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# Prevalence Of Pulmonary Hypertension And Associated Factors Among Rheumatic Heart Diseases Patients Having Follow Up At Public Referral Hospitals In Bahir Dar, Ethiopia, 2023 G.C

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**BAHIR DAR UNIVERSTY**

**COLLEGE OF MEDICINE AND HEALTH SCINCES**

**SCHOOL OF MEDICINE**

**DEPARTMENT OF INTERNAL MEDICINE**

# PREVALENCE OF PULMONARY HYPERTENSION AND ASSOCIATED FACTORS AMONG RHEUMATIC HEART DISEASES PATIENTS HAVING FOLLOW UP AT PUBLIC REFERRAL HOSPITALS IN BAHIR DAR, ETHIOPIA, 2023 G.C

BY:

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FEBRURARY, 2024 G.C
BAHIR DAR, ETHIOPIA

**BAHIR DAR UNIVERSTY**

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A THEISIS REPORT SUBMITTED TO DEPARTMENT OF INTERNAL MEDICINE, SCHOOL OF MEDICINE, COLLEGE OF MEDICINE AND HEALTH SCIENCE, BAHIR DAR UNIVERSITY, IN THE FULFILLMENT OF THE REQUIREMENTS FOR SPECIALTY IN INTERNAL MEDICINE.

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FEBRURARY, 2024 G.C

BAHIR DAR, ETHIOPIA

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# DECLARATION

This is to certify that the research thesis entitled “Prevalence of Pulmonary hypertension and associated risk factors among RHD patients attending Public referral hospitals , Bahir Dar, Ethiopia, 2023 ” submitted to Department of internal medicine, School of medicine, College of medicine and health science, Bahir Dar University, in the fulfillment of the requirements for specialty in internal medicine is a record of original work carried out by me and has never been submitted to this or any other institution to get any other degree or certificates. The assistance and help I received during the course of this investigation have been duly acknowledged.

By Asmamaw Gedefaw (internal medicine resident)

Bahir Dar, Ethiopia

# APPROVAL OF THESIS FOR DEFENSE



APPROVAL OF THESIS FOR DEFENSE

I hereby certify that I have supervised, read, and evaluated this research thesis titled "Prevalence of Pulmonary hypertension and associated risk factors among RHD patients attending Public referral hospitals , Bahir Dar, Ethiopia, 2023 G.C) " by Asmamaw Gedefaw (internal medicine resident) prepared under my guidance. I recommend the research thesis to be submitted for oral defense.

Approved by -

Dr Abiyot Teferi (MD, Cardiologist) _____ 16/07/2016

Clinical Advisor's name Signature Date

Gebeyaw Wudie (Assistant Professor of Epidemiology) _____ 16/07/2016

Public health advisor's name Signature Date

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# LISTS 0F ACRONYMS AND ABBREVATIONS

AR…… Aortic Regurgitation

ARF-----Acute Rheumatic Fever

AS …… Aortic Stenosis

COPD----- Chronic Obstructive Pulmonary Diseases

DM------ Diabetic Mellitus

ECG------ Electrocardiography

ECHO----- Echocardiography

HIV----- Human Immunodeficiency Virus

HF------- Heart Failure

HTN----- Hypertension

LA------- Left Atrium

LHD------ Left Heart Diseases

LV-------Left Ventricle

LVH----- Left Ventricular Hypertension

MPAP----- Mean Pulmonary Arterial Pressure

MS-------Mitral Stenosis

MR ------Mitral Regurgitation

NYHA----New York Heart Association

PAH------Pulmonary Arterial Hypertension

PH------ Pulmonary Hypertension

PE------ Pulmonary Embolism

PVR----- Pulmonary Vascular Resistance

RHC------ Right Heart Catheterization

RHD----- Rheumatic Heart Diseases

RHF------Right side Heart Failure

RVH----Right Ventricular Hypertrophy

RVSP----- Right ventricular systolic pressure

SPAP------Systolic Pulmonary Artery Hypertension

SSA----- Sub Saharan Africa

TB------ Tuberculosis

TR------- Tricuspid Regurgitation

TGSH----- Tibebe Ghion Specialized Hospital

WHO----- World Health Organization

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# ABSTRACT

**Background**: In patients with RHD, pulmonary hypertension (PH) is a common complication and significant contributor to associated morbidity and mortality. Rheumatic heart disease in particular mitral valve diseases remain as one of most common causes of PH in the developing countries.

**Objective:** To determine prevalence and factors associated with pulmonary hypertension (PH) among patients with rheumatic heart disease.

**Methods**: Institutional based cross sectional study was conducted and all the necessary data were obtained from patient's medical card or chart who had follow up at referral clinic.310 study participants were selected based on simple random sampling. Entered data was exported to Statistical Package of Social Science version 27 for analysis. Both bivariate and multivariable analysis were done to assess the association between each independent variable and the outcome variable using binary logistic regression model. A multivariable logistic regression model was conducted to identify factors associated with PH and presented by adjusted odds ratio (AOR) with 95% of CI. The model fitness was checked using Hosmer-Lemeshow at significance test at P values < 0.05.

**Result**: -Overall prevalence of pulmonary hypertension was 56.5% among patients with Rheumatic heart diseases having follow up at public referral hospitals. Among those who developed pulmonary hypertension 51.4% had severe pulmonary hypertension. Severe Mitral Stenosis (AOR 7.8, 95% CI 2.4-25.7), duration of illness (>= 3 years) (AOR 7.7, 95% CI 2.1-28.5) and diuretics use (AOR 5.6, 95% CI 2.2-14.3,) had statistically significant association with PH.Having Valve Intervention (AOR 0.06, 95% CI 0.01 0.29) and LVEF above 50% (AOR 0.14, 95% CI 0.02-0.81) were associated with reduced likelihood of PH.

**Conclusion:-**Rheumatic heart disease related pulmonary hypertension is still the major problem and severity of heart valve lesion, duration of illness and diuretic use which are prescribed for those with complication (HF) were determining factors for development of PH. Otherwise age, gender, residency were not associated with the presence of PH in RHD patients. Having valve intervention for advanced valvular lesion was associated with reduced PH and it is crucial to have cardiac centers that provide this service for large proportion of RHD patients.



**Keywords: pulmonary hypertension, rheumatic heart disease**

# 1. INTRODUCTION

## 1.1 Background

Pulmonary hypertension (PH) is a diverse disease resulting from pathogenic remodeling of the pulmonary vasculature, which raises pulmonary artery pressure and vascular resistance. Increased pulmonary blood flow, pulmonary vascular resistance, increased pulmonary venous pressure, or a combination of these factors are the responsible pathologic changes(1–3). It leads to structural and functional changes to the right side of the heart, eventually to decompensated right heart failure.

The current classification system distinguishes between five main groups of causes, each of which has a similar set of pathophysiological characteristics: pulmonary arterial hypertension (group 1), PH caused by left heart disease (group 2), PH caused by lung disease and/or hypoxia (group 3), chronic thromboembolic PH (group 4), and PH with unclear/multifactorial mechanisms (group 5). Most cases of PH are due to LHD which includes left side valvular heart diseases, LV systolic dysfunction and diastolic dysfunction(1,4)

Different studies use different modalities to diagnose pulmonary hypertension. Most hospital based studies use Trans – thoracic echocardiography to diagnose PH. Even though the gold standard to diagnose PH is right heart catheterization, it is invasive and not easily accessible in most centers in developing countries, including Ethiopia.

Trans - thoracic echocardiography measures the systolic pulmonary arterial pressure (sPAP) with acceptable accuracy in RHD patients(5). Echocardiography is recommended as the first-line, non-invasive, diagnostic investigation in suspected PH(1)

It is becoming an increasingly common global health issue complicating various common diseases in which its development is almost always associated with worsening of clinical symptoms and increased mortality. Rheumatic heart disease (RHD) in particular mitral valve lesions remains as one of most common causes of PH in the developing countries and presence of PH in RHD is a significant contributor to increased morbidity and mortality.

The World Health Organization (WHO) estimates Rheumatic Heart disease affects about 15.6 million people globally, with 282,000 new cases and 233,000 deaths occurring annually. Rheumatic heart disease (RHD) is one of the leading cause of non-communicable diseases in

low- and middle-income countries, mainly in sub-Saharan Africa and it accounts for up to 1.4 million deaths per year. RHD, one of the major causes of cardiovascular disease in most developing countries, is caused by a Group A streptococcal (GAS) bacterial infection which causes acute rheumatic fever (ARF) which can eventually end up with Rheumatic Heart Disease (RHD)(6).

## 1.2. Statement of the Problem

20 to 70 million people worldwide are estimated to have pulmonary hypertension, which affects roughly 1% of the world's population on average and up to 10% of persons over the age of 65. Due to the presence of cardiac and pulmonary causes of PH, prevalence is higher in individuals aged 65 years and above. About 80% of affected people reside in underdeveloped nations where most patients with pulmonary hypertension are younger and frequently linked to chronic infection such asrheumatic heart disease, HIV and schistosomiasis(4,7,8).

About 50% of newly diagnosed rheumatic heart disease patients present with advanced disease and complications. Heart failure and pulmonary hypertension were the most commonly observed complications in many hospital based studies. Majority of patients have moderate to severe valvular lesions which needs surgical intervention at presentation(9).

The prevalence of pulmonary hypertension in RHD is not well defined because of the different modalities used in different studies. Wide range of prevalence is reported in different centers ranging from 11% - 80%. In one large prospective cross-sectional study, which includes 3343 RHD patients from 25 hospitals including Ethiopia, India and Yemen, PH was reported to be 28.8%(9).

Another study described the prevalence of PH in patients with RHD at a tertiary center in Nigeria. From 1312 ECHO studies, 10% had evidence of rheumatic heart diseases (RHD) and secondary PH was present in 80% of patients(10). A similar study from Uganda showed a prevalence of PH of 33% among 309 newly diagnosed RHD patients(11). According to the study done in St.Paul’s Hospital Millennium Medical College cardiac unit, Ethiopia, which included 384 RHD patients, the prevalence of PH was 53.9 %(12).

Despite increased numbers of cases of pulmonary hypertension seen in our daily practice in particular patients with rheumatic heart diseases, there are only few studies which tries to identify factors associated with PH. A lot of factors may contribute toPH in patients with cardiac diseases including severity and type of valvular lesions,LA size and volume, LV function and diameter, duration and degree of symptoms and other non-cardiac co morbidities. However, factors for development of PH were not studied in the previous studies. Therefore the aim of the study is to describe the magnitude and factors associated with development of PH in RHD patients.

### 1.3. Significance of the Study

Establishment of accurate epidemiological data on PH and associated risk factors in this region may guide decision-making toward preventive interventions and early treatment.

It also increases awareness among health professionals about the diseases burden in particular in those who are at risk like patients with RHD and will serve as a base for future studies to be conducted on pulmonary hypertension. Early screening and detection of PH also help patients at risk to receive diseases specific and general management which slow or prevent progression.

## 2. LITRATURE REVIEW

### 2.1. Magnitude and Risk factors

Pulmonary hypertension has a distinctive history and challenges among non-communicable diseases. Although known for centuries, the diagnosis could only be made clinically after the invention of cardiac catheterization in the 1950s.The prevalence of PH, as determined by a central echocardiogram varies based on the causes and underlying conditions. Both in community and institution -based cohort studies, left heart disease (including RHD) and lung diseases were the most common causes of PH (4,38).Development of PH in this patients was associated with adverse outcomes and increased mortality(26, 27).

The prevalence of pulmonary hypertension in RHD is not well defined because of the different modalities used in different studies. Wide range of prevalence is reported in different centers ranging from 11% - 72.1%.

A tertiary hospital based study done in India which includes 2005 patients with RHD taken consecutively from 2011 – 2016 showed PH prevalence to be 30.5%. Most patients (69.3%) have moderate to severe valvular heart disease. In this study presence of PH was associated with major adverse cardiovascular event (MACE) which includes heart failure, stroke and PE(13) .

A retrospective study enrolling 558 consecutive RHD patients undergoing PBMC in a university-affiliated heart center in Iran between 2007 and 2015, which defines PH significant PH as mean PAP > 40 mmHg , shows prevalence of 27%. The echocardiographic findings, absolute MVA, indexed MVA, and mean trans-mitral valve gradient were associated with the presence of PH. Patients with PH were similar to the rest of the subjects in terms of demographics, body habitus, blood group, and incidence of atrial fibrillation. Mean age was, 28.6 ± 14.5 years (14).

Another retrospective study done in adults patients with RHD in Southern Yemen, PH was the most common identified complication(80.4%) and most of it (60.1%) was from patients with mitral valve stenosis(15).

A prospective study done in Saudi Arabia done between 1989 and 2003 among 559 RHD patients who undergone MBV for severe MS, the prevalence of PASP>50mmHg was 38%. The study also shows that the Doppler-monitored PASP fell to normal after 6 – 12 months of the intervention(16).

The epidemiology is poorly understood in Africa despite the high incidence of PH risk factors, unique genetic backgrounds and lifestyles, and low access to healthcare. According to PAPUCO (continent-wide Pan Africa registry-type cohort research), RHD and HF accounts for the large proportion of cases, 12.9 and 32.9% of patients respectively(17,18).

A large multi centered prospective cross-sectional study called REMEDY study which includes 3343 patients in 25 hospitals in 12 African countries (including Ethiopia), between January 2010 and November 2012 showed that the prevalence of PH in RHD is 28.8%. In this study moderate to severe mitral valve lesions and low income were found to be associated with PH(9).

A cross-sectional hospital based study which includes 309 patients with RHD done in Uganda where consecutive, newly diagnosed rheumatic heart disease patients were assessed and followed up for complications, indicates heart failure was the most common complication(46.9%),

followed by pulmonary hypertension (32.7%), atrial fibrillation (13.9%), recurrence of acute rheumatic fever (11.4%), infective endocarditis (4.5%) and stroke (1.3%) (11).

Another hospital based prospective cross-sectional study done in Uganda on 130 RHD patients where majority of the patients presented with moderate-to-severe valvular disease, Pure mitral regurgitation was the commonest valvular disease (40.2%), followed by mitral regurgitation plus aortic regurgitation (29%). In this study 45.9% of patients presented with severe heart failure in NYHA class III/IV, 53.3% with pulmonary hypertension, 13.9% had atrial fibrillation and 8.2% had infective endocarditis (32).

A large prevalence of PH (72.1%)was seen among 129 RHD patients based on a retrospective study done in Nigeria(10). A prospective hospital based observational study done in Egypt that included 153 HF patients, only diuretics usage ($P = 0.02$) and valve severity ($P < 0.0001$) were independent predictors for the development of PH among HFpEF patients including RHD patients (40).

According to study conducted in Saint Paul Hospital Millennium Medical College (SPHMMC) from 384 RHD patients, next to heart failure, pulmonary hypertension was the second most common complication that existed in 59.3% of patients. Among those who developed pulmonary hypertension almost half of them(51.8%) had severe pulmonary hypertension, 42.2% of them had moderate pulmonary hypertension and only 6% of them had mild pulmonary hypertension. Sever MS ($P =0.043$)was independent factor for the development of PH(12,19).

Based on study done in Jima which includes pediatric and adult RHD patients, PH was prevalent in 60.3%, where 42.3% had severe PH with female predominance (59.1%). Severity of aortic and mitral valve has a significant association with the presence of PH ($p=0.001$). Mitral stenosis was found in 39.5% of patients with PH. All with Severe MS has developed PH which was also statistically significant ($p \leq 0.001$)(20)

In a retrospective observational hospital based study of 419 patients from Spain with end stage HF from different causes, including RHD, different variables were analyzed to find predictors of PH (defined as a mean pulmonary pressure >25 mmHg). The prevalence was 62.2% and the presence of moderate-severe mitral regurgitation [OR 2.1 (1.2–3.7); P=0.006], moderate-severe

Mitral stenosis [OR 2.9 (1.3–6.4); P=0.005] and a duration of disease >=3 years [OR 1.7 (1.1–2.7); P=0.03] were independent risk factors associated with PH (38).

Based on prospective study done in UK from 2001 – 2008 which enrolled 1380 outpatient HF patients, Pulmonary hypertension was associated with the severity of Mitral valve lesion (OR = 6.74 CI (2.71–16.74) P value = 0.0001), raised filling pressures (OR=2.92 CI(1.22–6.94) P value = 0.016), LV systolic dysfunction, and LV dilation. PH was also found to be independent predictor of mortality(21,22).

In most patients with PH due to MS, AS, Valvular intervention was associated with a significant early and late reduction of PASP and lower risk of all-cause mortality(23,24)

The World Health Organization (WHO) estimates Rheumatic Heart disease affects about 15.6 million people globally, with 282,000 new cases and 233,000 deaths occurring annually. It is one of the leading non-communicable disease and major causes of cardiovascular death in low- and middle-income countries, mainly in sub-Saharan Africa accounting for up to 1.4 million deaths per year. It is caused by a Group A streptococcal (GAS) bacterial infection which causes acute rheumatic fever (ARF) and can eventually end up with Rheumatic Heart Disease (RHD)(6).

RHD was reported in 10 % echocardiographic study of 1500 patients which was done (January 1, 2018 to June 30, 2019 in teaching hospital found in Addis Ababa. Other institutional studies in the country also showed higher result, St. Paul hospital showed (30%), Jimma university specialized hospital (32.8%), Black Lion hospital (93.7%)(14), Mekelle University (20.9%)(15).

# 3.CONCEPTUAL FRAMEWORK

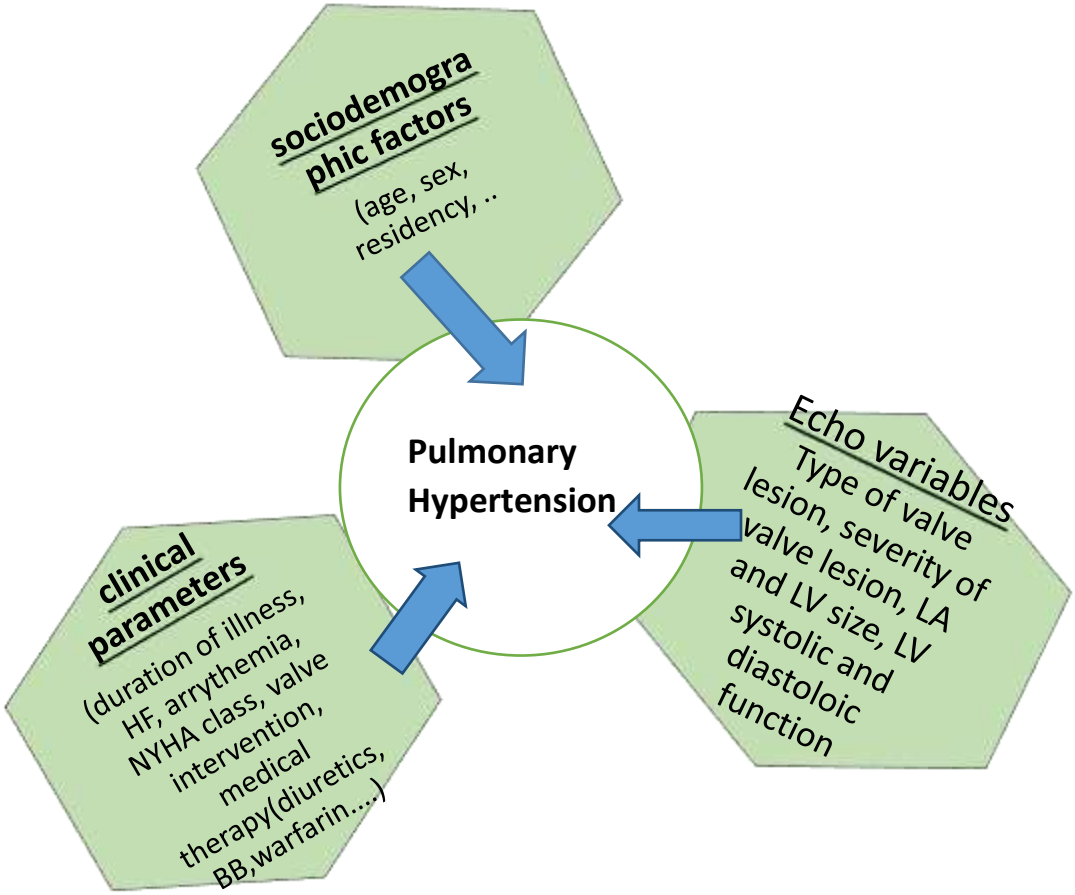


Figure 2: Conceptual framework of the relationship between the dependent and independent variables

# 4. OBJECTIVE OF THE STUDY

## 4.1 General objective

- To determine the prevalence of PH and associated factors among RHD patients attending public referral Hospitals in Bahir Dar city, from January 1 2022 to December 30 2023 G.C.

## 4.2 specific objectives

1) To determine the prevalence of PH among RHD patients having follow up at public referral Hospitals in Bahir Dar city.

2) To identify risk factors associated with pulmonary hypertension in RHD patients.

# 5. METHODS

## 5.1. Study design

Institutional-based cross-sectional study was conducted and data was obtained from patient's medical card using pre developed data collection format.

## 5.2. Study area

An institution based cross-sectional study was conducted among rheumatic heart diseases patients having follow up at 2 public hospitals in Bahir Dar (Tibebe ghion specialized hospital and Felege hiwot referral hospital) between January 1, 2022 to December 31, 2023.

Tibebe Ghion specialized hospital is located about 10km south from the city center and about 7 km from the new bus station ('Addisu Meneharia') on the way to Adet District and about 23 km from the Blue Nile Falls (locally called 'Tis abay' (Smoke of Fire). It is a tertiary university teaching hospital with 450 bed capacity out of which 72 are occupied by medical adult patients. The hospital receives patients who are referred from across the Amhara region and gives outpatient and inpatient services in all major departments.

Bahir Dar is situated on the southern shore of Lake Tana, the source of the Blue Nile (locally called Abay). Bahir Dar city (one of the ten most beautiful cities in Africa and one of the twelve UNESCO Learning Cities Awardee of 2015) .The city is located approximately 578 km (360

miles) north-northwest of Addis Ababa, and an elevation of 1,840 meters (6,036 foot) above sea level.

## 5.3. Source population

All RHD patients having follow up at MRCof public referral hospital.

## 5.4. Study population

All RHD patients having follow up at public referral hospital in the study period.

## 5.5. Inclusion criteria

We included patients whoare at least 15 years old and had clinical and Echocardiographic evidence of RHD.

## 5.6 Exclusion criteria

Patients without proper ECHO (not done by cardiologist)

Incomplete chart

Patient with RV out tract obstruction

Patients with diagnosis of other causes of PH.

## 5.7. Study Variables

### 5.7.1 Dependent Variables

PH

### 5.7.2. Independent Variables

- Sociodemographic variables (Age, sex, residency).
- Clinical factors ( duration of symptoms, history of admission, HF and NYHA class, treatment modalities including medication or definitive intervention, presence of other complication
- Echocardiography parameters (type and severity of valve lesion, LVEDD, LV size and volume, LA size and volume, LV systolic and diastolic function….

## 5.8. Operational definition

PH -defined as documented elevated right ventricular systolic pressure (eRVSP) >=35 mm Hg with or without other indirect findings on transthoracic echocardiography done by cardiologist in the absence of pulmonary stenosis, RVOTO and acute decompensated HF(25).

RHD - diagnosed by cardiologist doing the echocardiography based on 2012 World Heart Federation criteria (29)

LHD - includes patients with HF with reduced, mildly reduced, or preserved ejection fraction (HFrEF, HFmrEF, or HFpEF), left-sided valvular heart disease, and congenital/acquired cardiovascular conditions leading to post capillary PH) (1).

Left ventricular ejection fraction (LVEF) - is a measurement, expressed as a percentage of how much blood the left ventricle pumps out with each heartbeat. It is classified as reduced EF when EF <40%, mildly reduced when EF between 41 to 49% and preserved EF when >50%. But for data extraction purpose, we classified into reduced LVEF when EF <50% and preserved LVEF when EF >50% (39)

Left atrial (LA) diameter: - represents the anterior posterior dimension of the left atrium measured using Echocardiography.Normal LA diameter ranges between 20 to 40 mm (39).

Left ventricle end diastolic diameter (LVEDD):-represents the anterior posterior dimension of the left ventricle measured using Echocardiography at the end of diastole. Elevated if >=53 mm.

Type of heart valve disease: - represents either stenotic or regurgitant lesion of heart valves. There are four types of heart valves - mitral, aortic, pulmonic and tricuspid valve (MS, MR, TR, AR, AS)

Severity of heart valve disease: - describes the degree of stenosis or regurgitant lesion of affected heart valve and it is graded as mild, moderate or severe by Echocardiography (39).

Mitral Stenosis (MS):- type of heart valve disease and the severity of MS is assessed by Echocardiography based on mitral valve area (MVA) measurement, mild and moderate MS - > 2cm2, moderate 1.5 to 2 cm respectively, severe (including very sever)- < 1.5 cm2.

ADHF- is progressive worsening of sign and symptoms of HF (resulting from pulmonary or systemic congestion) in a patient with or without prior history of HF.

.

## 5.9. Sampling Size Estimation

The sample size was determined by using the following assumptions; prevalence of PHin RHD patients from previous study 28.8% (9), 95% confidence level (1.96), 0.5%level of precision.

$$\boldsymbol{n = \frac{Z^2_{\alpha/2} pq}{d^2}}$$

Z α/2 = is standard normal variant (at 5% type 1 Error (P <0.05) it is 1.96

d = margin of error was taken as 0.05.

p = expected proportion of the population with the event of outcome (prevalence) –the prevalence of PH…28.8%.

q =1-p: the probability of non-occurrence of the event of interest.

Using Epi info version 7 and based on the above assumptions. The estimated sample size was 315. Around 800 patients had follow up at referral clinic of TGSH and FHRH during 02 years period.

## 5.10.Sampling Technique

Simple random sampling was used to select participants' chart from the sampling frame.

## 5.11.Data Collection Procedures

Pre-developed data collection format was used to collect data from the medical record. The questionnaires contain different sections including demographics, clinical history, co morbidities, and other imaging and laboratory information.

## 5.12.Data Quality Assurance

The data was collected by trained health professionals (trained nurses& medical residents who work in the referral clinic. Data collection was supervised by senior internal medicine residents. Pretest was conducted in 5% of the sample before actual data collection to check consistency and ambiguity of the tool.

### 5.13. Data Processing and Analysis

The collected data was cleaned and checked for quality prior to data entry and then exported to SPSS version 27 for analysis. The descriptive analysis was computed by simple frequencies and proportions, and the results were presented by tables, bar graphs, and pie charts. Bivariate analysis were carried out to assess the relations of each independent variable and outcome variable using binary logistic regression model. Variables with P-value < 0.25 during the bivariate analysis were included in the multivariable logistic regression analysis. In the final multivariable logistic regression analysis, factors were considered significantly associated at p value less than 0.05.

AOR and their 95% confidence interval (CI) was used to measure the strength of the association.

## 6. ETHICAL CONSIDERATIONS

Ethical clearance was obtained from Bahir Dar University CMHS Ethics Review Board. A support letter was sent to Tibebe Ghion Specialized Hospital and Felege Hiwot Referral Hospital. Names will not be used in collecting the data from the medical files. Confidentiality was maintained by keeping the data collection forms locked in a secure cabinet and the electronic data file in a password protected computer. Data obtained in the course of study was handled by the research team.

## 7. DISSEMINATION

The finding of this study will be disseminated through publications, presentations on scientific meetings and conferences. The finding of the study will also be forwarded to Bahir Dar University, CMHS and Amhara National Health Bureaus.

# 8. RESULTS

## 8.1. Baseline characteristics

A total of 310 patients with diagnosis of RHD were recruited. Of these, 233 (71.9%) were females. The mean age of the study population was 29.9 ± 9.0 years ranging from 15 and 55 years respectively. Majority212 (68.4 %) were from rural area. The mean duration of illness at the time of first presentation was 17.9± 13.2 months.

Among the participants, 70.3% had a history of heart failure from which 93 (42.7 %) were NYHA class IV, 67 (31.9%) NYHA class III, 49 (22.9 %) NYHA class II and 7 (3.2 %) NYHA class I. Additionally, atrial fibrillation (32.6 %), left atrial thrombus (4.2 %), stroke (2.6 %), and infective endocarditis (1.6 %) were identified as other complications of RHD in the study population.

Pattern of valve involvement with severity based on the echocardiographic report has revealed MR (75.5 %), MS (66.8%), AR (27.1%), AS (4.2 %), and TR(34.8 %). Mixed mitral valve disease (MR +MS) was present in 59 % of study population. Majority of participants with MS 160 (77.3 %) had sever lesion, moderate 15 (7.2%), mild 32 (15.5%), whereas more than half (53%) cases of MR were mild, sever only in 20 % of cases. The mean LA, LVEDD diameter and LV EF(%) were 46.1 ± 11.9 mm, 45.5 ± 11.7 mm, 60.5 ± 11.7% respectively.

Diuretics were prescribed for 67.7%, whereas beta blockers for 34.5%, warfarin for 33.9 % study participants. 25 (8 %) had valve intervention, from which valve replacement was done for 13 participants.

Table 1: - Baseline sociodemographic, clinical and Echocardiographycharacteristics of study population including in relation to pulmonary hypertension

| Variables | Frequency (n) | Percentage (%) | Pulmonary hypertension<br>Yes (175) No (135) |
|---|---|---|---|
| Sex Male | 83 | 28.1 | 56 31 |
| Female | 233 | 71.9 | 119 104 |
| Age | 29.94±9.056 | | 30.90 ± 8.7728.69 ± 9.296 |
| Residency Urban | 98 | 31.6 | 50 48 |
| Rural | 212 | 68.4 | 125 87 |
| Duration(years) < 3 | 237 | 76.5 | 106 131 |
| >=3 | 73 | 23.5 | 69 4 |
| Heart failure | 218 | 70.3 | 162 56 |
| Atrial fibrillation | 101 | 32.6 | 92 9 |
| LA thrombus | 13 | 4.2 | 11 2 |
| Stroke | 8 | 2.6 | 3 5 |
| IE | 5 | 1.6 | 3 2 |
| Valve intervention | 25 | 8.1 | 14 11 |
| Diuretics | 210 | 67.7 | 162 48 |
| Beta Blocker | 107 | 34.5 | 92 15 |
| Warfarin | 105 | 33.9 | 90 15 |
| Other drug[a] | 6 | 1.9 | 3 3 |
| Echo finding MR | 234 | 75.5 | 126 108 |
| MS | 207 | 66.8 | 154 53 |
| AR | 84 | 27.1 | 52 32 |
| AS | 13 | 4.2 | 8 5 |
| LAD(mm) <40 | 102 | 32.9 | 12 90 |
| >=40 | 208 | 67.1 | 163 45 |
| LVEDD(mm)<53 | 267 | 86.1 | 142 125 |
| >= 53 | 43 | 13.9 | 33 10 |
| LV EF(%)< 50 | 32 | 10.3 | 29 3 |
| >= 50 | 278 | 89.7 | 146 132 |

a…. Angiotensin converting enzyme inhibitors, anti-thyroid medication

## 8.2 Magnitude and distribution of Pulmonary Hypertension

56.5 %study participants had pulmonary hypertension. The mean sPAP was 50.2 ± 25.0. Among those who developed pulmonary hypertension almost half of them 90 (51.4%) had severe pulmonary hypertension, 27.4 % of them had moderate pulmonary hypertension and only 21.1 % of them had mild pulmonary hypertension. The prevalence was higher in males 56/83(67%) than females 119/233 (51%) and participants from rural area had higher 125/212(58.9%) than those who are form urban area (51 %). The mean age among those with PH was 30.9±8.8 which is higher than those without PH (28.6± 9.3). On comparing those without PH, the mean cardiac chamber dimensions (LVEDD, LAD) were also higher among patients with PH.

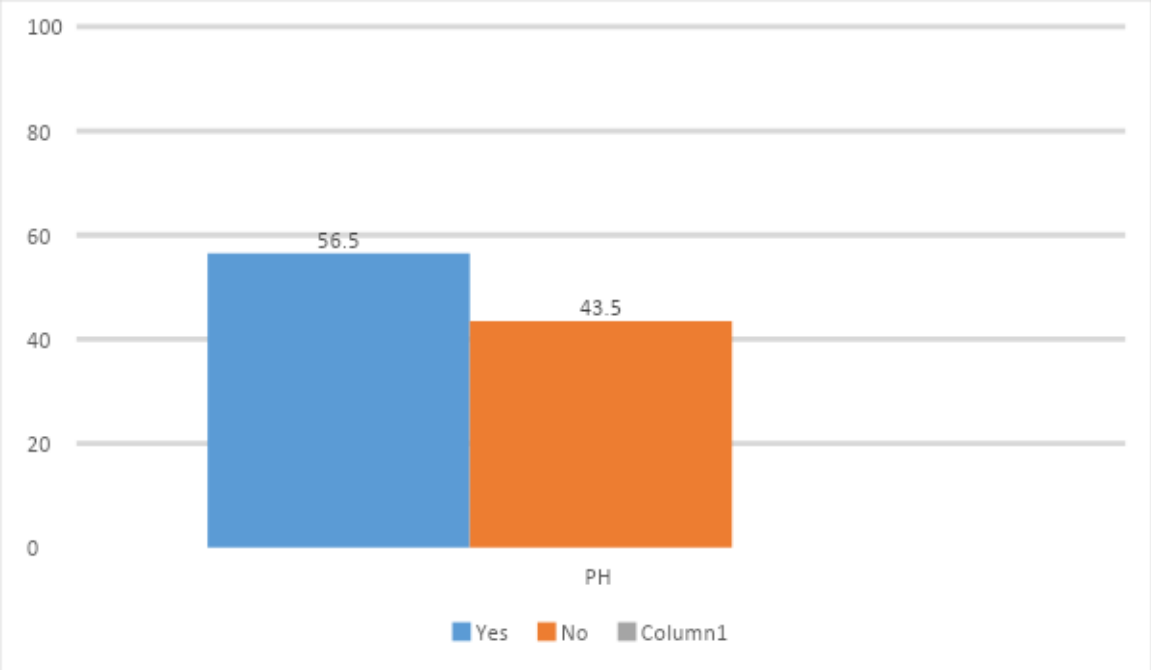


Figure 2: The proportion participants with pulmonary hypertension

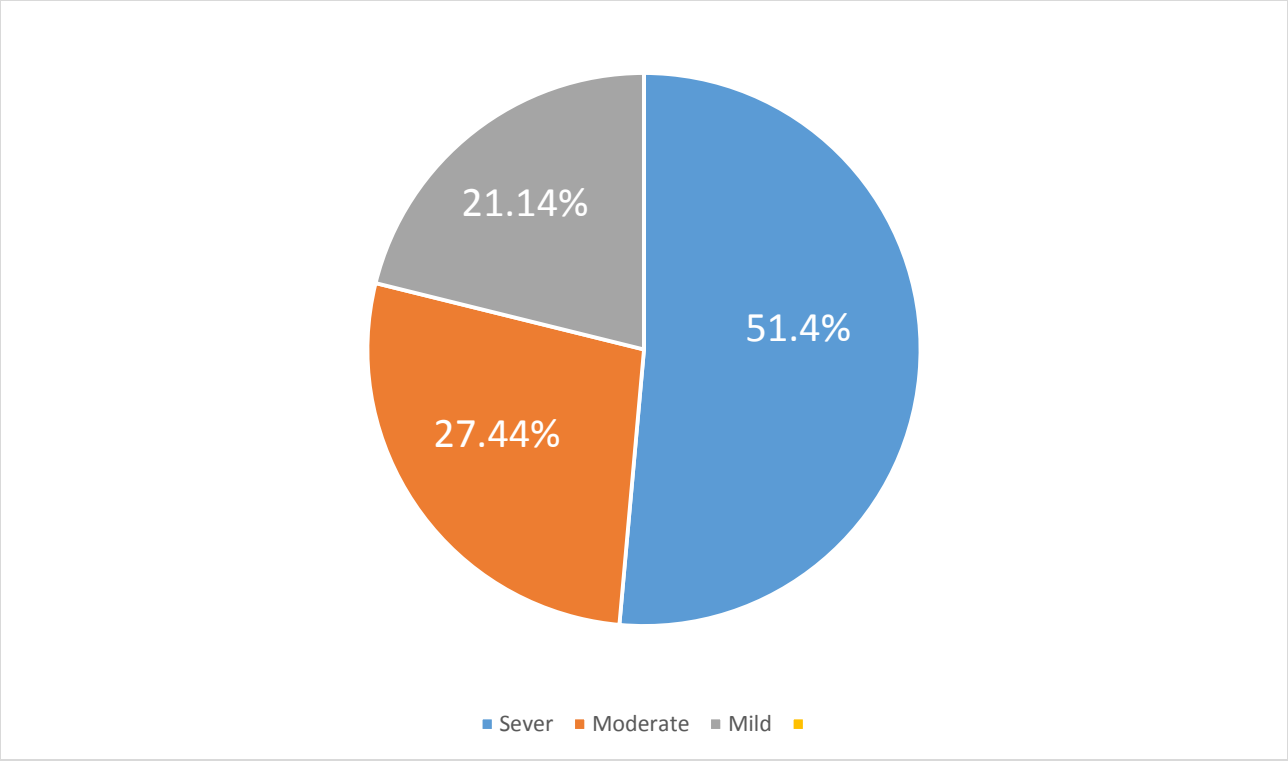


Figure 3:-The proportion participants with pulmonary hypertension based on severity.

Binary logistic regression model's goodness of fit was evaluated using the Hosmer and Lemeshow test and showed non-significant result ($\chi^2(8) = 7.3$, $p = 0.54$) suggesting that the model adequately fits the observed data and has satisfactory prediction of outcomes across various levels of the independent variable. The model was also statistically significant, $\chi^2(15) = 237.5$, $p < .001$. The model explained 53.5% (Cox & Snell R^2) and 71.8% (Nagelkerke R^2) of the variance in the dependent variable. Omnibus test of model of coefficients showed that the model as a whole was statistically significant.

Participants with diuretics use have a 5.6 times higher risk of developing PH compared to those without diuretic use (AOR 5.6, 95%CI 2.2-14.3, P = 0.001). Individuals in the study with longer duration of illness (>= 3years) were 7.7 times more likely to have PH than those less than 3 years (AOR 7.7, 95% CI 2.1-28.5, P= 0.02). Participants with Severe Mitral Stenosis were approximately 7.8 times more likely to develop Pulmonary Hypertension compared to those without (AOR 7.8, 95% CI 2.4-25.7, P<0.001).

The risk of developing Pulmonary Hypertension was reduced in participants who had Valve Intervention and higher LVEF (>=50%) by 94 % (AOR 0.06, 95% CI 0.01 0.29, P<0.001) and 86% (AOR 0.14, 95% CI 0.02-0.81, P=0.028) respectively.

Table 2:- Multivariable analysis of factors Associated with Pulmonary Hypertension among rheumatic heart disease patients.

| Variable | Categories | COR 95% CI | P value | AOR 95 % CI | P value |
|---|---|---|---|---|---|
| Sex | Male<br>Female | 1<br>1.57 (1.057) | <br>0.08 | 1<br>1.86(0.73-4.73) | <br>0.18 |
| Living area | Urban<br>Rural | 1<br>1.379 (0.852-2.232) | <br>0.19 | 1<br>1.27(0.53-3.01) | <br>0.58 |
| Duration illness | < 3years<br>>= 3 years | 1<br>21.3(7.59-50.31) | <br><0.001 | 1<br>**7.78(2.12-28.52)** | <br>**0.002** |
| Diuretics | No<br>Yes | 1<br>22.58(11.60-43.95) | <br><0.001 | 1<br>**5.66(2.24-14.29)** | <br>**<0.001** |
| Beta blocker | No<br>Yes | 1<br>8,86(4.80-16.37) | <br><0.001 | 1<br>2.13(0.82-5.50) | <br>0.11 |
| Warfarin | No<br>Yes | 1<br>8.47(4.58-15.63) | <br><0.01 | 1<br>1.38(0.49-3.83) | <br>0.53 |
| Valve intervention | No<br>Yes | 1<br>0.58 (0.25-1.32) | <br>0.19 | 1<br>**0.06(0.01-0.29)** | <br>**<0.001** |
| MS | No<br>Mild<br>Moderate<br>Sever | 1<br>1.56(0.61-3.70<br>3.41(1.11-10.49)<br>24.4(12.69-47.25) | <br>0.36<br>0.03<br><0.001 | 1<br><br>1.47(0.23-9.30)<br>**7.81(2.37-25.70)** | <br><br>0.68<br>**<0.001** |
| LA diameter | <40 mm<br>>=40 mm | 1<br>27.1(13.66-53.9) | <br>< 0.001 | 1<br>2.78(0.79-9.74) | <br>0.11 |
| LVEDD | <53 mm<br>>=53mm | 1<br>2.9(1.37-6.13) | <br><0.005 | 1<br>2.49(0.69-8.99) | <br>0.16 |
| LVEF | < 50%<br>>= 50% | 1<br>0.11 (0.03-0.38) | <br><0.001 | 1<br>**0.14(0.027-0.81**) | <br>**0.028** |

# 9. DISCUSSION

Based on this study, prevalence of PH among RHD patient was 56.5 % (95 % CI 50.9 –61.9) from which 51.4% had severe pulmonary hypertension. The result was similar to recent study done in Saint Paulo's Hospital which showed 59.3 % prevalence of PH and from which, half of them (51.8%) had also severe pulmonary hypertension (12).A hospital based studies from Jima and Uganda also showed similar result (20,32).

Based on a REMEDY study which was large multi centered and multi-national (including Ethiopia) prospective study, PH was present in 28.8% of RHD patients which was lower compared to our result (9). This may be due to the difference in the study population and early presentation and treatment given. Other studies done in Africa and Middle East countries also showed relatively higher prevalence of PH, Nigeria (72.1%), and Southern Yemen (80.4%)(10, 15).But, wide range of prevalence has been reported in different centers ranging from 11% - 80 %which may be due to differences in diagnostic criteria used, time of patient presentation, diagnosis and treatment given (definitive surgical intervention).The age grouped considered and studied is also different in some studies.

Prevalence of PH was 58.9% in rural setting and higher compared to urban setting (51%) which was similar to other studies. This may have been intensified by the lack of access to health care and delayed presentation seen in rural setting. The gender percentage was dominated by males (67%), while nearly half (51%) of the females had developed pulmonary hypertension, similar high prevalence of PH among males was observed in SPMSH (71.4%) and other studies (8,9)

PH was prevalent more in patients with other complications of RHD, it was prevalent in 73.4% of patients with HF as it was observed in similar studies (15, 19). Most patients had severe and multi-valvular lesions consistent with other studies (28).

Patients with severe Mitral Stenosis were approximately 7.8 times more likely to develop Pulmonary Hypertension compared to those without (AOR 7.8, 95% CI 2.4-25.7, P<0.001) which was supported by other studies, in Spain[OR 2.9 (1.3–6.4)] (38). PH development in MS is produced due to an elevation in the diastolic filling pressure, which results in a ‘‘passive’’ increase in pulmonary venous pressure. Longer duration of illness at the time of presentation was also found to have statistically significant association with PH (AOR 7.7, 95% CI 2.1-28.5, P=

0.02) which is supported by retrospective study in which duration of disease >=3years was associated with 1.7 times higher risk of PH than those with lesser duration of illness (39).

Participants with diuretics use had a 5.6 times higher risk of developing pulmonary hypertension (PH) compared to those without diuretic use (AOR 5.6, 95%CI 2.2-14.3) supported by study done in Egypt (40) . This is explained by the frequent need to use diuretics in those patients with overt HF and advanced diseases which also mark development of PH. Increased pulmonary blood flow and pulmonary venous pressure in patients with RHD leads to both pulmonary edema and venous PH. In patients with aortic and mitral valve disease the presence of pulmonary hypertension (PH) indicates a decompensated state of the disease with left ventricular and left atrial dysfunction and exhausted compensatory mechanism, i.e., a state of heart failure. It may also mark systemic congestion from development of Right side HF from sever and progressive PH.

Having valve Intervention and higher LVEF (>=50%) were found to associate inversely with development of Pulmonary Hypertension on multivariate analysis which is supported by previous studies as well (24, 35, 36).The maladaptive changes to the LV, LA, and finally pulmonary vasculature especially in the early course of the process may be reversed after valve intervention and resulting reduction in PH.

On comparing those without PH, the mean cardiac chamber dimensions (LVEDD, LAD) were also higher among patients with PH similar to other study results (27, 35).Pulmonary hypertension is initially passive or isolated post-capillary PH due to increased left sided filling pressures but later it is associated with LV heart chamber and pulmonary vascular structural remodeling changes.

# 10. CONCLUSION

In summary, the study has identified higher prevalence of PH among patients with RHD and involvement of heart valves was similar to other studies done previously, mitral valve being the commonest valve to be affected which was strongly associated with development of PH. Duration of illness and severity of heart valve lesion were risk factors for development of PH as

that of diuretic use for HF patients. Higher LVEF and having valve intervention for the underlying valve lesion were associated with reduced risk of PH.

## 11. LIMITATION OF THE STUDY

The biggest limitation of this study was the retrospective design -which was complicated by some incomplete data. Due to the current political issue and conflict in the study area, we did not perform additional tests and it was difficult to contact patients for additional information (not found in the patient card).Since the study was conducted in a hospital setting, its findings could not be applied to the broader public.

## 12. RECOMMENDATION

PH has complicated more than half of patients with RHD, most with sever range that is associated with poor outcome and increased mortality. Prevention, early screening and detection of PH by providing risk reduction measures and effective definitive treatment for those with indication is very important and advisable. Though most patients have advanced valvular lesion with complication, only few patients had valve intervention. Having valve intervention among patients with severe valvular lesion was associated with reduced PH and it is crucial to have cardiac centers in this area that provide the service for large proportion of RHD patients.
Further study is needed to assess the reason for late presentation and the difficulty towards the standard treatment practices before the development of sever pulmonary hypertension and other complication.

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# 14. ANNEX

## 14.1Information Sheet

**Title of Project:** Prevalence and associated risk factors of pulmonary hypertension among RHD patients having follow up at pubic referral hospitals, Bahir Dar, Ethiopia: A Cross Sectional Study

**Name of the Investigators:** Asmamaw Gedefaw,

**Background to the study**.

We would like to see the prevalence of pulmonary hypertension and associated risk factors among RHD patients having follow up at public referral hospitals. PH is an important cause of death and poor quality of life in many patients with heart diseases including RHD. However, data is scarce in Ethiopia and Africa. You will be interviewed with a prepared questionnaire; your chart will be revised for clinical, laboratory and imaging findings.

**Possible harms.** There is no harm in participating in this study.

**Benefits.** You will not directly benefit from this study. However, the findings of the study may help plan for care of patients with PH and RHD for strategic prevention/control of it in the general population with risk factors.

**Confidentiality.** All information which is collected about you during the course of the research will be strictly confidential.

**Autonomy.** All the information you give us is highly valuable to the study. It is up to you to decide whether to take part or not. If you decide to participate, you will be given this information sheet to keep and be asked to sign a consent form. Whether you consent or do not consent to be part of the study, your rights for care in the health care facility will not be compromised and you can withdraw from the study any time.

**What will happen to the research?** The data will be collected over four month's period and the result will be available in one months' time, and we hope to disseminate the result publishing it on national and/or international journals.

**Who is organizing and funding the research?** Research is funded by Bahir Dar University. The research will be reviewed by the Institutional Review Board of College of health Sciences, Bahir Dar University.

Thank you in advance!

**PI address**: Asmamaw Gedefaw, MD

Internal Medicine Resident at Bahir Dar University

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## 14.2 Informed Consent Form

PH is becoming an increasingly common global health problem complicating various common diseases in which its development is almost invariably associated with worsening of clinical symptoms and increased mortality. This study aims to look for the burden of PH in patients with RHD and associated risk factors. The information obtained will be used by policy makers and managing physicians for better care of individual patient and the strategic control of risk factors.

For this reason we kindly request you to participate in the study by responding to the interview, allowing to review your medical record and to undergo some investigations. We assure you that confidentiality of the information obtained is kept. If you have any questions we will be so happy to entertain them.

I confirm that I have understood what has been read/what I have read has been clear to me, and I have agreed to participate in the study.

Name_____

Signature_____

## 14.3 Questionnaire

**Prevalence and associated factors of pulmonary hypertension among RHD patients having follow up at Public referral hospitals, Bahir Dar, Ethiopia.**

After taking written informed consent and ethical approval, the following data will be retrieved by reviewing patient's charts and interviewing patients.

**A. Sociodemographic factors**

1. Card number (I care)
2. Age:
3. Sex:
    a. Male
    b. Female
4. Living area
    a. Urban
    b. Rural

B. **Clinical and lab parameters**

5. Duration of illness/symptoms in months
6. Hospital admission frequency
    a) No
    b) 01/year
    c) > 1/year

7. Does the patient have heart failure (history)?
    a. Yes
    b. No
8. If yes, NYHA class
    a. Class I
    b. Class II
    c. Class III
    d. Class IV
9. What medications is the patient taking?
    a. Diuretics
    b. Beta blockers
    c. Monthly B penicillin
    d. others
10. was definitive treatment/ valve intervention done
    a) yes
    b) no

11. If yes, what
    a) Repair
    b) Replacement
12. Other Complication of RHD
    a) Yes
    b) No
13. If yes, what
    a) IE
    b) Arrhythmia
    c) HF
    d) Thromboembolic event
    e) Others
14. ECG
    a. Sinus
    b. Atrial fibrillation
    c. Heart block (LBBB, RBBB, AV block)

**C. ECHO parameters/ variables**

1. Valvular lesion type and severity
    a) MR
    b) MS
    c) AR
    d) AS
    e) TR
2. LVEDD mm
3. LVESD mm
4. LV EF %
5. LA mm
6. RA mm
7. RV mm
8. LV mm
9. TAPSE %
10. Systolic PAP mmHg
11. Diastolic dysfunction
    a) Yes
    b) No
12. If yes
    c) Grade 1
    d) Grade 2
    e) Grade 3