (23.4%) had moderate or severe valve disease, the etiology of the valvular lesions was degenerative in 60%, functional in 15.5%, rheumatic in almost 10%, congenital in 6%, due to endocarditis in only 3%. The prevalence of VHD was increased with age (26). Calcification is one of the frequent findings in elderly cardiac valves. Prominent calcific deposits in the aortic valve are responsible for so-called degenerative (calcific) aortic stenosis (AS). Degenerative AS is also the third most common cause of cardiovascular disease, and the most common cause of valvular heart disease in industrialized countries. Other less frequent causes of AS include congenitally malformed valves (bicuspid, unicuspid), postinflammatory valvular disease, infectious endocarditis, and collagen vascular diseases (3). Similarly study done by Hollenberg SM et al (2017) reported degenerative disease is the most common etiology of MR, AS, and AR. Mitral stenosis, most often caused by rheumatic fever, which is uncommon in the United States (41).

In Euro Heart Survey, degenerative etiologies were the most frequent, followed by rheumatic, congenital diseases, endocarditis, ischemic and inflmmatory. An 85.4% of MS was rheumatic in

etiology while AS, MR and AR was mostly degenerative. At least one comorbidity was present in 36.3% of patients with AS and 41.7% with MR (42). Similary, Turkish registry of heart valve disease conducted prospectively between June 2009 and June 2011 at 42 centers, which included 1,300 medical patients showed, degenerative etiology (86%) was more frequent in aortic VHD, and rheumatic origin was the main cause in all VHDs. While the prevalence of aortic stenosis increased with age, mitral stenosis decreased with patient age. The mean age of the patients was 57±18 years and the female/male ratio was 1.5 (43).

A five year retrospective (January 2009 to December 2013) epidemiological survey of 19,428 consecutive patients screened by echocardiography with a mean age of 52.03±20.50 years from Southern china reported, it was rheumatic in 7,197 (37.0%) patients, congenital in 2,697 (13.9%), degenerative in 2,241 (11.5%), ischemic in 2,460 (12.7%). The prevalence decreased significantly in rheumatic VHD but increased markedly in congenital, ischemic and degenerative VHD (44). The other study from China, Cardiovascular Risk Survey (CRS) study, indicated the prevalence rates of VHD increased strikingly with age. The results of multinomial regression analysis indicated that VHD were related to age, smoking and hypertension (36). Similarly, a 4-year retrospective study from Tunisia reported, among 959 patients with a significant VHD, rheumatic was the most common cause of VHD in 66.6%, followed by degenerative in 17.2%. And rheumatic was the only cause of mitral stenosis and the most common cause of aortic regurgitation and multiple valve disease, whereas aortic stenosis was primarily degenerative, and mitral regurgitation was degenerative and ischaemic. Endocarditis, ischemic and congenital cause was also reported. As aortic stenosis increased with age, mitral stenosis decreased (38). Study done in Brazil (State of São Paulo) in 2009 revealed, out of 174 patients with severe valvular disease, the main cause of valve disease was rheumatic in 60%, followed by 15% of degenerative aortic disease and mitral valve prolapse in 13% (45).

In Uganda, among 140 heart failure (HF) patients, rheumatic heart disease (RHD) was the leading cause of HF in 31% of patients. Among children (age ≤ 16 years), congenital heart disease (CHD) was the first cause of HF (60%), followed by RHD (32%). RHD was the main cause of HF (30%) among adults (46). A recent systematic review of nine articles done in Ethiopia identified, valvular heart disease (42.3%), predominantly related to rheumatic heart disease, is the most commonly identified heart failure cause reported estimate ranged from 29.2 to 81.0% (47). Study done in

Lome (Togo) also reported, valvulopathies (2.6%) was mentioned among the reported cause of heart failure (48). In developing countries, malnutrition and crowded living conditions make children prone to throat infection with Group A streptococcal infection resulting in rheumatic fever in some cases. Many patients do not have access to optimum treatment including penicillin prophylaxis as well as other medical and surgical treatment modalities (49).

Endocardial involvement is relatively common in systemic lupus erythematosus (SLE), particularly in patients with antiphospholipid antibodies. Rheumatoid arthritis causes an immune complex valvulitis with infiltration of plasma cells, histiocytes, lymphocytes, and eosinophils, leading to fibrosis and retraction. Ankylosing spondylitis is associated with HLA-B27–mediated chronic inflammation and proliferative endarteritis of the aortic root and left-sided valves (8). Similarly, study also showed there is an increased risk of new-onset AS in patients with psoriasis, which was independent of age, gender, comorbidity, and socioeconomic status (50).

In 1967, anti-migraine drugs such as ergotamine and methysergide were associated with valvular insufficiency. In 2002, pergolide and cabergoline were also related to valvular changes among their users. Anorexigens such as fenfluramine, dexfenfluramine, and phentermine were also linked with human valvulopathies. More recently, the use of 3,4-methylendioxymetamphetamine (MDMA, 'Ecstasy') and benfluorexhave been found to be associated with DIVHD (51)(52)(53).

A review done by Iung and Vahanian revealed, the incidence of infective endocarditis is approximately 30 cases per million individiuals per year (54). A case series of 10 years from Dakar, Senegal reported, among ten cases of right sided infective endocarditis, valvulopathy was present in 3 patients (55). HIV itself is a risk factor for infective endocarditis in injecting drug users but not in drug nonusers (56). Echocardiographic abnormalities in HIV patients were common, especially LV hypertrophy and diastolic dysfunction (57). Study done by Lange et al reported, among 152 asymptomatic HIV-infected individuals with transthoracic echocardiography (TTE) and computed tomography (CT), 25% of individuals had mitral annular calcification, and 42% had coronary artery calcification, although CVD risk factors such as hypertension (35%), smoking (62%) and dyslipidemia (35%) were present (58).

Cardiovascular disease (CVD) is a common cause of death in patients with chronic kidney disease. A single center retrospective study of chinese inpatients with CKD reported, among 288 enrolled CKD patients, 22.9% had valve calcification, all of which exhibited aortic valve calcification,

while 21.2% exhibited mitral valve calcification. The valve calcification group were significantly older than the non-valve calcification group, and contained more patients with history of coronary artery disease or stroke. Up on subjective global assessment, more valve calcification patients were mid/severely malnourished (59). Other study also showed, there is significant interaction among CKD, AS/MR severity, and mortality, with increasingly worse outcomes for CKD patients with increasing AS/MR severity (60).

In a study of 2,553 AS patients included in the PARTNER trial, chronic obstructive lung disease (COPD) was present in 43% and was associated with increased 1-year mortality. Among those with COPD, oxygen dependence and poor mobility were each independently associated with increased mortality. Pulmonary hypertension (PH) is present in 50–65% of patients with severe AS and is classified as severe in up to 15–25% (61). Study done in USA (2000 to 2012) of patients with aortic valve disease (AVD) of >60 years reported; the most frequent coexisting conditions were hypertension, heart failure, renal failure, anemia, and diabetes. AVD hospitalizations increased most significantly in patients >80 years and those with higher burden of co-morbidities (62). As the population ages, the absolute number of patients with significant AS will rise substantially (63). Immunohistochemical analysis of stenotic aortic valves with different levels of severity have shown that early lesions of aortic stenosis have several common features with atherosclerosis, in particular inflammatory cell infiltrates, lipoproteins, and calcium deposits (64). A nationwide hospital-based register study at Swedish hospitals between 2003 and 2010, AS accounted 47.2% of VHD of which half of AS cases had concomitant atherosclerotic vascular disease (48.4%), whereas concomitant heart failure and atrial fibrillation were common in mitral valve disease and tricuspid regurgitation. Other common comorbidities were thoracic aortic aneurysms in AR (10.3%), autoimmune disorders in MS (24.5%) and abdominal hernias or prolapse in MR (10.7%) and TR (10.3%). Rheumatic fever was rare. The majority of VHDs were diagnosed in the elderly (68.9% in subjects aged ≥65 years), but pulmonary valve disease incidence peaked in newborns. Incidences of AR, AS and MR were higher in men (35).

In addition to intrinsic valve pathologies, cardiomyopathies or other causes of myocardial dysfunction can result in mitral and/or tricuspid regurgitation, even in the absence of intrinsic structural valve abnormalities presumably due to abnormal mechanical stresses that lead to the distortion of normal valves and of the subvalvular apparatus (1). Secondary mitral regurgitation

(functional mitral regurgitation), the valve leaflets and chordae are structurally normal and mitral regurgitation results from an imbalance between closing and tethering forces on the valve secondary to alterations in LV geometry. It is most commonly seen in dilated or ischaemic cardiomyopathies. Functional mitral regurgitation is associated with end-stage dilated cardiomyopathy. Annular dilatation in patients with chronic atrial fibrillation and LA enlargement can also be an underlying mechanism (12). Myocardial damage, either through ischemic events or from dilated cardiomyopathy, results in an anatomically normal valve to leak (65). Ischemic MR has been found to be associated with worse outcomes among patients with coronary artery disease (66).

From a systematic review of 28 articles done by Wang et al (2018), among the 21 studies reporting multivariable analysis, age was most frequently associated with aortic valve disease (AVD) (87% of studies). Male gender, body fat, blood pressure, lipids and smoking were associated with AVD in 40-50% of studies, while most studies (70%) did not find an association with diabetes. Black race independently predicted risk of AVD in two studies investigating race (67). Another prospective study, the Swedish Mammography Cohort, and the Cohort of Swedish Men, comprising 69,365 adults without cardiovascular disease at baseline, were followed for aortic valve stenosis (AVS) incidence and death. Over a mean follow-up of 15.3 years, 1,249 cases of AVS (494 in women and 755 in men) were recorded. The risk of AVS was significantly lower in current light drinkers (1–6 drinks per week compared to lifelong abstainers. The risk of AVS increased with increasing smoking intensity (68).

Mitral valve prolapse occurs when varying portions of one or both leaflets of the mitral valve extend or protrude abnormally above the mitral annulus into the left atrium. Although the prevalence of mitral valve prolapse was once thought to be as high as 15 percent in the general population, more recent studies using new echocardiographic criteria for diagnosis have suggested a prevalence of approximately 2.4 percent (69). Adem et al reported 1.6% of echocardiographic abnormalities was caused by mitral valve prolapse (39) Primary TR is due to intrinsic tricuspid valve disease seen in 15–30 % of all TR cases. Secondary or functional TR is much more common, seen in the absence of structural abnormalities of tricuspid valve which accounts for 70–85 % of all TR cases (70).

4.3. Patterns of valvular lesion involved

Echocardiography allows differentiation of valve disease from a flow murmur, identification of the specific valve involved, definition of the etiology of valve disease, and quantitation of the hemodynamic severity of the lesion along with LV size and function (8). In study done in entire Swedish population, three valve diseases (AS, MR, and AR) comprised the majority of VHDs (89.4% of all diagnosed cases). The incidence of pulmonary valve disease (TS) was the least common VHD (35). Hollenberg SM also indicated mitral regurgitation (MR) is the most common valve defect, followed by aortic stenosis (AS) and aortic regurgitation (AR) (41). Similarly, study done in Brazil reported mitral regurgitation (27.5%) was the most common isolated valve disease, followed by aortic stenosis (23%), aortic regurgitation (13%) and mitral stenosis (11%) (45). The Euro heart survey study also reported, aortic stenosis and mitral regurgitation are the two most frequent diseases among patients referred because of valvular disease in Europe (34). The 6 years study (HP-RHD Registry) done in India, among of 2,005 RHD patients, multivalvular involvement was 43.2%, mitral valve was the commonest affected valve (83.3%). The majority of the patients had moderate-to-severe valvular dysfunction (69.3%). Mitral and tricuspid valve involvement was more frequent in female subjects compared with more frequent aortic valve involvement in male subjects (71).

A study from Africa Tunisia reported, mitral stenosis was the most frequent lesion (44.1%), followed by multiple valve disease (22.3%) (38). Similary, a retrospective study from Tikur Anbassa Teaching Hospital (TAH) Ethioipa showed, combined mitral and aortic valve disease accounted for majority (42.6%) of the lesions followed by combined mitral regurgitation and stenosis (24.4%) (31). Adem et al, from Ayder referral Hospital also reported, among patients with rheumatic heart diseases (20.9%), co-occurrence of mitral and aortic valve disease was the commonest (39).

4.4. Clinical outcomes and Complications

In general, the heart can withstand significant amounts of stenosis and regurgitation before clinical symptoms appear. The different types of VHD may cause systolic and diastolic LV dysfunction and failure; infective endocarditis (IE); pulmonary arterial hypertension (PAH); AF or flutter and thromboembolic complications; absolute and relative myocardial ischemia and a tendency to develop larger MI. The end stage of most valvular heart disease is heart failure (6)(4).

Heart disease and stroke statistics (2011) from the American Heart Association reported, the pooled estimated 23,313 patients died from VHD in the United States, with aortic and mitral valve disease accounting for 15,183 and 2,644 deaths, respectively. Although, the overall incidence of RHD very low, the pooled mortality rate was 3,201. The same year, an estimated 98,000 patients were discharged with a diagnosis of VHD (72). A retrospective study from Southwestern Europe (Lisbon, Portugal) reported, among 287 VHD patients hospitalized over a 22-month period, the overall in-hospital mortality was 9.8% and cardiovascular mortality was 8.7%. Most (33.3%) of death was occurred in the context of ACS, followed by advanced refractory HF and cardiogenic shock due to VHD (29.6%), and to severe refractory pulmonary hypertension (related to valve disease and/or pulmonary embolism) in 7.4%. The remaining cause of death were infectious endocarditis of prosthetic valve or devices, acute complications after prosthetic valve implantation (surgical or percutaneous), and pericardial effusion (73). A study of deaths due to valve disease in the community and in hospital done by S. Talbot showed that, aortic valve disease was a more common cause of sudden death than was mitral valve disease. Mitral valve disease was a frequent cause of death in the elderly, these were often (66%) undiagnosed prior to death, particularly in men. Systemic embolism was an important factor influencing admission to hospital and was often the presenting feature (74).

HP-RHD Registry study reported, major adverse cardiovascular events (MACEs) were recorded in 23.4% patients and comprised mainly advanced heart failure (15.6%), peripheral embolism (4.1%), and stroke (3.9%). Advanced age, severe mitral stenosis, severe tricuspid regurgitation, presence of pulmonary artery hypertension and atrial fibrillation were the independent risk determinants of major adverse cardiovascular events (71). Another 12.6 years (between 1996 and 2013) retrospective study done at Siriraj Hospital of Thailand reported, out of 185 patients with isolated rheumatic MS, the incidence of long-term adverse outcome was 43.2% and included mortality in two patients (1.1%), hospitalization due to heart failure in 20 patients (10.8%), new-onset atrial fibrillation in 71 patients (38.4%), and embolic stroke in 14 patients (7.6%). Left atrial dimension greater than 50 mm and left ventricular end-systolic dimension less than 28 mm was associated with long-term adverse outcomes (75).

The survival of patients with aortic stenosis is nearly normal until the onset of symptoms, when survival rates decrease sharply. After the onset of symptoms, average survival is only two to three

years. Although the rate of progression of aortic stenosis is variable and difficult to predict, approximately 75 percent of patients with aortic stenosis will be dead three years after the onset of symptoms if the aortic valve is not replaced (76). Study done in USA of patients with Aortic Valve Disease (AVD) of >60 years revealed that, the overall AVD hospitalizations was increased by 59% from 2000 to 2012. This increase was most significant in patients >80 years and those with higher burden of co-morbidities. Overall inhospital mortality of patients hospitalized for AVD was 3.8%, which significantly decreased from 4.5% in 2000 to 3.5% in 2012. The length of hospital stay was decreased from 8.4 days in 2000 to 7.8 days in 2012 and was associated with a substantial increase in cost of hospitalization in the last decade from $31,909 to $38,172 (62). A similar study from New Zealand, in year 1998 to 2007, there were 8,876 deaths due to VHD in the collection, driven predominantly by an increase in aortic valve disease. The mean WHO age-standardized mortality rate over 20 years was 10.9 per 100,000 population per year. Nonrheumatic aortic valve disease was the most common cause of mortality, accounting for 49% of all deaths; while rheumatic heart disease decreased (77).

Study from Brazil showed, among a total of 174 patients with severe valvular disease, approximately half of patients (44%) presented with atrial fibrillation (45). Another retrospective study done in Portugal, Lisbon by Fátima et al reported, among 287 patients, 29 patients (10.1%) had complete AV block at presentation (16 patients with AS and 13 with MR; AS and MR coexisted in five patients) which was one among the other cause of syncope. The mean length of hospital stay was 11.98 ± 14.33 days. Most patient were discharged home from hospital (84.3%) and 5.2% were transferred to another hospital for continued care (73).

From Uganda, a prospective cohort study of 449 established RHD subjects (aged 5–60 years), followed up for 12 months, among 331 who had atleast one follow up, 35% (116/331) developed decompensated heart failure and, 63.7% (211/331) developed atrial fibrillation. Heart failure was associated with poor penicillin adherence and left ventricular end diastolic diameter greater than 55 mm. Atrial fibrillation was associated with left atrial diameter >40 mm. The 1-year mortality rate of 17.8% (59 deaths). Most deaths occurred within the first three months of presentation (81). A 6 year retrospective study from medical wards of Tikur Anbassa Teaching Hospital (TAH), Ethiopia from January 1995 to December 2001 reported, among a total of 457 cardiovascular deaths, including cerebrovascular accidents, 121 (26.5%) were due to rheumatic heart disease

(RHD). The overall mean age at the time of death was 25.89 ± 11.05 years. There were more female deaths accounting for 57.4 %. About 70% of RHD patients died from congestive heart failure. Eleven percent (13 patients) each died from systemic embolism and co-morbid conditions (31).

5. General objectives

To assess the incidence, clinical outcomes and associated factors of VHDs patients admitted to the medical ward of JUMC.

5.1. Specific objectives

- To assess the incidence of mortality among VHD patients admitted to medical wards of JUMC with in the study periods.
- To identify patterns of valvular disease among patients admitted to medical wards of JUMC
- To determine clinical outcomes of valvular disease among patients admitted to medical wards of JUMC
- To determine predictors of mortality of valvular heart disease patients among patients admitted to medical wards of JUMC.

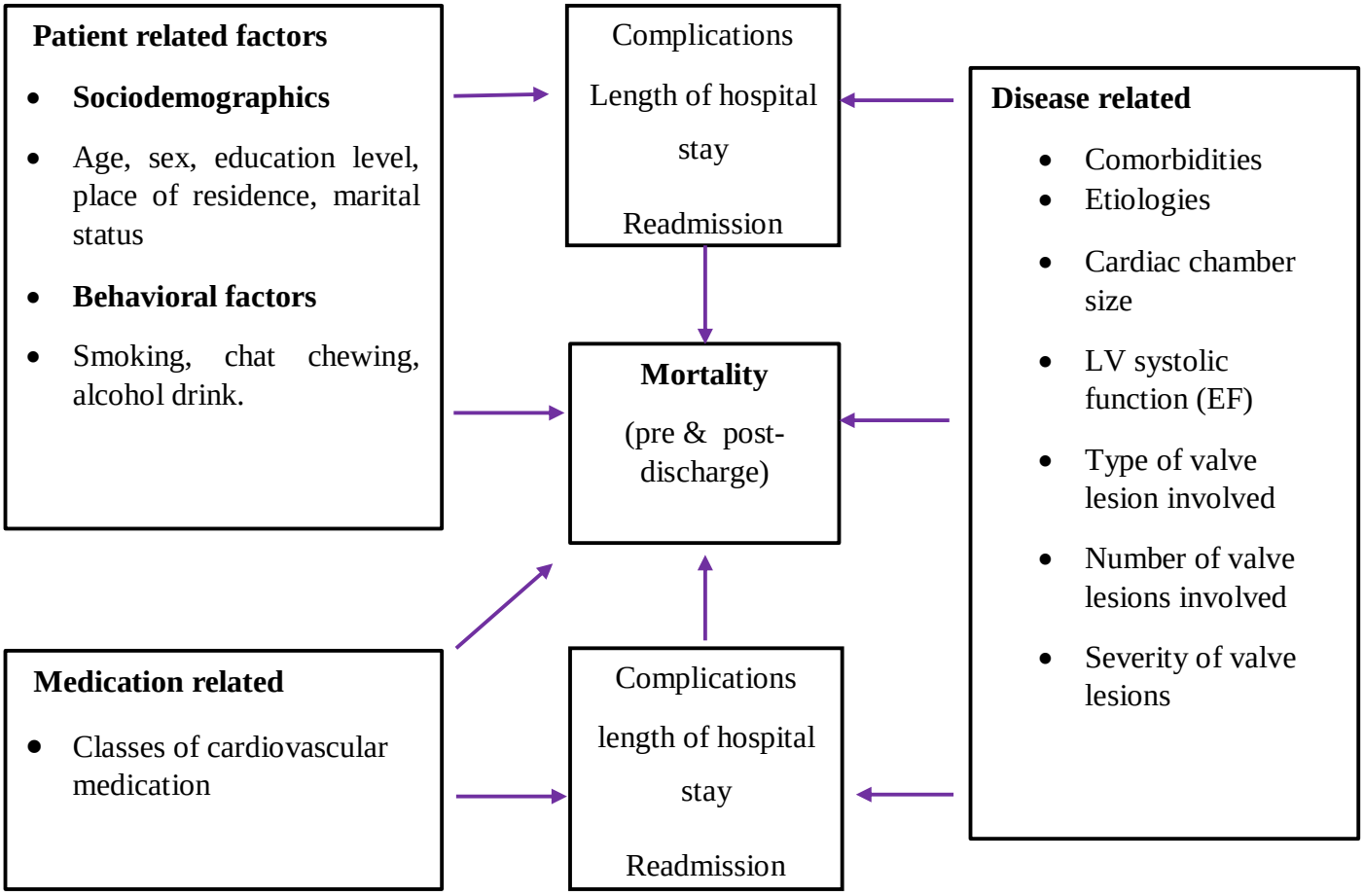


Figure 1: Conceptual framework for factors associated with VHD Clinical Outcomes, Jimma Medical center, 2019

7. Methods

7.1. Study area: The study was conducted at Jimma medical center (JUMC), a tertiary hospital in Jimma city, Jimma zone, Oromia regional state, Southwest Ethiopia, it is 352 kilometers away from Addis Ababa. Jimma is the largest city in south-western Ethiopia. The Hospital was established in 1930 E.C by Italian invaders for the service of their soldiers. Now, JUMC is one the referral hospital for the Southwest population of the country. The hospital provides service to 15 million people with 1600 staff members, 32 intensive care units, and 800 beds (78). The cardiology services in Ethiopia are still at a very early stage (79). In the country, there is only one cardiothoracic surgerical center in the capital city, Addis Ababa. Jimma University medical center has cardiologic unit which run by two cardiologists and medical residents. There is no cardiothoracic surgeon and the center do not have cardiac and thoracic surgery center.

7.2. Study design and period: A hospital based prospective observational study was carried out for consecutive 5 months starting from April 10 to September 10, 2019.

7.3. Source populations: All cardiovascular disease patients admitted to medical wards of Jimma University Medical center during the study period.

7.4. Study populations: Echocardiography (ECHO) confirmed valvular heart disease (VHD) patients and those fulfilled illigibility criteria admitted within the study period.

7.5. Sample size and sampling technique

All adults patients admitted to medical wards between April 10 to Semptember 10, 2019, diagnosed to have valvular heart disease by echocardiography imaging and fulfilled the inclusion criteria were included using consecutive sampling method. During the study period a total of 156 moderate and severe VHD patients were identified, included and followed up for consecutive 90 days.

7.6. Inclusion criteria

- Age 15 years and above
- Diagnosis confirmed by ECHO in addition to clinical diagnosis

7.7. Exclusion criteria

- Patient not willing to participate and give consent
- Patient to be referred for surgery
- Mild valve regurgitation and stenosis (80) (81)

7.8. Description of outcome endpoints

7.8.1: Primary outcome: Overall death (90 days-inhospital and post-discharge). Mortality was confirmed by the death summary written by physician treated the patients as well as through patient's relative witness through phone call and reviewing of the patients' medical **record.**

7.8.2: Secondary outcome: Complications, readmission, length of hospital stay (LoHS). The length of hospital stay was measured in number of days.

7.9. Variables of the study

7.9.1. Dependent variables

- Complications
- Length of hospital stay (in days)
- Readmission
- Death/mortality

7.9.2. Independent variables

7.9.2.1. Patient related factors

- Sociodemograhics and behavior
  - age
  - sex
  - residence
  - cigarette smoking
  - alcohol drink
  - chat chewing
  - educational level
  - marital status

7.9.2.2. Disease related factors

- Comorbidities
- Etiologies
- Severity of the valvular lesion
- Size of cardiac chambers
- Baseline ejection fraction
- Type of valvular lesions

7.9.2.3. Drug related factors

- Classes of cardiovascular medications

7.10. Data collection Instrument and procedures

Data collection tool has been developed after reviewing different relevant literatures, institutional guidelines and patient follow up charts. Before starting data collection, the tool was changed to the local language (Afan Oromo and Amharic) and then translated back to english. Data was collected through interview and reviewing the patient's medical record. The patient's care giver was asked when the patients failed to communicate. The data collected included patient's socio-demographics, comorbidities, echocardiographic findings, current medications, clinical outcomes. Data collection was carried out by trained 2 clinical nurses and 2 pharmacists and supervised by 2 medical residents and principal investigator.

7.11. Data Quality Assurance

Before starting data collection, pre-test was conducted on eligible patients, (5% of the final sample size) and the collection tool was modified accordingly. The trained nurses collected sociodemographics and discharge status of the patients while comorbidities, echocardiographic report, current medications and in hospital complications was collected by trained pharmacists. The collected data was checked appropriately for completeness, accuracy and consistency. Incomplete data was returned to the data collector and revised. The post-discharge mortality and readmission information was obtained through patient and/or relative's telephone interview and review of hospital medical charts by the principal investigator.

7.12. Data processing and analysis

Data was entered into Epi-Data 3.1 for cleaning and exported to SPSS Version 20 for analysis. Descriptive analysis was performed and results presented by mean, median, frequency tables and charts. Chi-square ($\chi 2$) with Fisher's exact test was used to compare the significance of

associations between categorical variables. Independent sample t-test and Mann whitney U test was used to compare mean of normal and median of non-normal distributed continuous variables respectively. Kaplan Meier with Log-rank test was used to assess and compare survival status between rheumatic and non-rheumatic VHDs. Variables identified with p-value < 0.25 in bivariate cox regression regression was considered candidate for multivariable cox regression. Multivariable Cox regression with backward elimination method was used to identify independent predictors of mortality. Hazard ratio (HR) was used as a measure of strength of association and p-value < 0.05 was considered declare statistical significance.

7.13. Ethical consideration

Ethical clearance (with a reference number, IHRPGJ/652/2019) was obtained from the Institutional Review Board (IRB) of Jimma University, Institute of Health. Prior to the start of data collection, the overall aim of the study was notified to participants. Written informed consent was obtained prior to the interview and review of the patient's record. Participants were assured that the study will not pose any risks or problems to their health. Confidentiality of their personal information was kept and assured through use of codes as identifier.

7.14. Dissemination plan

The result of the study will be presented and disseminated to school of pharmacy, Institute of health of Jimma University, JUMC, and other concerned bodies. Then, effort will be made to publish on reputable journal.

7.15. Operational definition

- **Comorbidity** is the presence of one or more additional diseases or disorders co-occurring with a valve lesions; in the countable sense of the term, is each additional disorder or disease.
- **A risk factor** is a habit or an environmental condition, that predisposes an individual to develop a particular disease
- **Length of hospital stay (LoHS)**. is the length of an inpatient episode of care, calculated from the day of admission to day of discharge.
- **A hospital readmission** is an episode when a patient who had been discharged from a hospital is readmitted within 90 days.
- **Clinical Outcome**: refers to the results of any healthcare intervention, including the entire range of activities performed. It include death, complications, LoHS, and readmission.
- **Complication** is an unfavorable evolution or consequence of a VHD, or a therapy. They include those directly (scientifally) related adverse consequences of VHD such congestive heart failure, atrial fibrilation, stroke and other embolic events, infective endocarditis, Cardiogenic pulmonary edema, pulmonary hypertension, bradyarrhthmia.
- **Burden** in this study is the impact of a VHD as measured by mortality, incidence, length of hospital stay, readmission.
- **Severity of VHD:** in this study, grading of the severity of valve lesion was reported in echocardiography as moderate and severe.
- **Etiology:** is identified cause of valve lesion confirmed/reported by echocardiography.
- **Incidence rate of death :** $\frac{\text{The number death of VHD cases within 3 months}}{\text{Total number of patients at risk of death within 3 months period}}$

Participants' enrollment

During the study period, a total of 191 valvular heart disease (VHD) patients had identified, among which 35 patients were excluded due to their valvular disease was mild (32 patients) and the remaining three patients were referred to other facilities for surgical intervention. Thus, VHD accounted about 22.6% of inpatient medical admissions. Finally, 156 VHD patients having atleast one moderate or severe valvular disease were enrolled and followup for 90 days. The was no loss to follow up. [Figure 2]

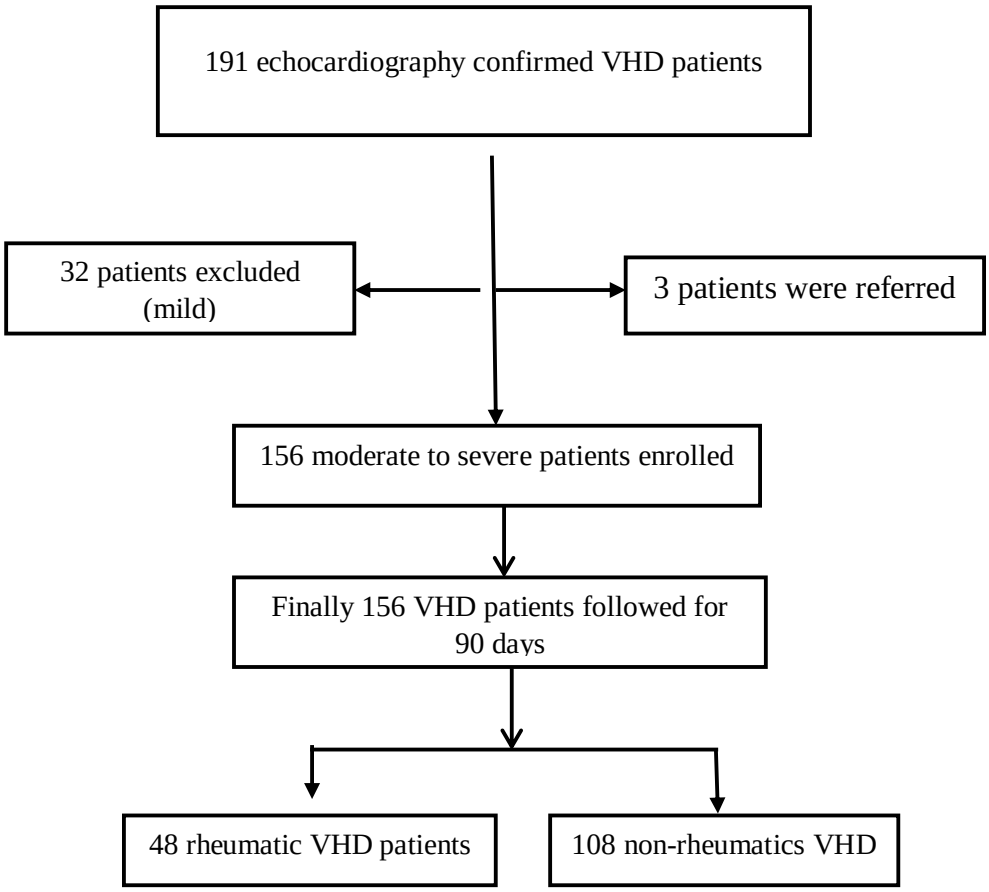


Figure 2: Flow diagram of participants' enrollment, JUMC, 2019

8 . Result

8.1: Baseline sociodemograhics characteristics

A total of 156 moderate to severe valvular heart disease patients were included in this study. Female accounted for 50.64% of the participants. The mean age of the participants was 45.62 ±19.126 years. More than half (57.1%) of the patients were in age greater than 40 years. Most of the patients were married 127 (81.4%) and reside in rural areas 103 (66.03%). Significant number of patients who were from urban area were died (50.0% vs. 30.20%, P=0.039). About half of them were illiterate 81 (51.92%) and farmer 81 (51.92%). From a total participants, 63 (40.38%) patients had history of and current khat chewer. Small number, 8 (5.1%) of patients reported had family history of cardiovascular disease. [Table 1]

Table 1: Sociodemograhics characteristics of study participants, Jimma Medical Center (JMC), 2019

Variables		Overall (156)	Died (n=30)	Survived (n=126)	P value
Age (mean ± standard deviation), years.		45.62 ± 19.126	42.23±19.625	46.43±18.995	0.282
	<40 years	67 (42.9%)	15(50.0%)	52 (41.3%)	0.385
	>40 year	89 (57.1%)	15(50.0%)	74 (58.7%)	
Sex	Male	77 (49.36%)	14(46.7%)	63 (50.0%)	0.743
	Female	79 (50.64%)	16(53.3%)	63 (50.0%)	
Residence	Urban	53 (33.97%)	15 (50.0%)	38 (30.2%)	0.039
	Rural	103 (66.03%)	15(50.0%)	88 (69.8%)	
Marital status	Single	29 (18.60%)	8 (26.7%)	21 (16.7%)	0.206
	Married	127 (81.40%)	22 (73.3%)	105 (83.3%)	
Education level	Illiterate	81 (51.92%)	14 (46.7%)	67 (53.2%)	0.214
	Primary	62 (39.74%)	11 (36.7%)	51 (40.5%)	
	Secondary & above	13 (8.34%)	5 (16.7%)	8 (6.3%)	

Occupation	Farmer	81 (51.92%)	13 (43.3%)	68 (54.0%)	0.279
	Merchant	26 (16.67%)	5 (16.7%)	21 (16.7%)	
	Student	19 (12.20%)	4 (13.3%)	15 (11.9%)	
	Private job	12 (7.70%)	2 (6.7%)	10 (7.9%)	
	Housewife	10 (6.40%)	5 (16.7%)	5 (4.0%)	
	Governmental	8 (5.12%)	1 (3.3%)	7 (5.6%)	
Khat chewing	Yes	63 (40.38%)	11 (36.7%)	52 (41.3%)	0.644
	No	93 (59.6%)	19 (63.3%)	74 (58.7%)	
Smoking	Yes	17 (10.90%)	4 (13.3%)	13 (10.3%)	0.744
	No	139 (89.1%)	26 (86.7%)	113 (89.7%)	
Alcohol drink	Yes	14 (8.97%)	3 (10.0%)	11 (8.7%)	0.734
	No	142 (91.0%)	27 (90.0%)	115 (91.3%)	
Family history of cardiovascular disease	Yes	8 (5.12%)	2 (6.7%)	6 (4.8%)	0.651
	No	148 (94.9%)	28 (93.3%)	120 (95.2%)	

8.2: Patterns of co-morbidities

Hypertension (23.1%) was the most frequently identified comorbid disease followed by ischemic heart disease (IHD) (9.0%), thyrocardiac diseases (7.7%), chronic obstructive lung disease (COPD) and asthma (7.7%). More number of patients who had CKD as a co-morbidity were died (20.0% vs. 3.2%, P= 0.004). None of the patients who had diabetes mellitus (DM) and severe acute malnutrition (SAM) as a co-morbidity were died. [Table 2]

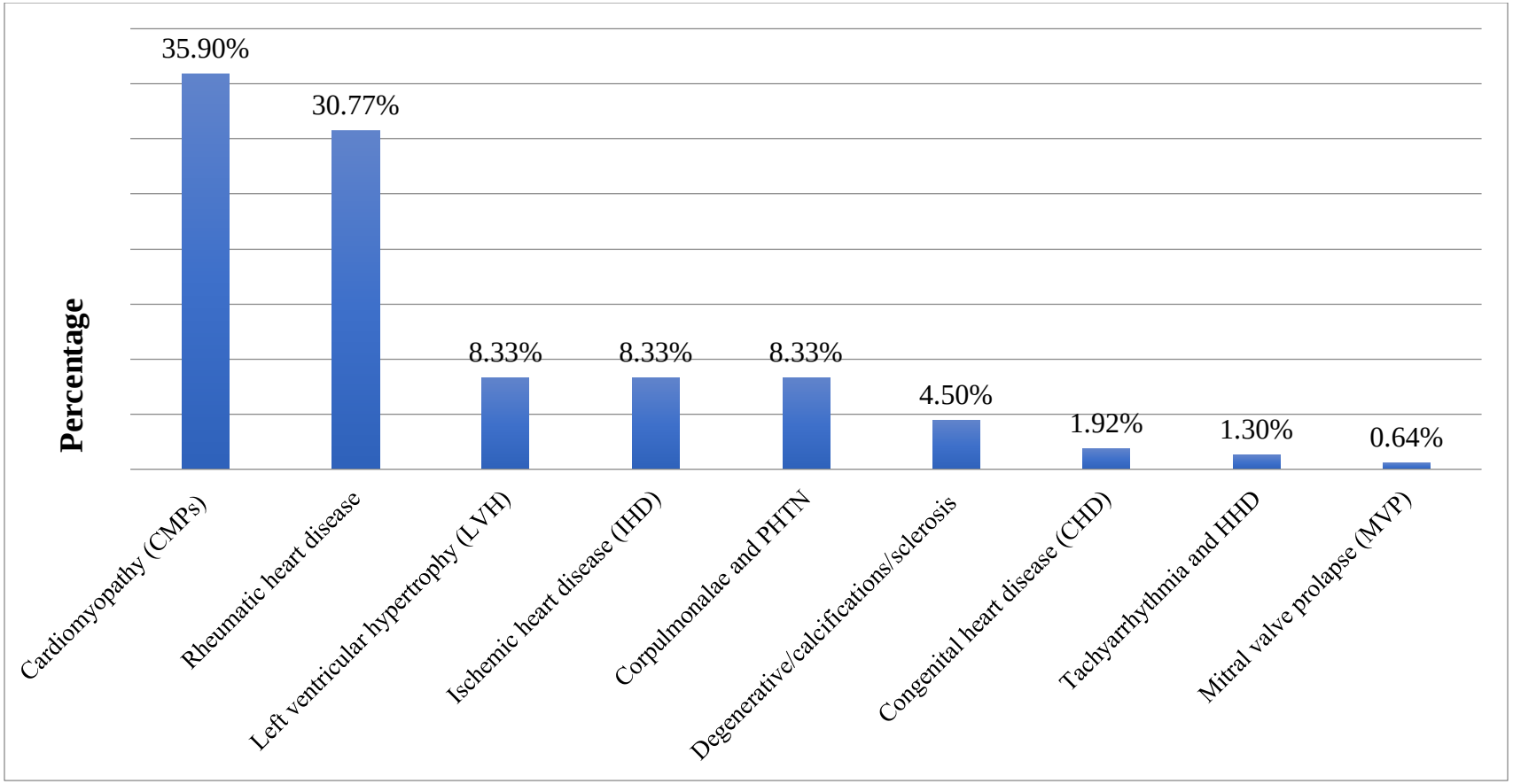
Table 2: Patterns of Co-morbidities of the participants, JMC, 2019

Conditions	Frequency	Percentage
Hypertension	36	23.1%
Ischemic heart disease	14	9.0%
Thyrocardiac disease	12	7.7%
COPD & Asthma	12	7.7%
Tuberculosis	11	7.1%
Chronic kidney disease	10	6.4%
Diabetes Mellitus	5	3.2%
Retroviral infection	5	3.2%
Severe acute malnutrition	3	1.9%

COPD: chronic obstructive lung disease

8.3: Echocardiography identified etiologies

Cardiomyopathy (35.90%) was the most commonly reported etiology causing valvular lesion followed by rheumatic heart disease (30.77%). There was no significant difference in mortality interms of etiologies of valve disease (P= 0.426). Rheumatic cause of valvular heart disease (VHD) was more common in younger patients (age less than 40 years) while, non-rheumatic causes were common in age greater than 40 years old (P < 0.001). Degenerative VHD (4.5%) was only reported in those age greater than 40 years. It was the most common cause of aortic stenosis (AS) (36.4%), while rheumatic VHD was the most common cause of mitral stenosis (MS) (95.2%). The mean (SD) left ventricular (LV) ejection fraction was 41.51 ± 16.24 %. There was no significant difference in mean LV ejection fraction between VHD patients who were died and survived (P= 0.935). Majority (86.50%) of the patients had at least one cardiac chamber dilation. [Figure 3]



HHD: hypertensive heart disease, PHTN: Pulmonary hypertension

Figure 3: Etiologies of valvular heart disease of participants, JMC, 2019

8.4: Patterns of involvement of cardiac valves and Doppler findings

Mitral valve (38.5%) was the most common affected valve morphology followed by aortic valve (30.1%). Pulmonic valve was involved in around 1.9 % of patients. In rheumatic heat disease (RHD) patients, the most common valve structure affected were mitral valve (91.7%) and aortic valve (54.2%).

From the study participants, 63.5% of the patients had at least one severe valve lesion. The remaining 36.50% had a moderate valve lesion. There was no significant difference in severity of valvular lesions between patients who were died and survived (P= 0.39). Compared to non-rheumatic VHD, rheumatics patients had more severe valvular lesions (75% vs. 58.3%, P= 0.046). Mitral regurgitation (84.0%) and tricuspid regurgitation (79.5%) was the most common doppler finding in all VHD patients followed by aortic regurgitation (35.25%). Aortic stenosis (7.05%) and pulmonic valve regurgitation/stenosis (7.05%) were rarely reported. Majority (84.6%) of VHD patients had at-least two valvular lesions and the remaining 15.4% had isolated single valvular disease. Rheumatic heart disease (RHD) patients had more multi-valvular lesions compared to non-rheumatics (93.8% vs. 80.6%, P = 0.035). Mitral stenosis (P= 0.001) and aortic regurgitation (P= 0.01) was significantly the most common echocardiographic (ECHO) finding in RHD patients compared to non-rheumatic valvular diseases. [Figure 4]

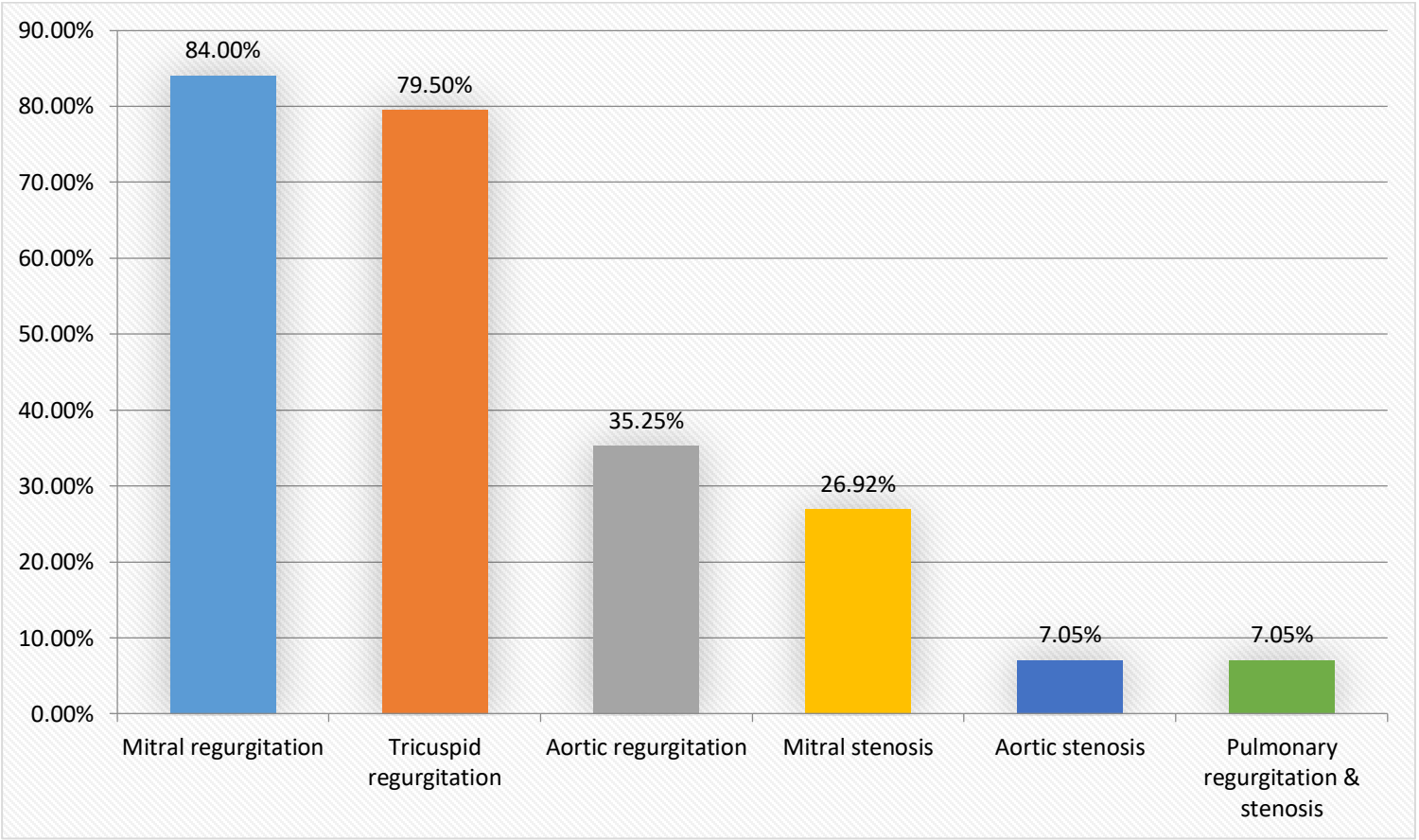


Figure 4: Patterns of echocardiographic Doppler finding of participants, JMC, 2019

8.5: Cardiovascular medications used in valvular heart disease (VHD) patients

Diuretics (92.90%) were the most commonly prescribed followed by beta-blockers (BBs) (37.20%) and angiotensin converting enzyme inhibitors (ACEIs) (36.50%). Significant number of VHD patients who survived prescribed ACEIs compared to patients who were died (41.3% vs. 16.7%, P= 0.012). However, more number of patients who died were prescribed digoxin (33.3% vs. 16.7%, P= 0.040). Rheumatic VHD patients were more likely prescribed anti-coagulants and digoxin compared to non-rheumatic causes (P<0.05). Regarding treatment of infective endocarditis (IE), ceftriaxone and gentamycin was prescribed empirically for four rheumatic heart disease (RHD) patients with native valve subacute bacterial infective endocarditis while vancomycin and gentamycin was prescribed for one RHD patients co-morbid with RVI infection.[Table 3]

Table 3: Classes of cardiovascular medications use in VHD patients, JMC, 2019.

Classes	Frequency	Percentage
Diuretics	145	92.90%
Beta blockers	58	37.20%
ACEIs	57	36.50%
Anti-platelets	49	31.40%
Statins	47	30.10%
Anticoagulants	44	28.20%
Digoxin	31	19.90%
Amlodipine	9	5.80%

ACEIs: angiotensin converting enzyme inhibitors

8.6. Clinical Outcomes

8.6.1: Admission complications

The patients were presented or developed different major cardiovascular complications. About 83.33% of patients were presented with congestive heart failure followed by pulmonary hypertension (44.23%) and atrial fibrillation (28.20%). Relatively small number of valvular heart disease (VHD) patients who died were presented with congestive heart failure as admission complication compared those patients who survived (70.0% vs. 86.5%, P= 0.029). However,

significant number of patients who died were presented with atrial fibrillation compared to those who survived (43.3% vs. 24.6%, P= 0.04). When rheumatic and non-rheumatic etiology was compared, atrial fibrillation, pulmonary hypertension and infective endocarditis were significantly reported complications in rheumatic etiology (P< 0.05). [Table 4]

Table 4: Major cardiovascular events as admission complications of VHD patients, JMC, 2019

Major cardiovascular events		All (n=156)	Died (n=30)	Survived (n=126)	P value
Congestive heart failure	Yes	130 (83.33%)	21 (70.0%)	109 (86.5%)	0.029
	No	26 (16.7%)	9 (30.0%)	17 (13.5%)	
Pulmonary hypertension	Yes	69 (44.23%)	11 (36.7%)	58 (46.0%)	0.353
	No	87 (55.8%)	19 (63.3%)	68 (54.0%)	
Atrial fibrillation	Yes	44 (28.20%)	13 (43.3%)	31 (24.6%)	0.040
	No	112 (71.8%)	17 (56.7%)	95 (75.4%)	
Left ventricular thrombus	Yes	18 (11.54%)	3 (10.0%)	15 (11.9%)	1.000
	No	138 (88.5%)	27 (90.0%)	111 (88.1%)	
Cardiogenic pulmonary edema	Yes	15 (9.61%)	2 (6.7%)	13 (10.3%)	0.737
	No	141 (90.4%)	28 (93.3%)	113 (89.7%)	
Infective endocarditis	Yes	5 (3.20%)	0 (0.0%)	5 (4.0%)	0.584
	No	151 (96.8%)	30 (100.0%)	121 (96.0%)	
Stroke	Yes	5 (3.20%)	1 (3.3%)	4 (3.2%)	1.000
	No	151 (96.8%)	29 (96.7%)	122 (96.8%)	
Brady-arrhythmia	Yes	4 (2.56%)	0 (0.0%)	4 (3.2%)	1.000
	No	152 (97.4%)	30 (100.0%)	122 (96.8%)	
Polycythemia/cyanosis	Yes	1 (0.64%)	1 (3.3%)	0 (0.0%)	0.192
	No	155 (99.4%)	29 (96.7%)	126 (100.0%)	

8.6.2: Lengths of hospital stay (LoHS)

The median (IQR) length of hospital stay for a total patients was 12.0 (8, 21) days. There was no statistical significance difference in length of hospital stay between patients who were died and survived (P= 0.461).

8.6.3: Readmission rate

The patient was observed if they were rehospitalized after discharged improved till the end of the study period. Seventeen (10.90%) patients were rehospitalized after the first discharged. The mean time (SD) to readmission was 42.23 ± 24.52 days. There was no significant difference in number of readmission between patients who were died and survived (P= 0.744).

8.6.4: Mortality

During the 90 days follow-up, 30 (19.2%) of patients were died from all causes. The total person time for all patients at risk of death was 12, 609 days. Thus, the overall incidence rate of death of VHD within 90 days was 2.38 cases per 1000 person-day. The mean (SD) age at death was 42.23 ±19.62 years. Overall mean (SE) survival time was 80.80 ± 1.84 days (95% confidence interval (CI), [77.20-84.40]). There was no statistical significant difference in mean (SE) of survival time between rheumatic and non-rheumatic VHD patients respectively (Log-rank (P=0.526)). [Figure 5]

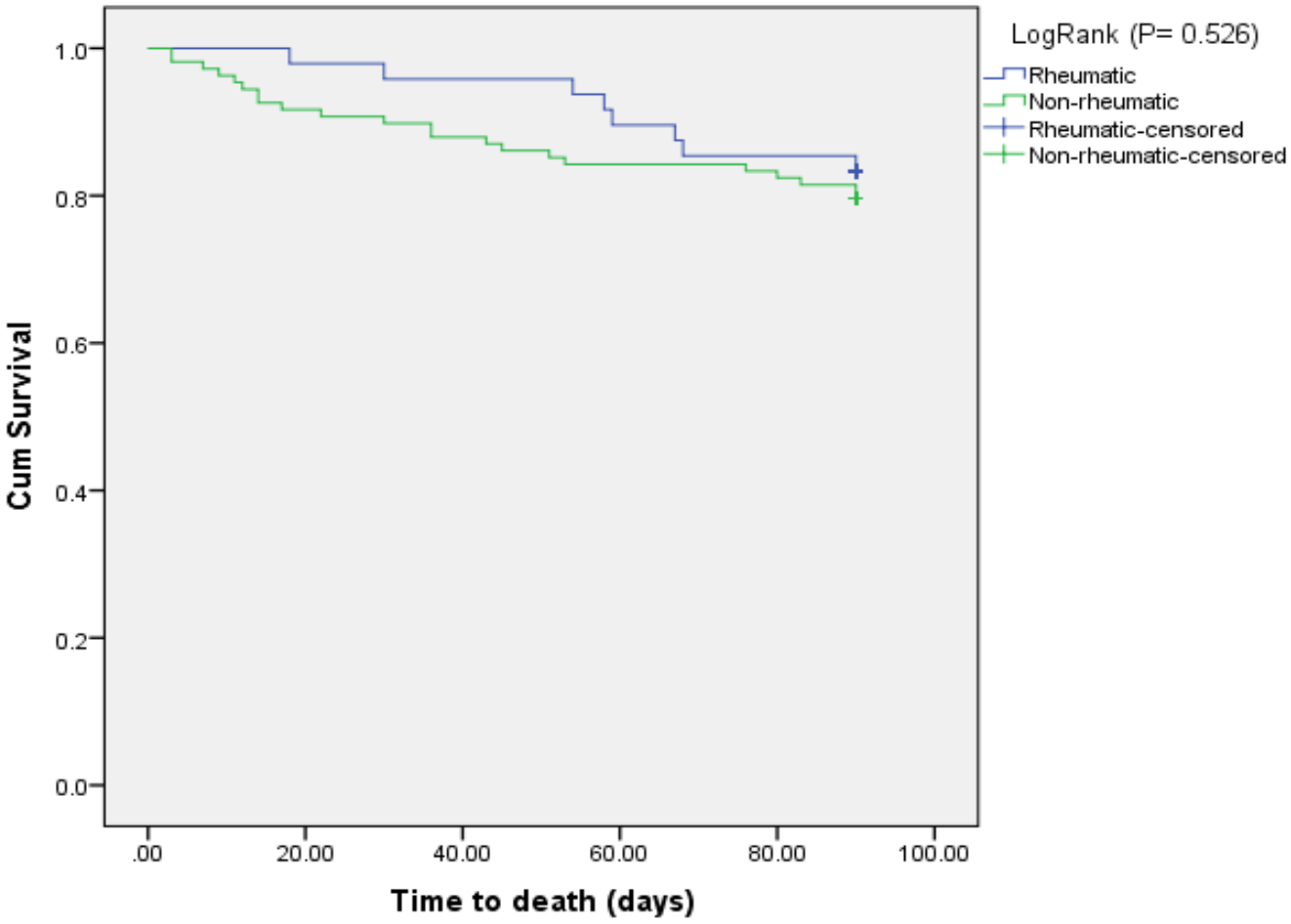


Figure 5: Kaplan Meier survival function of rheumatic vs. non-rheumatic valvular heart disease patients, JMC, 2019

8.6.5: Predictors of mortality

Variables identified with p-value < 0.25 in bivariate cox regression regression was entered into multivariable cox-regression with backward ellimination method. Those variables were urban residence, chronic kidney disease (CKD), thyrocardiac disease, retroviral infection (RVI), cardiac chamber dimension, severe pulmonary stenosis (PS), congestive heart failure (CHF), atrial fibrillation (AF), angiotension converting enzyme inhibitors (ACEIs), beta blockers (BBs), digoxin, anti-platelets, statins, and amlodipine.

From multivariate cox-regression, patients who were from urban area had 59.8% increased risk of death compared to those who were from rural areas (AHR= 1.598, 95% CI, 1.108-2.305). Presence of CKD as a comorbidity were associated with 2.56 times at risk of death (AHR= 2.562, 95% CI, 1.62-4.06). Atrial fibrillation (AF) as admission complication was associated with 52.0% increased risk of death (AHR= 1.52, 95% CI, 1.051-2.195). Similarly, patients with severe pulmonary stenosis had more than 3 times at risk of death (AHR= 3.339, 95% CI, 1.194-9.337). Having congestive heart failure (CHF) as admission complication was associated with 38.6% reduced risk of death (AHR=0.614, 95% CI, 0.413-0.912). Patients who prescribed angiotensin converting enzyme inhibitors (ACEIs) were around 64.0% less likely to die (AHR= 0.360,95%CI,0.135-0.958).[Table5]

Table 5: **Bivariate and multivariate Cox-proportional hazard regression for predictors of death of the participants, JMC, 2019 (N= 156).**

Covariates		Died (n=30)	Survived (n=126)	CHR	95% CI	P value	AHR	95% CI	P value
Residence	Urban	15(50.0%)	38 (30.2%)	1.482	1.036-2.12	0.031	1.598	1.108-2.305	0.012
	Rural	15 (50.0%)	88 (69.8%)						
Chronic kidney disease	Yes	6 (20.0%)	4 (3.2%)	2.325	1.484-3.642	0.000	2.562	1.617-4.06	<0.001
	No	24 (80.0%)	122 (96.8%)						
Thyrocardiac disease	Yes	4 (13.3%)	8 (6.3%)	1.450	0.856-2.454	0.167	1.63	0.900-7.65	0.074
	No	26 (86.7%)	118 (93.7%)						
Retroviral infection	Yes	2 (6.7%)	3 (2.4%)	1.612	0.786-3.305	0.193	1.784	0.848- 3.75	0.127
	No	28 (93.3%)	123(97.6%)						
Atrial fibrillation (AF)	Yes	13 (43.3%)	31 (24.6%)	1.427	0.995-2.048	0.053	1.52	1.051-2.20	0.026
	No	17 (56.7%)	95 (75.4%)						
Severe PS	Yes	1 (3.3%)	0 (0.0%)	2.386	0.878-6.481	0.088	3.339	1.19-9.337	0.022
	No	29 (96.7%)	126(100.0%)						
Chamber diameters	Normal	7 (23.3%)	14 (11.1%)	1.530	1.002-2.337	0.049	1.541	1.005-2.36	0.057
	Dilated	23 (76.7%)	112 (88.9%)						
Congestive heart failure	Yes	21 (70.0%)	109 (86.5%)	0.629	0.425-.929	0.020	0.614	0.413-.912	0.016
	No	9 (30.0%)	17 (13.5%)						

ACEIs	Yes	5 (16.7%)	52 (41.3%)	0.308	0.118-0.80	0.016	0.360	0.135-.958	0.041
	No	25 (83.3%)	74 (58.7%)						
Beta blockers (BBs)	Yes	8 (26.7%)	50 (39.7%)	0.588	0.262-1.32	0.198	0.647	0.282-1.48	0.304
	No	22 (73.3%)	76 (60.3%)						
Anti-platelets	Yes	5 (16.7%)	44 (34.9%)	0.414	0.158-1.08	0.072	0.536	0.200-1.44	0.216
	No	25 (83.3%)	82 (65.1%)						
Statins	Yes	6 (20.0%)	41 (32.5%)	0.576	0.235-1.41	0.227	3.172	0.549-18.34	0.197
	No	24 (80.0%)	85 (67.5%)						
Digoxin	Yes	10 (33.3%)	21 (16.7%)	2.180	1.020-4.66	0.044	1.916	0.889-4.13	0.097
	No	20 (66.7%)	105 (83.3%)						
Amlodipine	Yes	5 (16.7%)	4 (3.2%)	4.996	1.90-13.10	0.001	3.690	1.380-9.86	0.009
	No	25 (83.3%)	122 (96.8%)						

Key: ACEIs**:** Angiotensin Converting Enzyme Inhibitors, PS: Pulmonary Stenosis, CI: Confidence Interval, C/AHR: Crude/Adjusted Hazard Rate

9. Discussion

In this study, we assessed co-morbidities and echocardiographically identified etiologies of moderate to severe valvular heart disease. Burden of valvular lesion, mainly mitral regurgiation, tricuspid regurgitation, and multivalvular was idenfied. We also assessed admission and inhospital compalications and its medical management. Few patients were referred for valvular surgeries and majority of our patients were medically managed. Finally, we identified all cause mortality was high.

Burden, risk factors, patterns and management of valvular heart disease

More than half (57.10 %) valvular heart disease (VHD) patients were aged 40 years and above. This is consistent to a study by Nkomo et al, where it indicated the prevalence of VHD was increased with age (82). Euro Heart Survey (EHS) also reported, patients with VHD are often elderly (34). In this study, rheumatic heart disease patients had lower mean age compared to non-rheumatic VHD. This finding is consistent with "the REMEDY study"(24) and study done by Adem et al from Mekele, Ethiopia (39). Regarding social drug use, 40.38% of patients had history of and current khat chewer. And 5.1% of patients had family history of CVD. This is in-contrast to EHS, where smoking and family history of CVD was reported as a risk factors in 38.7% and 25.7 % of VHD patients respectively (34). This might because of high prevalence of khat chewing in our area.

Regarding comorbidities, hypertension was commonly reported as co-morbid disease in valvular heart disease patients. This is consistent with Euro Heart Study (EHS) (34) and Turkish registry of heart valve disease (83). However, it is in-contrast to study done in Portugal by Esteves et al where coronary heart disease (28.21%) and chronic kidney disease (20.9%) was reported the most common comorbidities (73).

With regard to echocardiography identified etiologies, cardiomyopathy was the common cause of valvular lesion. This is consistent with study done by Nawaz et al where the major complications of dilated cardiomyopathy was mitral (92%) and tricuspid (50%) regurgitation respectively (84). Adem et al from Mekele University, Ethiopia reported dilated cardiomyopathy caused 6.8% of echocardiographic abnormalities (39). However, this finding is in-contrast to the Turkish registry of Heart valve disease in which rheumatic was the most common cause of all VHDs (83). Ischemic and congenital etiology in Turkish registry (83) and Triki et al (38) from Tunisia was comparable

to our study. Mitral valve prolapse caused mitral regurgitation in 0.64% of patients which was comparable to study done by Adem et al, where 1.6% of mitral valve prolapse caused pathologic mitral regurgitation (MR) (39). However, it was reported as the cause of VHD in 13% of patients in Brazil (45). Majority of mitral stenosis (MS) and aortic regurgitation (AR) etiology was rheumatic and most cases of aortic stenosis (AS) was degenerative. This is consistent with Euro Heart survey (34) and Turkish registry (83).

In this study, mitral regurgitation (MR) was the most common valvular disease. Similarly, in Turkish registry, native MR was the most common (83). However, our finding was in-contrast to the Euro Heart Survey, in which native aortic valve stenosis was the most common (34). This difference is because of epidemiological difference in etiology between developed and developing countries, where degenerative aortic valve disease is prevalent in developed countries (85). Rheumatic heart disease (RHD) patients had significantly more multi-valvular lesions compared to non-rheumatics. Our finding was similar with HP-RHD Registry (86) and study doneby Tadele et al, (87). Mitral valve was the most common affected valve morphology. Animasahun et al, from Nigeria also reported the most common valve affected in RHD was mitral valve (88).

In valvular heart disease (VHD), drug therapy stabilizes the patient's condition when the disease is due to abnormal valve structure, and in treating the underlying condition when the condition is due to a functional abnormality [14]. In this study, diuretics, beta-blockers and angiotensin converting enzyme inhibitors (ACEIs) were the most frequently prescribed cardiovascular medications. This finding is comparable to study done in Brazil by de Moraes et al (45). Anticoagulants and digoxin was more frequently utilized in rheumatic group. This is consistent with ‘the Remedy study’ (24).

Clinical outcomes of valvular heart disease

Congestive heart failure (CHF), pulmonary hypertension (PAH), atrial fibrillation (AF), were the frequent admission complications of valvular heart disease (VHD) patients. This finding is comparable to HP-RHD Registry (86), ‘the REMEDY study’ (24) and De Moraes et al (45).

During the 90 days follow up, 19.2 % of patients were died from all-causes. This result was comparable to “the REMEDY study” (24) and study done by Okello et al (89) in which the mortality rate of rheumatic heart disease (RHD) patients were 16.9% and 17.8% respectively.

Similarly, mortality rate of unoperated severe symptomatic mitral rigurgitation patients from Ohio, US of America was 20% (90). However, our finding is higher than retrospective study done in Lisbon, Portugal in which in-hospital mortality of VHD was 9.8% (73). This lower death rate compared to our finding might be due to absence of surgical management in our setting.
Te mean (SD) age patients at death was 42.23 ± 19.625 years. This is not comparable to the REMEDY study (24) and Oli K and, Asmera J from Ethiopia (31), where the median and mean age at time of death was 28.7 and 25.89 ± 11.05 years respectively. This might because of most of the included patients in the those studies were younger and RHD patients compared this study.

Patients residing in urban areas were at increased risk of death. There was no evidence to support this, however, it might due to lifestyle and environmental changes due to urbanization added to suboptimal health care. In this study, presence of chronic kidney disease (CKD) as a co-morbidity was associated with 2.56 times more likely at risk of death. Samad et al, also reported significant interaction was occurred among CKD, AS/MR severity, and mortality; the CKD hazard ratio was 2.0 (severe AS) and 2.6 (severe MR) (60). Similarly, presence of severe pulmonary stenosis was associated with more than 3 times increased risk of death. This is in-contrast to study done in Olmsted County, Minnesota by Petty GW et al, in which severe aortic stenosis was independent predictor of cerebrovascular events and death (91). Patients who prescribed angiotension converting enzyme inhibitors (ACEIs) were around 64.0% less at risk of death. This finding is supported by study done by Nadir et al, in which aortic stenosis (AS) patients treated with ACEIs or ARBs had a significantly lower all-cause mortality with an AHR (0.76) and fewer cardiovascular events with an AHR (0.77) (92).

In this study, atrial fibrillation (AF) was significantly increased the risk of death (AHR= 1.52). Similarly, Thomas et al, reported patients with AF had the highest risk of death (HR, 1.32) (93). However, presentation with congestive heart failure (CHF) was associated with reduced risk of death compared to presentation with other complications (AHR=0.614). However, this is in-contrast to the REMEDY study (24) and study done by Dujardin KS et al (94) where both functional class (AHR =1.29) and atrial fibrillation (AHR= 3.28) were predictors of survival. This difference might be due to the fact that VHD patients who were presented with out CHF were presented with AF, stroke, and corpulmonalae, which increased the risk of mortality.

The median (IQR) length of hospital stay for all valvular heart disease patients was 12.0 (8, 21) days. This is comparable to the study done by Esteves et al, which was mean 11.98±14.33 days (73). Seventeen (10.90%) patients were rehospitalized during 90 days of follow up. This is in-contrast to study done by Rezzoug et al, in Belgium, where 50 % of VHD patients aged greater 80 years needed rehospitalization (95). This is higher than our finding which might be due to the included patients were elder and the follow up duration was longer.

9.1: Limitation and strength of the study

Being prospective observational study was one of the important strength of this study. As per to our understanding of the topic, there was no such study in Ethiopia which investigated clinical outcomes of non-rheumatic etiologies of valvular disease. However, this study was not without limitations. Data was collected from single institution and relatively small in the sample size. The echocardiography was not always done by same cardiologists/radiologists, therefore inter-individual variation in interpretation should take into account. Some of important echocardiography parameters were not available. Almost all patients were admitted with complications of valvular heart disease, during the study period there was no identified new complications except exacerbation of the previous complications. Due to lack of proper documentation of prescription of benzathine penicillin during follow visit for rheumatic heart disease patients, it was not evaluated wether the patients were given on regular monthly schedule or not.

10. Conclusion

The incidence of all-cause mortality of valvular heart disease (VHD) in our study was high. The overall mean survival time was approximately 81 days. There was no statistical difference in mean survival time between rheumatic and non-rheumatic etiology. Hypertension was the common co-morbid cardiovascular disease reported in VHD patients. Cardiomyopathy and rheumatic heart disease accounted about two-third of etiologies of valvular heart disease. Mitral regurgitation and tricuspid regurgitation was the common valvular disease. Most of the VHD was multi-valvular. Majority of mitral stenosis was caused by rheumatic and aortic stenosis caused by degenerative VHD. Congestive heart failure, pulmonary hypertension and atrial fibrillation was the frequent admission complications. Presence of CKD as a co-morbidity, living in urban areas, presence of severe pulmonary stenosis, and atrial fibrillation as admission complication was statistically increased the risk of death. While presence of congestive heart failure and use of angiotensin converting enzyme inhibitors was statistically reduced the risk of death.

11. Recommendation

We recommend JUMC cardiologists to pay attention to the care of valvular heart disease patients, as the mortality and morbidity of the disease was high. Particularly more emphasis should be given to VHD patients presenting with AF and co-morbid with CKD. We also recommend further multicenter research to be done in the area to recommend Ethiopian Federal Ministry of Health, Health policy makers to fund and implement cardio-thoracic and vascular surgery center and improve the care the patients.

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13. Annexes

13.1. Informed written consent

Name of the organization: Jimma University

Principal investigator: Temesgen Mulugeta

Study site: Jimma Medical Center (JUMC)

Purpose of the Study: To assess burden, clinical outcomes and associated factors valvular heart disease patients admitted to medical wards of JUMC.

Duration: April 10 to August 10/2019

Possible risk and benefit: There will be no risk or problem happen to you. The result of this study will help improve the awareness, care and future prevention of valvular heart disease.

Confidentiality: The response you give will be used only for the purpose of the study. The data/information we gather will be kept confidential and not be given to any third party.

Right: your current and future medical services will not be affected if you refused to participate or withdraw from the study

Contact address: email: temesgenmulugetaf@gmail.com Mob: +251917734764

CONSENT FORM

I am informed fully in the language I understand about the aim of the above mentioned research. I understood the purpose of the study entitled with, "***burden, clinical outcomes and associated factors valvular heart disease patients".*** I have informed for this study data will be collected. I have also read the information sheet or it has been read to me. In addition, I have been told all the information collected throughout the research process will be kept confidential. I understood my current and future medical services will not be affected if I refused to participate or withdraw from the study. I _____, after being fully informed about the detail of this study, hereby give my consent to participate in this study and approve my agreement with signature.

Patient name: _____signature _____ date: _____

Investigator/data collector name: _____signature: _____date: _____

Afaan Oromootiin

Maqaa waajjiraa: yuunivarsiitii Jimmaa

Maqaa qorataa: Tamasgeen Mulugetaa Fayisaa

Bakka qorannoo: Giddu Galeessa Fayyaa Jimmaa

Kaayyoo qorannoo: balbal'insa, wantoota qabsiisuu danda'anii fii wantoota dhukkubni huutuu onnee fiduu danda'u adda baasuufi dha.

Yeroo qorannoo: Eebla 22 hanga hagayya 22, 2011 ALH.

Miidhaa fi bu'aalee qorannoo kanaa: miidhaan kami iyyuu kan sirra gahu hin jiru. Garuu bu'aan qorannoo kanaa babal'insa dhukkichaa uummata keessa maal akka fakkaatu, wantoota dhukkubicha fiduu danda'an erga adda baafamee booda, yaala dhukkubichaa fooyyessuu fi dhukkubicha ittisuu ta'a.

Iccittii eguuu: Deebii gaafatamteef/taniif kan laattu/ttan hundi qorannichaaf qofa kan oolu ta'a. Odeeffannoo kan sirraa fudhatnu kundi nama/qaama biraatti dabarfamee hin kennamu, maqaan kees hin barraa'u.

Mirga: yoo hirmaachuu didde yookaan qorannicha keessaa bahuu yoo barbaaddes, yaala siif kennamu irratti rakkoo kan fidu hin ta'u.

Iimeelii: temesgenmulugetaf@gmail.com Mob: +251917734764

Unka waliigaltee

Akka gadi fageenyaan afaan danda'uun natti himamuu yaalametti, kaayyoo qorannichaa sirriitti hubadheera. Mata duree qorannichaa" ***balbal'insa, wantoota qabsiisuu danda'anii fii wantoota dhukkubni huutuu onnee fiduu danda'u adda baasuu***" jedhuufii kaayyoo isaas hubadheera. Kanaafis oddeeeffaanoon akka funaanamu hubadheera. Anis unka odeeffannoo qorannichaa dubbiseera yookaan naaf dubbisaniiru. Deebii gaafatamuuf kan laadhu hundi qorannichaaf qofa kan oolu akkasumas odeeffannoo narraa fudhatanu kundi nama/qaama biraatti dabarfamee akka hin kennamne, maqaan koos akka hin barroofne natti himameera. Kan biraas, yoon hirmaachuu dide fii qorannicha keessaa bahuu yoon barbaade, yaala ammaa fi gara fuula duraa naaf kennamu irratti rakkoo kan fidu miti. Kanaafuu, ani_____ erga wantootni kuni hundi natti himamee, irratti hirmaachuu kootiif waliigalee mallattoo kootiin nan mirkaneessa.

Maqaa dhukkubsataa: _____mallattoo: _____ guyyaa_____

Maqaa qorataa/ nama odeeffannoo funaanu: _____ mallattoo_____guyaaa____

የድርጅቱ ስም: የጅማ ዩኒቨርሲቲ

ዋና ተመራማሪ: አቶ ተመስገን ሙሉጌታ

የጥናት ማዕከል፡ ጅማ የሕክምና ማዕከል (ጃኤምሲ)

የጥናቱ ዓላማ: በጅማ ዩኒቨርሲቲ የሕክምና ማዕከል የልብ መሰከት በሽታ ሕመምተኛ ጫና፣ የህክምና ውጤቶች እና ተጓዳኝ ነገሮች ለማጥናት

የሚፈጀው ጊዜ: ሚያዝያ 22 እስከ ነሐሴ 22/2011

ሊከሰቱ የሚችሉ ስጋቶችና ጥቅሞች: ምንም አደጋ ወይም ችግር አይኖርም። የዚህ ጥናት ውጤት የበሽታውን ግንዛቤ፣ እንክብካቤ እና የወደፊት መከላከልን ለማሻሻል ይረዳል

ሚስጢራዊነት: የሚሰጡት ምላሽ ለጥናቱ ዓላማ ብቻ ያገለግላል። የምንሰበስበው መረጃ በምሥጢር ተጠብቆ ለሌላ ሶስተኛ ወገን አይሰጥም።

መብት: ለመሳተፍ ፈቃደኛ ካልሆኑ ወይም ከጥናቱ ካቆሙ የአሁኑ እና የወደፊት የህክምና አገልግሎቶች አይነኩም

አድራሻ: ኢሜይል: temesgenmulugetaf@gmail.com ሞባይል: +251-917734764

<u>የፈቃድ ፎርም</u>

ከላይ የተጠቀሰውን ምርምር በተመለከተ በሚገባኝ ቋንቋ ሙሉ በሙሉ ተረድቻለሁ። " **የልብ መሰኮት በሽታ ሕመምተኛ ጫና፣ የህክምና ውጤቶች እና ተጓዳኝ ነገሮች** " በሚል ርዕስ የያዘውን የጥናቱ አላማ *ተረዲቻለሁ።* የመረጃ ወረቀቱን አንብቤያለሁ ወይም ለእኔ በሚገባኝ ቋንቋ ተነቦልኛል። በተጨማሪም፣ በጥናቱ ሂደት ውስጥ የተሰበሰበውን መረጃ በሙሉ በሚስጥር ይያዛል። ለመሳተፍ ፈቃደኛ ካልሆንኩ ወይም በጥናቱ ምክንያት ሳደርግ የአሁኑ እና የወደፊት የሕክምና አገልግሎቶቼ ምንም አይሆኑም።. እኔ ---------- የዚህ ጥናት ዝርዝር መረጃ ሙሉ በሙሉ ከተረዳሁ በኋላ፣ በዚህ ጥናት ለመሳተፍ ከፈርማ ጋር ያለኝን ስምምነት ኣረጋግጫለሁ።

የታካሚ ስም: _____ ፈርማ _____ ቀን: _____

መረጃ ሰብሳቢ ስም _____ፊርማ: _____ ቀነ: _____

13.2. Data collection tool

The aim of this study is to assess the burden, clinical outcomes and associated rsik factors of patients admitted and diagnosed with valvular heart disease at Jimma Medical Center from April 10 to September 10, 2019 GC.

1. **Sociodemographics**
   - Card.No _____ current admission date (to ward):_____ Ward:_____
   - Contact No. (Patient) _____ Relative: _____
   - **Sex** : male ☐ female: ☐
   - Age (in years): _____
   - **Residence**: Urban ☐ Rural ☐
   - **Religion**: orthodox ☐ Muslim ☐ protestant ☐ catholic ☐ others_____
   - **Ethinicity**: Oromo ☐ Amhara ☐ SNNP ☐ Gambella ☐ Tigre ☐ others _____
   - **Marital status**: single ☐ married ☐
   - **Educational status**: primary ☐ secondary & above ☐ illetrate ☐
   - **Occupation**: government ☐ Private Job ☐ student ☐ merchant ☐ farmer ☐ housewife ☐ others (specify) _____
2. **Social drug use and family history**
   - Smoking (tobacco): yes ☐ No: ☐
   - Alcohol drink (any type) Yes ☐ No: ☐
   - Khat chewing: yes ☐ No: ☐ if yes, duration _____
   - Other substance use (list): _____
   - Family history of CVD/VHD yes: ☐ No: ☐ If yes (list): _____

3. Co-morbidity:

- ☐ Hypertension
- ☐ Diabetes
- ☐ Dyslipidemia
- ☐ CAD (IHD, ACS, angina)
- ☐ Arrhythmias
- ☐ COPD
- ☐ Asthma
- ☐ Pregnancy
- ☐ Others _____
- ☐ Old stroke
- ☐ Renal failure (CKD, AKI, NS, etc.)
- ☐ Thyroid disease
- ☐ Adult onset malnutrition
- ☐ HIV
- ☐ TB
- ☐ None

4. ECHO findings:

A. Cardiac chamber size (e.g. LV internal diameter end systole/diastole, LA size, mid RV diameter)

- ☐ normal:
- ☐ dilated (*mm*): _____

  _____

  _____
- ☐ decreased: _____

B. Aortic root dimension (*in mm, if dilated*): _____

C. Main pulmonary artery dimension *(in mm, if dilated*): _____

D. Regional wall motion abnormalities: _____

E. LV systolic function (LVEF): _____

F. Global LV wall thickness (in *mm*)

- ☐ increased: _____
- ☐ decreased: _____

G. Wall of the LV

- ☐ dyskinesia: _____
- ☐ hypokinesia: _____

H. Valve structures: normal ☐ abnormal ☐

- Mitral valve (leaflets…)
  - _____
  - _____
  - _____
- Aortic valve (cusps, annulus)
  - _____
  - _____
  - _____
- Tricuspid valve
  - _____
  - _____
- Pulmonic valve
  - _____
- Mitral valve prolapse: _____

I. Intracardiac mass, thrombus, or vegetation: _____

J. Septum (inter atrial and inter ventricular): _____

K. Spontaneous echo contrast (grade): _____

L. Pericardium:

- ☐ normal
- ☐ effusion:_____
- ☐ thickening: _____
- ☐ calcification: _____

M. Inferior Vena Cava (IVC) size (*in mm, if dilated*): _____

N. Doppler (CW, PW, color flow)

- Transvalvular inflow velocity: _____
- Shunt: _____
- Regurgitation (with Vmax)
  - _____
  - _____
  - _____
  - _____
- Stenotic lesion (with valve area):
  - _____
  - _____
  - _____
- Pulmonary Hypertension (RVSP):
  - _____
- **Conclusion**:

  _____

  _____

5. Etiology or underlying cause (from ECHO result)

- ☐ Rheumatic
- ☐ Degenerative aging/calcification
- ☐ Infective endocarditis
- ☐ Aortic scelerosis
- ☐ Idiopathic
- ☐ Inflammatory condtions:
  SLE ☐ RA ☐ Ankylosing spondylitis ☐ Psoriasis ☐
- ☐ Syphilitic aortitis
- ☐ Ischemia (IHD) (Esp. inferior MI)
- ☐ Pulmonary arterial hypertension (Idiopathic)
- ☐ Congenital Heart disease/defect:
  bicuspid _____, tricuspid_____,
  ASD_____, VSD _____ ,TOF _____
- ☐ Myxomatous degeneration (frequent cause MVP)
- ☐ Marfan syndrome
- ☐ Aortic dissection
- ☐ Cardiomyopathies
  _____
- ☐ Trauma
- ☐ Cardiac neoplasm
- ☐ Malignant hypertension
- ☐ Drugs, if yes, list _____
- ☐ IVD use: if yes list _____
- ☐ Others (e.g: HIV,): _____

6. Current confirmed diagnosis:

_____

7. Admission complications:

- ☐ CHF class:____, stage: ____
- ☐ Atrial Fibrillation (AF)
- ☐ Bradyarrhythymias: _____
- ☐ Cardiac thrombus
- ☐ stroke (ischemic :___hemorhag: ___)
- ☐ Pulmonary edema (cardiogenic shock)
- ☐ PE _____ _____
- ☐ Infective endocarditis
- ☐ Pulmonary hypertension
- ☐ Sepsis
- ☐ Others _____

8. Medications prescribed after admission, including for established and potential complications

- _____
- _____

- _____
- _____
- _____
- _____
- _____

9. **Discharge**
   - **Date** : _____
   - **Reason for discharge**: self-discharge ☐ physician's decision ☐
   - **Status**: improved ☐ The same ☐ referred: ☐ died : ☐
     - If died, date of death: _____
     - Suspected cause of death (from complications or any):

       _____

10. **Length of hospital stay (LOHS)**: *counted from admission to discharge*
    - Days _____
    - weeks _____

- **Discharge medications including for secondary prophylaxis:**
  - _____
  - _____
  - _____
  - _____
  - _____
  - _____

11. **Time to first appointment after discharge**: _____
12. **Follow up after discharge**:
    - ☐ On regular follow up
    - ☐ On follow up but irregular
    - ☐ Lost to follow up
13. **Readmission to ward within 3 months**. Yes ☐ No ☐ If yes,
    - reason for readmission (*including new Dx/complications*):

      _____

      _____

- time to the first readmission: _____
- number of readmissions/---: _____

14. Death within 3 months. Yes ☐ No ☐ If yes,

- Date of death: _____
- Suspected cause of death (from complications or any) : _____

Kaayyoo qorannoo kanaa balbal'insa, wantoota qabsiisuu danda'anii fii wantoota dhukkubni huutuu onnee fiduu danda'u adda baasuufi dha.

1. Haala Jireenya Hawwaasaa

- Lakk. kaardii: ---------- guyyaa ward galan: ---------- bakka: ----------
- lakk. bilbilaa (kan dhukkubsataa): ---------- kan firaa: ----------
- Saaala dhiira: ☐ dubara: ☐
- Umurii: ----------
- Bakka Jireenyaa: baadiyyaa ☐ magaalaaa ☐
- Amantaa: ortodoksiii ☐ Muusiliima ☐ protestaantii ☐ kaatolikii ☐ kan biraa
- Gosaa: Oromo ☐ Amhara ☐SNNP ☐ Gambella ☐Tigre ☐ kan biro: ------
- **Haala fuudhaa fi heerumaa**: kan hin fuune ☐kan fuudhe ☐kan wal hike ☐ kan irraa du'e ☐
- **Sadarkaa barnootaa**: sadarkaa tokkoffaa ☐sadarkaa lammaffaa fi isaa ol ☐ dubbachuu fi dubbisuu hin danda'u ☐
- **Hojii**: hojii mootummaa ☐ kan dhuunfaa ☐ barataa ☐daldalaa ☐ Qotee bulaa ☐ haadha manaa ☐ kan biraa yoo jiraate ☐

2. Wantoota suusii ta'anii fi dhukkuba sanyiin daddarbu

- **Tamboo aarsuu** eyyeen ☐ lakki ☐
- **Dhugaatii alkoolii:** eyyeen ☐ lakki ☐
- **Caatii qama'uuu: eyyeen** ☐ lakki ☐
- **Kan biraa yoo fayyadamu ta'e ibsi: ----------**
- **Maatii keesssa dhukkubni onnee/ujummoo dhiigaa akkasumas kan huutuu onnee:** eyyeen ☐ lakki ☐ yoo jiraate ibsi: ----------

የዚህ ጥናት ዓላማ በጅማ የሕክምና ማዕከል የልብ መሰኮት በሽታ ሕመምተኛ ጨና፣ የህክምና ውጤቶች እና ተጓዳኝ ነገሮች ለማጥናት ።

1. ማህበራዊግራፊክስ

- ካርድ ቁጥር፡ ---------- የአሁን የማመልከቻ ቀን፡ ---------- ዋርድ፡ ----------
- የእውቂያ ቁጥር (የታካሚ)፡ ---------- የዘመድ፡----------
- **ፆታ፡** ወንድ ☐ ሴት ☐
- **ዕድሜ** (በዓመታት)፡ ----------
- **መኖሪያነት:** - ገጠር ☐ የገጠር ☐
- **ሃይማኖት:** ኦርቶዶክስ ☐ ሙስሊም ☐ አብያተ ክርስቲያናት ☐ ካቶሊካዊ ☐ ሌሎች --------
- **ብሔር / ብሔረሰብ:** ኦሮሞ ☐ አማራ ☐ ደቡብ ☐ ጋምቤላ ☐ ትግሬ ☐ ሌሎች _____
- **የጋብቻ ሁኔታ**- ያላገባ ☐ ያገባ ☐ የተፋታ ☐ ሚስቱ የሞተች ☐
- **የትምህርት ደረጃ**: የመጀመሪያ ደረጃ ☐ ሁለተኛ-ደረጃ እና ከዛ በላይ ☐መናገር እና ማንበብ አይቻልም ☐
- **ሥራ:** የመንግሥት ☐የግል ስራ ☐ተማሪ ☐ነጋዴ ☐ገበሬ ☐ ሌሎች፡----------

2. ማህበራዊ መድሃኒት አጠቃቀም እና የቤተሰብ ታሪክ

- ማጨስ (ትምባሆ): አዎ☐ አይደለም:☐
- አልኮል መጠጥ (ማንኛውም አይነት) አዎ ☐ አይደለም ☐
- **ጫት ማኘክ፡** አዎ☐ አይደለም ☐
- ሌሎች (ዝርዝር): _____
- የቤተሰብ ታሪክ የ CVD / VHD አዎን ☐ አይደለም ☐ አዎ ከሆነ (ዝርዝር): _____

የጋራ መጓደል: ማንኛውም በሽተኛ ካርድ ወይም ሪፖርት / ታሪክ ቀደም ብሎ ምርመራ

- ከፍተኛ የደም ግፊት
- የስኳር ህመም
- ዲልሲፒዲያሚያ
- የልብ ድካም በሽታ (IHD, ACS, angina)
- ሥር የሰደደ የልብ ድካም (CHF)
- Cardiomyopathies
- የአስፈራ በሽታ (arrhythmias)
- ኮፒዲ (COPD)
- አስም
- ድንገት (stroke)
- የኩላሊት ችግር (CKD, AKI, NS, ወዘተ)
- የደም ማነስ
- የታይሮይድ በሽታ
- አስከፊ በሽታዎች ------
- በአዋቂዎች የተመጣጠነ ምግብ እጥረት
- ቶንሲሊየስ
- ሪትሚቲ ትኩሳት